Electrical Stimulation for the Treatment of Chronic Wounds

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1.0 Executive Summary

Electrical stimulation (ES) has been studied as a possible therapy for accelerating wound healing. Preclinical studies have shown that externally applied electrical stimulation can increase ATP (adenosine triphosphate) concentrations in tissues, increase DNA synthesis, promote healing of soft tissue or ulcers, cause epithelial and fibroblasts to migrate into wound sites, accelerate the recovery of damaged neural tissue, reduce edema, and inhibit the growth of some pathogens.

ES has been used or studied for many different therapeutic applications. It has been used for stimulating the healing of fractures in the lower leg, spine, and wrist and for relieving chronic intractable pain in the spine. Studies have also tested the effectiveness of ES to heal jaw fractures, reduce pain and swelling in soft tissue injuries, alleviate spinal cord lesions, eliminate intermittent claudication, improve healing from assorted hand injuries, reduce cerebral edema in cases of head trauma, reduce swelling in grades I and II ankle sprains, and accelerate healing after foot, dental, or oral surgery.

We identified several types of ES for wound healing:

- direct current (DC);
- pulsed current (PC), which includes pulsed direct current (PDC) and high-voltage pulsed current (HVPC) devices;
- alternating current (AC);
- pulsed electromagnetic induction (PEMI), which includes pulsed electromagnetic field (PEMF) and pulsed electromagnetic energy (PEE) devices; and
- spinal cord stimulation (SCS).

ECRI conducted extensive analyses of studies of ES for the treatment of chronic wounds (≥30 days duration) that included

- a qualitative analysis of all ES studies,
- a quantitative analysis of the normalized healing rates of ES studies,
- a meta-analysis of the normalized healing rates of ES studies,

- a meta-analysis of proportion of lesions completely healed in ES studies,

- a comparison of the quality of ES studies compared to conventional and alternative therapies for the treatment of venous and decubitus ulcers, and

- a control-matched comparison of ES therapies for venous ulcers and for decubitus ulcers compared to conventional and alternative therapies.

Based on these analyses, we make the following overall conclusions about ES for chronic wound healing:

Qualitative Conclusions—

- Although all ES studies have at least 1 weakness, not all are potentially confounded.

- ES controlled studies for venous ulcers are about equal to or slightly inferior in quality compared to other controlled studies for venous ulcers.

- ES controlled studies for decubitus ulcers are about equal to or slightly superior in quality compared to other controlled studies for decubitus ulcers.

Quantitative Conclusions—

- ES facilitates the healing rate of chronic ulcers.

- ES facilitates the complete healing of chronic ulcers.

- The relationship between outcomes and ES can be affected by wound size and type of stimulator.

- Decubitus ulcers are more likely to heal completely in response to ES than venous ulcers.

Based on these analyses, ECRI draws the following conclusions for different types of electrical stimulators for chronic wound healing:

Direct Current (DC)—

There is

- No evidence that DC stimulation improves the healing rate of chronic, decubitus, or diabetic ulcers.

Pulsed Current (PC)—

There is

- Evidence that PC stimulation improves the normalized healing rate of stage II through IV decubitus ulcers. This improvement in the healing rate of decubitus ulcers appears to be roughly comparable to that in many conventional and alternative therapies for stage II and III decubitus ulcers. (Randomized controlled trials would be needed to determine if these rates significantly differ.)

- No evidence that PC stimulation improves the healing rate of chronic venous or diabetic ulcers.

- Insufficient data for comparison of stage IV decubitus ulcers treated by ES therapy to other therapies.

Alternating Current (AC) or Transcutaneous Electrical Nerve Stimulation (TENS)—

There is

- Evidence that AC devices improve the normalized healing rate of decubitus ulcers.

- No evidence that AC or TENS improves the healing rate of chronic venous or diabetic ulcers.

- Insufficient data to compare AC therapy findings to those for any other therapy.

Pulsed Electromagnetic Induction (PEMI)—

There is

- Evidence that PEMF stimulation improves the normalized healing rate of venous ulcers. However, this improvement appears to be small and may not be clinically useful.

- Evidence that PEE stimulation improves the normalized healing rate for stage II decubitus ulcers. The improvement of stage II decubitus ulcer healing appears to be roughly comparable to conventional and alternative therapies for stage II and III decubitus ulcers. (Randomized controlled trials would be needed to determine if these rates significantly differ.)

- No evidence that PEMF stimulation improves the healing rate of chronic decubitus or diabetic ulcers.

- No evidence that PEE stimulation improves the healing rate of chronic venous or diabetic ulcers.

- Insufficient data to determine whether PEE stimulation improves the normalized healing rates for stage III or IV decubitus ulcers.

General Findings

- ES devices are safe when used appropriately.

- Most types of ES are more effective than minimal treatment (e.g., saline-soaked gauze).

- ES is not markedly superior to or inferior to conventional or alternative therapies (defined in Sections 7.1.1 and 7.2.2). There is insufficient evidence to determine if clinically significant differences exist.

2.0 Healing Process and Ulceration

2.1 Phases of Wound Healing

The normal wound healing process consists of 3 phases:

- inflammatory (substrate),
- proliferative, and
- remodeling.

INFLAMMATORY (SUBSTRATE) PHASE[1]—After initial damage to blood vessels at the wound site, smooth muscle cells of injured vessels cause vasoconstriction (from circulating catecholamines and serotonin), which leads to hemostasis. Circulating platelets subsequently adhere to injured vessel walls, become activated, and release substances such as adenosine diphosphate (ADP); platelet-activating factor (PAF), which stimulates additional platelet aggregation and activation; and growth factors such as platelet-derived growth factor (PDGF) and alpha and beta transforming growth factors (TGF-a and TGF-ß). Leukocytes (neutrophils, monocytes, and lymphocytes) enter the injured site. Neutrophils, stimulated by PAF, interleukin-1 (IL-1), and tumor necrosis factor (TNF), first adhere to the capillary endothelium then clear the wound of foreign debris and organisms by producing hydrogen peroxide and proteins that destroy bacteria. Monocytes, the most important leukocyte, are attracted by chemotactic agents in wounds, such as TGF-ß, and are transformed into macrophages. The main function of macrophages is releasing biological agents called monokines (including IL-1, TNF, TNF-a, TGF-a, TGF-ß, and colony stimulating factors) that regulate other inflammatory cells. T-lymphocytes secrete lymphokines (including interferon-?, TGF-ß, fibroblast-activating factor, and IL-2 through IL-8). Fibroblasts, also critical to wound healing, are attracted by PDGF. Agents such as epidermal growth factor (EGF), insulin-like growth factor-1, and TGF-ß in the presence of PDGF assist fibroblast replication.

PROLIFERATIVE PHASE[2]—During this phase, which begins 2 days post-trauma and lasts for 3 weeks, the wound fills in with new tissue. Primary activities during this period are

- epidermal regeneration,
- neoangiogenesis,
- collagen synthesis, and

- wound contraction.

Most activity is carried out by fibroblasts, epithelial cells, endothelial cells, and macrophages.

During **epidermal regeneration**, epidermal cells migrate over the wound at a rate of 2 to 3 cell diameters per hour, assisted by fibronectin and vitronectin. Proliferation begins at the wound edge and is affected by numerous factors (fibroblastic growth factor {FGF}, Ca, EGF, keratinocyte growth factor, PDGF, IL-1, TGF-a, and TGF-ß). **Neoangiogenesis**, new capillary formation, begins from venules at the wound edge and is stimulated by angiogenic factors including TNF-a and FGF. **Collagen synthesis** begins in cellular rough endoplasmic reticulum of fibroblasts with production of procollagen that is transported by the Golgi apparatus to extracellular space, where it is degraded by proteolytic enzymes, yielding collagen monomers. These are cross-linked and assembled into collagen. Oxygen is essential to collagen synthesis. Fibroblasts also produce the ground substance (proteoglycans), which act as adhesive agents. **Wound contraction** begins within 1 to 2 weeks of injury, resulting from fibroblast movement and myofibroblast interaction. Fibronectin and other factors regulate the process.

REMODELING PHASE[3]—Approximately 3 weeks after injury, the wound begins a continual process of collagen synthesis and breakdown that leads to remodeling of the site. There are several different types of collagen compounds. Type I is synthesized by more mature fibroblasts and is associated with fiber-rich scar tissue. Type III appears within 24 to 48 hours after injury in children. Type IV is associated with the rebuilding of the basement membrane and attaching the newly formed epidermal layer to the dermis. Type VII contains anchoring fibrils. Changes also occur in the ground substance to increase wound tensile strength.

2.2 Wounds and Ulcerations

Many factors can interrupt or alter wound healing, including[4]

- aging;
- obesity;
- inadequate perfusion (e.g., atherosclerosis);
- anemia—due to blood loss (volumetric);
- edema—interstitial edema increases the distance between capillary beds and the wound site, which makes O_2 diffusion more difficult;
- repeated trauma to site;
- foreign bodies in site;
- infection—local or systemic;
- nutritional deficiencies—including proteins and vitamin, C which affect collagen synthesis; vitamins A and B, which lower host defense mechanisms and immunity; and trace elements (e.g., Zn, Fe, Cu);
- smoking;
- radiation;
- medications (e.g., exogenous steroids); and
- topical agents (e.g., Betadine, Dakin's solution, and H_2O_2).

Some diseases that can predispose patients to develop chronic wounds include[5,6]

- diabetes mellitus—leading to artherosclerosis, neuropathies, immune compromise;
- chronic venous stasis ulceration;

- inherited disorders of wound healing—such as (a) Ehlers-Danlos syndrome, an inability to produce normal collagen; (b) epidermolysis bullosa, wherein there is inadequate adhesion of epidermis, dermis, and basement membrane of skin; and (c) Marfan's syndrome (associated with abnormalities in collagen maturation and cross-linking);

- neoplasms;

- connective tissue disorders—such as osteoarthritis, rheumatoid arthritis, scleroderma;

- blood abnormalities—such as sickle cell anemia, thalassemia, multiple myeloma, macroglobulinemia, cryoglobulinemia;

- lymphedema; and

- other disorders such as inflammatory bowel disease and ulcerative necrobiosis lipoidica.

VENOUS ULCERS—Venous insufficiency can develop as a result of thrombosis, obstruction, dilation (varicosity), or hemorrhage.[7] These disruptions in venous return can lead to inadequate oxygenation and nutrition of subcutaneous tissue, causing breakdown and necrosis. Ambulatory venous hypertension is the most common pathway leading to venous ulceration.[8] The valves of leg veins are usually incompetent, leading to venous reflux, retrograde flow of blood, and subsequent tissue breakdown. The resulting ulceration may have a covering of fibrous debris with a firm bed of granulation tissue.[9]

Venous ulcers are shallow with flat borders, often wet with exudate, and frequently painless. These lesions develop slowly over years and can lead to loss of ankle function and bony ankylosis.

Venous ulcerations are common. Approximately 1% of the population will develop such poorly healing ulcers during their lifetime.[10] Between 1990 and 1992, there were 1.3 million outpatient visits in the United States for the treatment of venous ulcers.

ARTERIAL (ISCHEMIC) ULCERS—Arterial ulcers result from inadequate perfusion to a site. Diseases associated with arterial ulcers include arteriosclerosis obliterans, thromboangiitis obliterans (Buerger's disease), necrotizing vasculitides (e.g., polyarteritis nodosa, rheumatoid arthritis, systemic lupus erythematosus), sickle cell anemia, and diabetes mellitus.[11] Ischemic ulcers usually present as punched-out lesions with a well-demarcated border (without epithelium) over toes, interdigital spaces, the lateral malleolus, or dorsum of the foot. The ulcer base is very deep (possibly with exposed tendons),

black, necrotic, and has no granulation tissue. Such lesions are very painful. Surrounding tissue also shows signs of arterial insufficiency (e.g., loss of nail growth, absence of hair, atrophic skin).

DECUBITUS (PRESSURE SORE) ULCERS—Pressure ulcers occur when soft tissue is compressed over a period of time. These localized areas of tissue necrosis tend to develop when soft tissue is compressed between a bony prominence (e.g., femoral trochanter) and an external surface (e.g., mattress). They may also be caused or aggravated by friction or shearing forces. Pressure ulcers are also known as decubitus ulcers, bedsores, and pressure sores.

Staging (or grading) of pressure ulcers has been inconsistent and chaotic. In 1989, the National Pressure Ulcer Advisory Panel (NPUAP) issued a consensus statement classification of decubitus ulcers:[12]

Stage I: Nonblanchable erythema of intact lightly pigmented skin or a darker tone or violet hue to darkly pigmented skin; heralding lesion or skin ulceration.

Stage II: Partial-thickness skin loss involving the epidermis and/or dermis; ulcer is superficial and presents clinically as an abrasion, blister, or shallow crater.

Stage III: Full-thickness skin loss involving damage or necrosis of subcutaneous tissue that may extend down to, but not through, underlying fascia; ulcer presents clinically as a deep crater with or without undermining of adjacent tissue.

Stage IV: Full-thickness skin loss with extensive destruction, tissue necrosis or damage to muscle, bone, or supporting structures (e.g., tendon, joint capsule).

Decubitus ulcers are common. NPUAP reports a 1% to 5% annual incidence (number of new cases per year) and a 3% to 14% annual prevalence (new and old cases per year) among hospitalized patients.[13] Prevalence rates may reach 15% to 25% in skilled nursing facilities. Twenty-six percent of patients with nonhealing decubitus ulcers develop osteomyelitis.[14] Patient risk factors for developing decubitus ulcers include immobility, inactivity, malnutrition, fecal and urinary incontinence, decreased level of consciousness, advanced age, chronic systemic illness, and (nonambulatory) fractures.[15]

2.3 Evaluation and Therapies for Wound Healing

2.3.1 Evaluation

Patients with chronic wounds should initially undergo complete vascular and neurological evaluations. Their nutritional status should also be established.[16] Wounds should be staged and photographed at each visit. Wound parameter measurements performed each visit should include[17,18]

- accurate measurement of wound volume (critical)[see section 4],
- accurate measurement of surface area (critical),
- length,
- width,
- depth,
- degree of undermining,
- location,
- stage, and
- presence of sinus tracts, granulation tissue, necrotic tissue, and epithelialization.

Wounds can be measured by planimetry, direct tracing, or stereophotogrammetry. Noninvasive vascular testing should be performed to determine possible arterial insufficiency. These procedures include segmental pressure measurements, pulse-volume recordings, and transcutaneous oxygen levels (T_cPO_2) at the level of the chest and upper wall.[19] An absolute T_cPO_2 of 30 mm Hg or PO_2 index ≥ 0.2 are positive prognostic factors for healing; PO_2 values <0.2 suggest that the wound will not heal unless additional oxygen is provided to the site.

2.3.2 General Therapies

Conservative therapy for venous ulcers is based on compression and includes (1) below-the-knee graded elastic stockings (providing 30 to 40 mm Hg at the ankle), (2) Unna boots, and (3) pneumatic compression devices.

Pressure relieving devices for decubitus ulcers include (1) static devices that immobilize sites and rely on materials that cushion and mold to body surfaces (e.g., foam overlays; devices filled with gel, water, or air; heel and elbow pads) and (2) dynamic pressure-relieving devices that use electricity to alternate currents of air which redistribute pressure against the body, removing pressure from affected sites.[20] (Frequent and routine repositioning of bedridden patients may prevent the formation of these ulcers.)

Weingarten[21] classified direct wound care therapies into 2 basic categories: passive and active. Passive therapies are those that alter the wound environment through application of various topical agents such as antiseptics or debriding agents. Such therapies enhance, but do not alter, natural wound healing processes. Passive therapies include antibacterial and antiseptic agents, debriding agents, and various dressings. Active therapies are defined as agents applied to a wound site to directly stimulate the wound healing process. These include hyperbaric oxygen (HBO) therapy, electrical stimulation (ES), ultrasonography (US), ultraviolet light (UV), and growth factors such as platelet-derived growth factor-BB (PDGF-BB), platelet-derived wound healing factors (PDWHF), and epidermal growth factor (EGF).

ECRI conducted an extensive evaluation of guidelines for ulcer therapy. [See section 2.4 and **Table 2.1**.]

DEBRIDEMENT—Debridement includes[22,23]

- wet-to-dry dressings,
- surgical (sharp) debridement,
- dextranomers,
- enzymatic debridement agents, and
- autolytic debridement.

Wet-to-dry dressings can be effective. They initially adhere to devitalized tissue, then once dressings are dry (usually 4 to 6 hours), they can be removed along with devitalized tissue and exudate. A disadvantage is that they are nonselective and can remove both viable (e.g., granulation tissue, new epithelial tissue) and nonviable tissues. **Dextranomers** are absorbent beads placed into wound beds. They absorb exudate, bacteria, and other debris. Disadvantages include costs and difficulties in applying them to wounds in some anatomical locations. **Enzymatic debridement** with topical agents (e.g., Collagenase®, Elase®) can remove devitalized tissue. Such therapy may be appropriate in patients with noninfected wounds and who are confined to long-term care facilities, who receive care at home, or who are not surgical candidates.

Autolytic debridement utilizes synthetic dressings that cover a wound and allow devitalized tissue to self-digest from enzymes normally present in wound fluids.

The Agency for Health Care Policy and Research (AHCPR)[a] 1995 recommendations for debridement of decubitus ulcers are as follows:[24]

- Remove devitalized tissue in pressure ulcers when appropriate for the patient's condition and consistent with patient goals. (Strength of Evidence = C.[b])

- Select the method of debridement most appropriate to the patient's condition and goals. Sharp, mechanical, enzymatic, and/or autolytic debridement techniques may be used when there is no urgent clinical need for drainage or removal of devitalized tissue. If there is an urgent need for debridement, as with advancing cellulitis or sepsis, sharp debridement should be used. (Strength of Evidence = C.)

- Use clean, dry dressings for 8 to 24 hours after sharp debridement associated with bleeding; then reinstitute moist dressings. Clean dressings may be used in conjunction with mechanical or enzymatic debridement techniques. (Strength of Evidence = C.)

- Heel ulcers with dry eschar need not be debrided if they do not have edema, erythema, fluctuance, or drainage. Assess these wounds daily to monitor for pressure ulcer complications that would require debridement. (Strength of Evidence = C.)

- Prevent or manage pain associated with debridement as needed. (Strength of Evidence = C.)

WOUND CLEANSING—AHCPR (1995) recommendations for cleansing of decubitus ulcers are as follows:[25]

- Cleanse wounds initially and at each dressing change. (Strength of Evidence = C.)

- Use minimal mechanical force when cleansing ulcers with gauze, cloth, or sponges. (Strength of Evidence = C.)

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a The Strength-of-Evidence ratings for AHCPR guidelines are shown in Appendix III.

b According to the AHCPR rating scale, a `C' rating means that the conclusion is based on (a) results of 1 controlled trial, (b) results of at least 2 case series or descriptive clinical studies, or (c) expert opinion.

- Do not clean ulcer wounds with skin cleansers or antiseptic agents (e.g., povidone iodine, iodophor, sodium hypochlorite solution {Dakin's solution}, hydrogen peroxide, acetic acid). (Strength of Evidence = B.[c])

- Use normal saline for cleansing most pressure ulcers. (Strength of Evidence = C.)

- Use enough irrigation pressure to enhance wound cleansing without causing trauma to the wound bed. Safe and effective ulcer irrigation pressures range from 4 to 15 pounds per square inch (psi). (Strength of Evidence = B.)

- Consider whirlpool treatment for cleansing pressure ulcers that contain thick exudate, slough, or necrotic tissue. Discontinue whirlpool when the ulcer is clean. (Strength of Evidence = C.)

DRESSINGS—Synthetic dressings types include:[26]

- hydrocolloid,

- polyurethane, and

- biodressings and gels.

Hydrocolloid dressings are adhesive, gel-producing, water-impermeable membranes that can be left on sites for ≤1 week. These dressings typically have an adhesive wound contact surface, an impermeable outer face, a carboxymethylcellulose exude absorbing component, and varying amounts of pectin and/or gelatin. Examples include Duoderm, Comfeel ulcer dressing, J & J ulcer dressing, and Restore. **Polyurethane** dressings have transparent adhesive materials necessitating frequent redressing. Examples include Mitraflex, Op-Site, Bio-occlusive, Tegaderm, Synthaderm, and Primaderm. **Biodressings and gels** are dressings composed of hydrogels of water and polyethylene oxide reinforced with polyethylene film. These hydrogels are nonadherent and are more appropriate for abrasion-like wounds. Examples include Vigilon, Spenco Second Skin, Biobrane, Metro Gel, and Spand-Gel.

These synthetic (occlusive) dressings are intended for noninfected wounds in which there is no cellulitis, extensive erythema, purulence, fever, or abnormally high number of organisms in cultures.[27] These dressings are easy to use and have many advantages; they (1) absorb exudate, (2) require few dressing changes,

[c] An AHCPR rating of `B' means that the conclusion is based on (a) 2 or more controlled clinical trials in humans that provide support, or (b) when appropriate, the results of 2 or more controlled trials in an animal model that provide indirect support.

(3) protect the wound from external contaminants, (4) enhance wound repair, and (5) minimize wound disruption. There are disadvantages; they (1) may cause excessive tissue maceration, (2) may be inefficient for wounds with excessive exudate, (3) require healthy tissue margins, (4) may be messy to apply and use, and (5) may not be well retained in areas subject to excessive motion. They are contraindicated in ischemic ulcers; if bone or tendon is exposed; or in patients with wounds that are infected or that have draining sinus tracts, excessive necrosis, excessive exudate, or osteomyelitis.

AHCPR (1995) recommendations for dressings of decubitus ulcers are as follows:[28]

- Use a dressing that will keep the ulcer bed continuously moist. Wet-to-dry dressings should be used only for debridement and are not considered continuously moist saline dressings. (Strength of Evidence = B.)

- Use clinical judgment to select a type of moist wound dressing suitable for the ulcer. Studies of different types of moist wound dressings showed no difference in pressure ulcer healing outcomes. (Strength of Evidence = B.)

- Choose a dressing that keeps the surrounding intact (periulcer) skin dry while keeping the ulcer bed moist. (Strength of Evidence = C.)

- Choose a dressing that controls exudate but does not desiccate the ulcer bed. (Strength of Evidence = C.)

- Consider caregiver time when selecting a dressing. (Strength of Evidence = B.)

- Eliminate wound dead space by loosely filling all cavities with dressing material. Avoid overpacking the wound. (Strength of Evidence = C.)

- Monitor dressings applied near the anus, since they are difficult to keep intact. (Strength of Evidence = C.)

ELECTRICAL STIMULATION (ES)—ES therapy is the application of an externally applied electrical current to wound sites to accelerate healing. ES is extensively assessed in the balance of this report.

The AHCPR (1995) recommendation for ES therapy for decubitus ulcers is as follows:[29]

- Consider a course of treatment with electrotherapy for stage III and IV pressure ulcers that have proven unresponsive to conventional therapy. ES may also be useful for recalcitrant stage II ulcers. (Strength of Evidence = B.)

HYPERBARIC OXYGEN (HBO) THERAPY—HBO therapy is a treatment designed to administer oxygen to tissues at a much higher content than is available at sea level.[30] Usually patients undergo therapy in a sealed tank, but some techniques have utilized topical applications. Although many case reports and case series evaluating HBO therapy for wound healing have been published,[31,32,33,34,35,36,37,38,39,40,41,42,43,44,45] there are fewer controlled trials.[46,47,48,49]

The AHCPR (1995) recommendation for HBO therapy for decubitus ulcers is as follows:[50]

- The therapeutic efficacy of hyperbaric oxygen has not been sufficiently established to permit recommendation for the treatment of pressure ulcers. (Strength of Evidence = C.)

GROWTH FACTORS—A number of studies have evaluated different topical growth factors for the treatment of ulcers including recombinant PDGF-BB,[51,52,53,54,55,56] autologous PDWHF,[57,58,59,60] TGF-ß,[61] basic fibroblast growth factor (bFGF),[62,63] and EGF.[64,65]

The AHCPR (1995) recommendation for growth factor and/or cytokine therapy for decubitus ulcers is as follows:[66]

- The therapeutic efficacy of miscellaneous topical agents (e.g., sugar, vitamins, elements, hormones), growth factors, and skin equivalents has not yet been sufficiently established to warrant recommendation of these agents at this time. (Strength of Evidence = C.)

ULTRASOUND (US), ULTRAVIOLET (UV), AND LASERS—A few studies have evaluated the efficacy of US,[67,68,69,70,71] UV,[72] or helium-neon lasers[73] for the treatment of ulcers.

The AHCPR (1995) guideline states that[74]

- the therapeutic efficacy of ultraviolet, low-energy laser irradiation, and ultrasound have not been sufficiently established to permit recommendation of these therapies for the treatment of pressure ulcers. (Strength of Evidence = C.)

2.4 Guidelines and Evidence of Present Practice Patterns

Our research identified 12 guidelines, 4 technology assessments, and 4 studies with evidence of present practice patterns for the treatment of chronic ulcers. Guideline publications include formal practice guidelines or consensus statements (e.g., Wound Ostomy and Continence Nurses Society {WOCN}, AHCPR) and review articles intended to identify optimal treatments for chronic ulcers. Chosen technology assessments evaluated technologies relevant to the treatment of chronic ulcers. Studies with evidence of present practice patterns were surveys. Summaries of these guidelines are presented in **Table 2.1**; summaries of technology assessments for specific wound healing therapies are presented in **Table 2.2**.

2.4.1 Consensus

There is a consensus about several aspects of treating chronic wounds.

Maintenance therapy is usually sufficient to arrest stage I (nonblanchable erythema of skin) decubitus ulcers. Treatments include

- regular repositioning of the patient;
- avoiding positioning the patient directly on the trochanter;
- reducing friction and shear forces by using protective dressings;
- protecting wounds from excessive moisture, particularly in incontinent patients;
- reducing pressure on sites, particularly on heels;
- avoiding the use of donut-type ring cushions; and
- maintaining adequate nutrition, especially protein and vitamin C.

Open ulcers (decubitus stage II to IV, venous, and arterial) require a moist healing environment relatively free from impediments to healing (e.g., infection, necrotic tissue, excessive exudate). Continuous moist gauze dressings are good for maintaining a moist ulcer bed.

The periulcer surface should be protected from moisture by a film or dressing to prevent maceration.

Mechanical, surgical, enzymatic, and autolytic debridement all effectively remove devitalized tissue. However, autolytic debridement is not appropriate for infected

wounds. Forceful irrigation with warm normal saline (through a 35 mL syringe fitted with a 19-gauge angiocatheter, generating 8 psi) is a good method of mechanical debridement that removes devitalized tissue and debris without injuring granulation tissue.

Systemic antibiotics are only indicated in the presence of sepsis, advancing cellulitis, or osteomyelitis.

Swab cultures are not appropriate for determining infection at wound sites because all open wounds are colonized by bacteria.

Venous leg ulcers require treatments that increase the venous return. Therapies include

- compression bandages with 20 to 40 mm Hg pressure at the ankle that gradually decreases toward the knee,
- elevation of legs above the level of the heart, and
- surgery as needed to repair superficial and perforating veins.

2.4.2 Lack of Consensus

There is a lack of consensus on several aspects of treating chronic wounds.

Topical Antibiotics and Antiseptics—Some of the guidelines that address the use of topical antimicrobials do not address treating local infection, cleansing the wound, or moistening the gauze dressing.

Frantz and Gardner[75] recommend topical antimicrobial therapy for infected wounds that are otherwise free of nonviable tissue and debris. They recommend against the use of antiseptics (e.g., povidone iodine, Dakin's solution, hydrogen peroxide) for wound cleansing or moistening dressings. They also suggest that several commercially prepared wound cleansers (e.g., Shur Clens, Biolex, Puri-Clens) are toxic to cells essential for wound healing. WOCN[76,77] and the University Hospital Consortium (UHC)[78] recommend using topical antimicrobial agents. WOCN recommends topical therapy to keep the wound surface clean, moist, and free from secondary infection. Although it notes the possible harm from povidone iodine, hydrogen peroxide, Dakin's solution, and acetic acid, WOCN does not specifically recommend against their use. In fact, WOCN recommends Dakin's solution to control odor, help liquefy necrotic tissue, and combat staphylococcal and streptococcal infections. However, in its 1993 guideline for the treatment of venous, arterial, and neuropathic leg ulcers,[79] WOCN notes that ". . . controversy exists regarding the deleterious effects of

various solutions[antiseptics, antibiotics] in open wounds. . .” and that caregivers should review the current literature before reaching a decision about topical treatment. The UHC guideline states that topical antiseptics may be used for ≤1 week; topical antibiotics may be used for fixed durations to avoid sensitization, selection of resistant organisms, and systemic toxicity.

Smith's[80] guideline for pressure ulcers recommends against topical antibiotic agents. The Douglas & Simpson[81] guideline for venous leg ulcers states that there is little evidence that bacteria impair ulcer healing. The Goldman & Fronek[82] guideline for venous leg ulcers recommends against topical antibiotics. The 1995 AHCPR[83] guideline recommends against cleansing wounds with antiseptics or skin cleansers. The other guidelines do not address antimicrobial treatment.

Grafting and Operative Closure—There are no specific recommendations for candidate selection or use of grafting. Douglas & Simpson recommend it for patients with venous leg ulcers that have not healed after 1 year of properly applied support and compression bandaging. They prefer mesh grafting over split-skin or pinch grafting. However, Goldman & Fronek recommend split-skin and pinch grafting for non-healing ulcers. UHC recommends split thickness grafting or myocutaneous flaps, but does not specify selection criteria. AHCPR recommends operative repair of clean stage III or IV ulcers that do not respond to optimal treatment (as defined in its guideline) using direct closure, skin grafting, skin flaps, musculocutaneous flaps, and free flaps.

Hyperbaric Oxygen (HBO) Therapy—The 1992 British Columbia Office of Health Technology Assessment (BCOHTA) concludes that HBO therapy for chronic osteomyelitis (COM) and osteoradionecrosis (ORN) is questionable. At that time, only 1 small randomized controlled trial of HBO therapy for ORN had been published. More recent guidelines offer conflicting views. The 1992 AHCPR guideline states that there is inconclusive evidence. On the other hand, WOCN recommends HBO therapy for venous leg ulcers but acknowledges that it is controversial.

Other Topical Pharmacologic Agents—Many topical agents, such as sugar, antacids, vitamins A and D, growth factors, and hormones, have been proposed to aid wound healing. None of the guidelines recommend these adjuvant treatments. AHCPR's 1992 technology assessment[84] of Procuren (PDGF-BB) concluded that results were uninterpretable because the 3 existing trials were small and because 2 of them were uncontrolled.

Other Systemic Pharmacologic Agents—AHCPR, Douglas & Simpson, and Goldman & Fronek guidelines state that pentoxiphylline (a vasodilator) has not been shown to be an effective therapy for chronic wounds.

Irradiation—Infrared, ultraviolet, and low-energy laser irradiation have been proposed as adjuvant therapies for chronic wounds. AHCPR found inadequate evidence to recommend any of these treatments for pressure ulcers.

Hydrotherapy—The 1995 AHCPR guideline recommends whirlpool treatment for ulcers with thick exudate, slough, or necrotic tissue.

Ultrasound (US) Therapy—AHCPR does not recommend US therapy. However, Goldman & Fronek suggest that it may a useful treatment for venous leg ulcers.

Electrical Stimulation—The UHC guideline considers ES an unproven adjunctive therapy for wound healing. On the other hand, AHCPR recommends ES for recalcitrant stage II to IV pressure ulcers (based on ≥2 controlled clinical trials).

2.4.3 Practice Patterns

Summaries of reports of practice patterns for the treatment of wounds are presented in **Table 2.3**.

In 1994, Roe et al.[85] surveyed 146 community nurses (primary caregivers for chronic leg ulcers) in England. The survey revealed that

- 51% routinely cleansed sites,
- 1% never cleansed sites,
- 79% used an antiseptic cleaner,
- 17% used an antibiotic tulle,
- 18% used an antibiotic cream,
- 65% used a dry dressing,
- 6% never used a dry dressing,
- 91% applied compression bandages,
- 66% applied compression bandages exclusively, and
- 23% used products providing 20 to 40 mm Hg compression at ankle graduated to 50% at the knee.

Margolis & Cohen[86] analyzed the methodology sections of all English language RCTs (since 1966), evaluating therapies for venous leg ulcers to determine the standard of care. Forty-six percent of studies cleansed wounds with saline, 8% with water, and 22% with antiseptics and/or disinfectants.

Frantz et al.[87] collected data from all patients treated for pressure ulcers at a Veterans Administration hospital between 1983 and 1988. Sixty-three percent of ulcers were treated with antiseptics, 48% with topical agents (e.g., antacids), 18% with antiseptic impregnated gauze, and 8% with dry packing strips. One-third received no dressing at all.

2.5 Tables

Table 2.1. Summary of Guidelines for Wound Healing Therapy

Study	Ulcer Types	Recommended	NOT Recommended	Comments
Douglas & Simpson[88] (1995)	Venous (leg)	• support or compression bandaging • leg elevation • if skin grafting, use mesh grafting rather than pinch or split-skin grafting • superficial vein surgery if deep veins are competent	• routine swabbing for bacterial culture • crêpe or elastic tubular bandages, except shaped bandages • oxpentiphylline or other drug therapy, including enhancers of fibrinolysis • grafting with cultured keratinocytes	No specifics on dressings, antiseptics, antibiotics.
WOCN[89] (1992)	Pressure	• pressure relief/reduction devices • position changes, at least every 2 hours for bedfast patient • friction/shear force relief/reduction devices • reduce excessive moisture • nutrition — tissue hydration and positive nitrogen balance • remove impediments to healing, including infection, necrotic tissue, and excessive or pooled exudate • debridement: conservative instrumental debridement of clearly necrotic tissue; enzymatic; autolytic using a moisture-retentive dressing; mechanical using wet-to-dry dressings and/or water propulsion therapy • forceful irrigation of dirty wounds (35 mL syringe with 19-gauge needle) • gentle flushing with noncytotoxic solution for clean/granulating wounds • absorption dressings • wound cleansing at each dressing change • topical therapy to keep wound surface clean, moist, and free from secondary infection • evaluation of healing on a regular basis • referral to surgical consultation in nonhealing wounds • educate the patient • follow-up	• debride non-infected, dry ischemic wounds • debride dry eschar • occlusive dressings in infected wounds or in wounds with potential for anaerobic infection • tight wound packing Authors do not actually recommend against the following, but they emphasize the adverse qualities: • surgical debridement involves surgical and anaesthesia risks (but it is rapid and effective) • improperly diluted povidone iodine inhibits and/or destroys macrophages and fibroblasts • H_2O_2 is a nonselective debriding agent (destroys fibroblasts) • Dakin's solution destroys fibroblasts unless properly diluted (but controls odor, may be used against staphylococcal and streptococcal infections, and helps liquefy necrotic tissue) • acetic acid destroys fibroblasts	Nursing guideline.

Table 2.1. Summary of Guidelines for Wound Healing Therapy (continued)

Study	Ulcer Types	Recommended	NOT Recommended	Comments
WOCN[90] (1993)	Arterial (leg) Venous (leg) Neuropathic (leg)	• optimize blood flow: to lower extremities by maintaining legs in a dependent or neutral position (arterial + neuropathic);[d] for venous return by keeping legs elevated above the heart (venous); avoid crossing legs (a + v) or sitting with acute angulation (v); avoid exposure to cold (a + n); avoid smoking (a); avoid constrictive clothing (all) • reduce pressure for bony prominences (all) • orthotics consult for patient with altered gait (n) • moisturize skin after bathing with nonirritating agent such as petrolatum and xipamide (all) • ambulate patient to tolerance (a + v) • avoid standing for prolonged periods (v) • use of vascular support devices (v) • prevent moisture between toes (a + n) • avoid friction (a + n) • maintain routine foot care for toenails, corns, and calluses; avoid self-treatment of corns and calluses (a + n) • use of proper footwear (a + n) • evaluate diabetes management (n): blood glucose control, nutritional status, compliance • remove impediments to healing, including infection, necrotic tissue, and excessive or pooled exudate (all) • debridement: surgical consult for sharp debridement (n); enzymatic (all); autolytic using moisture vapor permeable transparent dressings (all), hydrogels (all), hydrocolloid dressings (all), or foam dressings (v); mechanical using wet-to-dry dressings (all) or water propulsion therapy (v) • gentle wound cleansing at each dressing change for non-necrotic ulcers (all)	• debride dry gangrene	Nursing guideline.

[d] The specific wound type for which a particular treatment is recommended by the authors is in parenthesis, abbreviated as arterial (a), venous (v), or neuropathic (n).

Table 2.1. Summary of Guidelines for Wound Healing Therapy (continued)

Study	Ulcer Types	Recommended	NOT Recommended	Comments
		• absorption dressing for non-necrotic wounds with crater formation or pooled exudate (n) • dressings: moisture vapor permeable transparent adhesive dressings (all), hydrocolloid dressings (all), hydrogel dressings		
Frantz & Gardner[91] (1994)	Not specific, but including pressure and venous ulcers	• remove nonviable tissue, such as necrotic tissue and slough, and foreign debris, such as residual material from dressings • debridement: autolytic; biochemical (enzymes); mechanical; or sharp (surgical) • cleansing: vigorous technique confined to wounds with large segments of foreign debris or nonviable tissue; gentle irrigation (8 psi, equivalent to solution forced through 35 mL syringe with 19-gauge angiocath) for wounds with granulation tissue; using a gentle patting technique with a soft, moist gauze • physiologically compatible solutions, such as normal saline and lactated Ringer's, for cleansing and moistening gauze dressings • topical antimicrobial therapy (e.g., Silvadene) to treat wound infections • dressings that provide a moist healing environment and do not disrupt the skin surrounding the wound: moist gauze; polyvinyl or hydrocolloid dressings on partial-thickness wounds free of infection; absorptive dressings (e.g., calcium alginate) on wounds with large amounts of drainage. • positioning techniques for pressure ulcers • pressure-reducing devices for pressure ulcers • supportive boots, foam wedges, and specially fitted shoes, especially for diabetics with pressure ulcers • compressive stocking, Unna's paste boots, and pneumatic compression devices to enhance venous return for venous insufficiency ulcers	• swab culture to diagnose a wound infection • autolytic debridement in immune compromised individuals • wet-to-dry dressings (mechanical debridement) once the wound begins to granulate • vigorous cleansing for wound with granulation tissue • antiseptic solutions to cleanse wounds or moisten gauze dressings • polyvinyl or hydrocolloid dressings on wounds that are infected and/or full thickness • sterile technique for dressing application • body weight in detecting malnourishment	

Table 2.1. Summary of Guidelines for Wound Healing Therapy (continued)

Study	Ulcer Types	Recommended	NOT Recommended	Comments
		• proper nourishment: 1.25 g to 1.5 g protein per kg body weight per day and 30 to 35 calories per kg body weight per day, unless contraindicated; daily multivitamin; zinc supplement if there is a zinc deficiency; iron supplement only if there is no active infection • assess wound on 5 parameters: wound location; wound size; level of tissue involvement; characteristics of the wound surface; and characteristics of the periwound surface		
UHC[92] (1990)	Pressure	• maintain adequate nutrition, particularly protein; Vitamin C 500 mg orally twice daily; zinc sulfate 220 mg orally 3 times daily may be helpful for recalcitrant ulcers • rehabilitative measures to improve mobility • repositioning according to a regular schedule: turning the patients alternately from the 30° left side-lying position, the supine, and the 30° right side-lying positions; avoid positioning directly over greater trochanter; avoid prolonged sitting upright in a chair; avoid excessive elevation of upper torso • carefully monitor bony prominences every 2 to 4 hours (development of stage I pressure ulcer requires more frequent monitoring) • systemic antibiotics only if ulcers are complicated by cellulitis, osteomyelitis, bacteremia, or other sepsis • bacterial endocarditis prophylaxis for persons with cardiac valvular lesions • surgical debridement of all necrotic tissue with appropriate antibiotic therapy for sepsis • surgical debridement of lesions totally covered by eschar accompanied by use of moist dressing • enzymatic debridement • topical antiseptics (povidone-iodine, acetic acid, Dakin's solution, H_2O_2) may be used for periods of 1 week or less	• routine swab cultures to diagnose infection • foam pads less than 4″ thick	Guideline focus is pressure relief/reduction devices.

Table 2.1. Summary of Guidelines for Wound Healing Therapy (continued)

Study	Ulcer Types	Recommended	NOT Recommended	Comments
		• topical antibiotics may be used for fixed periods of time to avoid sensitization, selection of resistant organisms, and systemic toxicity • keep wound moist, but protect surrounding skin from moisture • therapeutic foam or air mattress/overlay • air-fluidized beds, esp. for patients who fail treatment on foam, air mattresses, or overlays, or who have multiple ulcers so that repositioning off the ulcers is difficult • trauma/oscillating beds for patients with unstable spines • split thickness skin grafts or myocutaneous flaps		
Smith[93] (1995)	Pressure	• 4″ to 6″ deep solid foam mattresses are the most inexpensive and effective pressure-relieving products • polyurethane dressings can protect area from friction (i.e., for stage I ulcers), and are more effective for saline wet-to-dry dressings for stage II ulcers • necrotic material must by removed — enzymatic debridement in good for smaller eschars; polyurethane and hydrocolloid dressings (autolytic) are more effective for stage III ulcers; hydrogels for dry deep stage III and stage IV ulcers; hydrophilic foam, alginates, or saline-impregnated gauze for packing deep wounds with significant exudate • surgical debridement for stage IV ulcers • higher protein intake and vitamin C supplements	• foam pads less than 4″ thick • donut-type devices or ring cushions • wet-to-dry dressings can damage granulation tissue • the is no consensus on the use of low air-loss and air-fluidized beds • swabs to establish clinical infection • topical antibiotic agents	Guideline restricted to nursing home patients aged 65 years or older.
Wiseman et al.[94] (1992)	Leg ulcers	• occlusive nonabsorbent dressings for stage I ulcers and stage II ulcers with light (1-2 mL/day) drainage • nonadherent absorbent dressings for stage II ulcers with light drainage • hydrocolloid dressings for stage II ulcers with light to moderate (3-5 mL/day) drainage and stage III-IV ulcers with moderate to heavy (>5 mL/day) drainage • occlusive absorbent composite dressings for stage III-IV ulcers	• hydrogels	Book chapter about wound dressings.

Table 2.1. Summary of Guidelines for Wound Healing Therapy (continued)

Study	Ulcer Types	Recommended	NOT Recommended	Comments
		with moderate drainage • nonadherent nonabsorbent primary dressing kept moist to prevent adherence with adherent absorbent secondary dressing for stage II-IV ulcers with moderate drainage and stage III-IV ulcers with heavy drainage		
Edlich et al.[95] (1992)	Not specified	• cleanse wounds at high pressure — 35 mL syringe with 19-gauge needle, normal saline (= 8 psi) — ONLY for heavily contaminated wounds		Book chapter about surgical management of wounds.
Goldman & Fronek[96] (1992)	Venous (leg)	• elevate legs above the level of the heart while at rest • compression therapy with stockings or bandages: should exert a resting pressure of at least 20 to 30 mm Hg at the ankle; should be applied to produce a pressure gradient where the pressure is higher at the ankle and lower at the knee • encourage walking and exercise • ultrasound therapy and intermittent pneumatic compression may also be beneficial • cover ulcer with a local dressing that should reduce pain and pruritus; allow excess fluid and exudate to escape without permitting desiccation; not cause an allergic reaction; be easy to change with the least discomfort possible; not leave dressing material in the wound when changed • surgical correction of venous insufficiency of superficial veins, perforating veins, and insufficiency of deep veins • split-skin or pinch grafting • sclerotherapy for venous hypertension in some patients • systemic antibiotics only in patients with cellulitis • diuretics only as a short course in cases with severe edema	• regard occlusive arterial disease as an absolute contraindication for compression therapy • topical pharmacologic agents (e.g., antibiotics) • surgical or systemic pharmacologic treatments as stand-alone therapy • vein valve transplants • valvuloplasty • venous transposition	Consensus paper.
Rodeheaver et al.[97] (1994)	Pressure + vascular insufficiency	• mechanical/surgical debridement of necrotic tissue of ulcers in the lower extremity • sharp surgical debridement	• debridement with wet-to-dry dressings	Interdisciplinary roundtable.

Table 2.1. Summary of Guidelines for Wound Healing Therapy (continued)

Study	Ulcer Types	Recommended	NOT Recommended	Comments
		• autolytic debridement • enzymatic debridement		
AHCPR[98] (1992)	Pressure (stage I)	• systematic skin inspection at least once daily, paying particular attention to bony prominences • routine cleansing: avoid hot water; use a mild cleansing agent; minimize force and friction against skin • minimize factors leading to dry skin (<40% humidity, exposure to cold); moisturize dry skin • protect skin from excessive moisture (e.g., due to incontinence) • minimize friction and shear forces on skin: proper positioning, transferring, and turning techniques (avoid dragging by using trapeze or bed linen); lubricants (e.g., corn starch, creams); protective films; protective dressings (e.g., hydrocolloids); protective padding • maintain adequate nutrition, especially in terms of calories, protein, and iron • maintain physical activity, when possible • reposition at least every 2 hours; avoid positioning directly on the trochanter • pillows or foam wedges to keep bony prominences from direct contact with one another • use device that totally relieves pressure on the heels in people who are completely immobile • maintain head of bed at lowest possible elevation • pressure-reducing mattress: foam, static air, gel, or water • patient education	• massage over bony prominences • donut-type ring cushions	Focus is on prediction and prevention.
AHCPR[99] (1995)	Pressure (stages II-IV)	• avoid positioning on a pressure ulcer • follow same procedures as in AHCPR 1992[100] for repositioning • static support surface (e.g., foam overlay) if a patient can assume a variety of positions without bearing weight on an ulcer and without bottoming out	• donut-type ring cushions • autolytic debridement of infection ulcers • debride heel ulcers with dry eschar that do not have edema, erythema, fluctuance, or drainage • cleanse wounds with skin cleansers or antiseptics	

Table 2.1. Summary of Guidelines for Wound Healing Therapy (continued)

Study	Ulcer Types	Recommended	NOT Recommended	Comments
		• dynamic support surface if patient cannot assume a variety of positions without bearing weight on an ulcer or without bottoming out, or if the ulcer does not heal • low-air-loss or air-fluidized bed for patient with large stage III or IV pressure ulcers on multiple turning surfaces (may also help avoid excessive moisture on skin) • debride devitalized tissue: sharp debridement if need is urgent (e.g., advancing cellulitis or sepsis); mechanical, enzymatic, and autolytic may be used when there is no urgent need • cleanse wounds at each dressing change: use minimal mechanical force; use normal saline • safe and effective irrigation pressures range from 4 to 15 psi • whirlpool treatment for ulcers with thick exudate, slough, or necrotic tissue • dressings that keep ulcer bed continuously moist; protect surrounding skin dry • eliminate dead space by loose packing • electrotherapy for stage III and IV ulcers that have proved unresponsive to conventional therapy or recalcitrant stage II ulcers (as an adjunctive therapy) • systemic antibiotic therapy for bacteremia, sepsis, advancing cellulitis, or osteomyelitis • protect ulcers from exposure to feces • follow body substance isolation procedures • use sterile instruments to debride • use clean dressings, rather than sterile ones • operative repair of clean stage III or IV ulcers that do not respond to optimal patient care: direct closure; skin grafting; skin flaps; musculocutaneous flaps; free flaps • education	• systemic antibiotics for local infection • hyperbaric oxygen • infrared, ultraviolet, or low-energy laser irradiation • ultrasound • miscellaneous topical agents (e.g., sugar, vitamins, elements, hormones, other agents) • growth factors • skin equivalents • systemic agents other than antibiotics (e.g., vasodilators, pentoxiphylline) • use swab cultures to diagnose infection • prophylactic ischiectomy	

Table 2.2. Summary of Technology Assessments for Wound Healing Therapies

Study	Technology Assessed	Conditions/Diseases	Conclusions
AHCPR[101] (1992)	Procuren (PDGF-BB)	Unhealed wounds	The existing trials are small, and 2 out of 3 are uncontrolled, making any interpretation impossible. There is insufficient evidence.
BCOHTA[102] (1992)	Hyperbaric Oxygen (HBO)	Chronic osteomyelitis (COM) Osteoradionecrosis (ORN)	*COM* — There is conflicting data regarding HBO efficacy. Case series data report fairly high recovery rates, while the 1 RCT showed no beneficial (possibly deleterious) effect. Proponents of HBO say it is an adjunct therapy. *ORN* — HBO for ORN of the mandible is supported by the 1 small published RCT. Possibly useful in this situation, HBO is still an adjunct therapy.
NCHSR[103] (1981)	Ultraviolet (UV) radiation	Pressure ulcers	The effectiveness of UV radiation in treating pressure ulcers has not been satisfactorily demonstrated. All data are from case studies; there are no controlled trials. Data is confounded by, for example, UV radiation treatment started simultaneously with more vigorous local measures.
NCHSR[104] (1981)	Hydrotherapy/whirlpool (WP)	Pressure ulcers	Hydrotherapy (whirlpool bath) is a safe and effective treatment for pressure ulcers.

Table 2.3. Summary of Reports of Practice Patterns for the Treatment of Chronic Wounds

Study	Study Type (Locale)	Ulcer Type	Practice Pattern
Brandeis et al.[105] (1995)	Survey (U.S.)	Pressure	**2,011 nursing home residents ³ 60 years of age in 270 nursing facilities** • 79% of patients with stage II - IV were on a repositioning program • 72.8% received protective/preventive skin care • 72.8% had a pressure-relieving bed
Margolis & Cohen[106] (1994)	Review article	Venous	**Literature review of methods section from all English language RCTs on treatments for venous ulcers since 1966.** • 26% of studies used a multilayer inelastic bandage, 26% used a two-layer or thinner inelastic bandage, 20% used a single-layer elastic bandage, 4% used elastic stockings, and 2% used a combination of compression pump and stocking • 58% of studies did not indicate if debridement was performed, 6% used surgical debridement, 12% used enzymatic debridement, and 12% debrided the patients but did not specify which technique • 46% of studies used saline as a cleansing agent (most did not mention sterility), 8% used water, and 22% used disinfectants and antiseptics (including cetrimide, acetic acid, mercurochrome, chlorhexidine, gentian violet, hydrogen peroxide, and potassium permanganate) • 30% of studies used occlusive dressings (hydrocolloids, paraffin, foam), 20% used zinc-impregnated gauze, and 4% used saline-soaked gauze

Table 2.3. Summary of Reports of Practice Patterns for the Treatment of Chronic Wounds (continued)

Study	Study Type (Locale)	Ulcer Type	Practice Pattern
Roe et al.[107] (1994)	Survey (G.B.)	Chronic leg ulcers associated with venous disease, arterial disease, rheumatoid arthritis, and diabetes	**Survey of 146 community nurses opinions.** • 68 (47%) sometimes cleanse, 74 (51%) routinely cleanse, and 2 (1%) never cleanse a leg ulcer • 78 (53%) use saline, 104 (71%) use warmed saline; 38 (26%) use either exclusively • 94 (64%) never use cetrimide • 115 (79%) never use hypochlorite • 69 (47%) never use H_2O_2 • 98 (67%) never use chlorhexidine • 26 (18%) never use potassium permanganate, 82 (56%) use it (significantly higher rate of use in 1 of the 3 health authorities) • 128 (88%) use a combination of different dressings layered over the ulcer • 53 (36%) had used all of the dressing listed on the survey at one time or another: ❍ 133 (91%) use hydrocolloid dressings, 5 (3%) never use them ❍ 127 (87%) use alginate dressings, 2 (1%) never use them ❍ 81 (55%) use hydrogel dressings, 6 (4%) never use them ❍ 50 (34%) use foam dressings, 16 (11%) never use them ❍ 25 (17%) use an antibiotic tulle, 54 (37%) never do ❍ 27 (18%) use an antibiotic cream, 38 (26%) never do ❍ 73 (50%) use some other tulle, 30 (21%) never do ❍ 98 (67%) use polysaccharide beads, 3 (2%) never do ❍ 60 (41%) use a semipermeable film, 21 (14%) never do ❍ 27 (18%) use an odor absorbing dressing, 5 (3%) never do ❍ 95 (65%) use a dry dressing, 9 (6%) never do ❍ 90 (62%) use impregnated NA, 4 (3%) never do ❍ 84 (58%) use flamazine, 5 (3%) never do ❍ 76 (52%) use an enzymatic agent, 9 (6%) never do ❍ 105 (72%) use paste bandage, 3 (2%) never do • 133 (91%) apply compression bandages to venous ulcers, but only 93 (66%) do so exclusively, and only 33 (23%) used products that could provide an adequate level of compression (20 to 40 mm Hg at the ankle, graduated to 50% of that pressure at the knee)

Table 2.3. Summary of Reports of Practice Patterns for the Treatment of Chronic Wounds (continued)

Study	Study Type (Locale)	Ulcer Type	Practice Pattern
Frantz et al.[108] (1992)	Retrospective (Iowa, U.S.)	Pressure	**Veterans Administration facility charts; part also from prospective study of ES.** • 118 (49.4%) of ulcers were treated with enzyme debriding treatments, 112 (95%) of these by trypsin enzymatic spray • 69 (28.9%)[e] of ulcers were treated with cleansing treatments, 52 (75.4%) of these with soap, and 16 (23.2%) of these with normal saline • 152 (63.6%) of ulcers were treated with some type of antiseptic: 131 (86.2%) of these with H_2O_2, 39 (25.7%) of these with povidone-iodine, and 22 (14.5%) of these with sodium hypochlorite • 105 (43.9%) of ulcers were treated with hydrocolloid dressings, 79 (33.1%) of ulcers were dressed with gauze squares, 56 (23.4%) of ulcers were treated with polyurethane dressings • 80 (33.5%) of ulcers were treated on a no-dressing protocol, 20 (8.4%) of ulcers were dressed with dry packing strips and dry gauze-type dressings applied to wound with no topical agents, 14 (5.9%) of ulcers were treated with Dakin's dressings, 11 (4.6%) with acetic acid dressings, 9 (3.8%) with saline dressings, 8 (3.3%) with povidone-iodine dressings, 1 (0.4%) with a H_2O_2 dressing, and 1 (0.4%) with iodoform gauze packing strips • 115 (48.1%) of ulcers were treated with topical treatments, 40 (34.8%) of these with antacids, and 35 (30.4%) of these with silver sulfadiazine

[e] Frequency is printed as 69 (out of 239) ulcers, or 28.9% in the first sentence of the paragraph, and 89 (out of 239), or 28.9% in the last sentence of the paragraph. Assuming 28.9% is the correct percentage, 69 out of 239 ulcers is the correct proportion.

3.0 Electrical Stimulation for Wound Healing

3.1 Basic Description

Living cells produce electrical potentials by piezoelectric, pyroelectric, and streaming mechanisms.[109] Piezoelectric potentials are generated by stress, typically at the interface between bone and surrounding ion-containing fluid.[110] Pyroelectric potentials are created from the heating of fluids.[111] Streaming potentials are created by charged liquids flowing next to each other.

Human skin itself may act as a battery capable of driving substantial currents into a wound.[112] If so, this electrical current may accelerate wound healing.

Preclinical studies have shown that externally applied ES can

- increase ATP (adenosine triphosphate) concentrations in tissues,[113]
- increase DNA synthesis,[114]
- promote healing of soft tissue or ulcers,[115,116]
- cause migration of epithelial and fibroblasts into a wound site,[117,118]
- accelerate the recovery of damaged neural tissue,[119]
- reduce edema,[120] and
- inhibit the growth of various pathogens.[121,122]

Examples of preclinical studies of electrical stimulation are presented in **Table 3.1**.

ES has been used or studied for many different therapeutic applications. ECRI has conducted extensive technology assessments on Electrical Bone Growth Stimulation for the Lower Leg,[123] Electrical Bone Growth Stimulation for the Spine,[124] Electrical Bone Growth Stimulation for the Wrist,[125] and Spinal Cord (Dorsal Column) Stimulation for Chronic Intractable Pain.[126] Studies have also been conducted to test the efficacy of ES for healing jaw fractures,[127] reducing pain and swelling in soft tissue injuries,[128] alleviating spinal cord lesions,[129] eliminating intermittent claudication,[130] improving healing from assorted hand injuries,[131] reducing cerebral edema in cases of head trauma,[132] reducing swelling in grades I and II ankle sprains,[133] and accelerating healing after foot surgery,[134] dental surgery,[135] and oral surgery.[136,137]

3.2 Types of Electrical Stimulation and Treatment Protocols

All electrical stimulators are not the same. We classified ES devices for chronic wound healing into several basic categories:

- direct current (DC) [which we also refer to as low-intensity direct current (LIDC) throughout this report],
- pulsed current (PC),
- alternating current (AC),
- pulsed electromagnetic induction (PEMI), and
- spinal cord stimulation (SCS).

These categories are primarily based on the type of electrical current.

Just as all ES studies do not use the same type of current, the types of devices within each category may not be the same. Devices categorized within each group may differ technically and/or by mode of action. We did not assume *a priori* that all devices within a category are homogeneous. We used these categories to describe and present the diversity of ES devices for chronic wound healing.

3.2.1 Direct Current Applications

Some electrical stimulators used DC, which is a continuous, unidirectional, constant current. **Table 3.2** displays therapy synopses for DC stimulation for wound healing.

The published studies of DC stimulation for the treatment of wound healing used low-intensity direct current (LIDC).[f] (One study, however, {Akers & Gabrielson[138]} used an unspecified level of DC.) Clinicians applied 20 to 100 microamps (μA) of current at low voltage (<8 volts). The cathode (negative electrode) was usually wrapped in saturated saline-gauze and placed directly over the wound site; the anode (positive electrode) was placed on the skin surface near the wound. Patients underwent 2-hour sessions 2 or 3 times daily. After several days or if the wound apparently stopped healing, clinicians reversed (switched) the polarity of the electrode by placing the anode directly over the

[f] We use the term "low-intensity direct current" (LIDC) throughout this report. Although the term low-intensity may be redundant because all studies in this report used a microamperage current, this nomenclature reminds the reader that these devices use very low currents, that are unlikely to cause electrolytic tissue destruction.

wound and the cathode at a nearby site. They reversed polarity 1 or more times (depending on the regimen) to stimulate healing if the wound had not improved or reached a "growth plateau."

The regimen used by Wolcott et al. appears typical of published DC therapies for wound healing.

Representative LIDC Regimen: Wolcott et al. 1969[139]

(1) The ulcer base was covered with dry sterile gauze. The negative electrode was placed on gauze packing, covered with additional gauze, and secured by waterproof tape. The positive electrode was placed on gauze 15 cm proximal to lesion. Both electrode packs were saturated with Ringer's solution.

(2) A 600 μA current was applied for ≥2 hours.

(3) If there was extensive ulcer drainage without bleeding, the current was increased to 800 μA for 1 or 2 hours. If the ulcer bled, the current was reduced to 400 μA.

(4) In subsequent treatments, current was maintained 200 μA below level producing bleeding in ulcer.

(5) The daily cycle consisted of 2 hours current on, then 4 hours current off. (6 hours of stimulation delivered in 2-hour sessions TID {3 times daily}.)

(6) If the ulcer was not infected after 3 days, polarity was reversed. (The positive electrode was placed over the lesion, and the negative electrode was placed proximally.) If the ulcer was infected, therapy continued at same polarity, but was reversed 3 days after the infection cleared.

(7) Daily procedures consisted of (a) substituting fresh gauze; (b) cleansing the ulcer; (c) adjusting the current as needed; (d) evaluating for granulation tissue formation and re-epithelialization at ulcer margins; and (e) evaluating for possible growth cessation ("growth plateau"), usually 14 to 21 days after treatment onset.

(8) If the ulceration had reached the growth plateau, polarity was reversed (negative electrode over lesion).

(9) If another growth plateau in ulceration occurred, polarity was reversed again (positive electrode over lesion).

(10) Thereafter, polarity was reversed every 24 hours until the lesion healed.

3.2.2 Pulsed Current Applications

Some electrical stimulators used PC, which is a periodic, nonsinusoidal pulsed wave current. **Table 3.3** displays therapy synopses for PC stimulation for wound healing.

We classified published studies of PC stimulation for the treatment of wound healing into 2 subcategories: (a) pulsed direct current (PDC), in which the delivered current has a DC component and (b) high-voltage pulsed current (HVPC), in which the delivered current has little or no DC component.

Pulsed DC studies generally used 30 to 40 mA (generated by a 6 to 12 V battery) at 128 pulses per second (Hz), although 1 study (Wood et al.[140]) used 300 to 600 μA at only 0.8 Hz. PDC studies include Wood et al.,[141] Gentzkow et al.,[142] Feedar et al.,[143] Mulder,[144] and Weiss et al.[145] (The study reported by Mulder appears to be a duplicate of results reported by Feedar et al. based on the study size, outcomes, regimen, device, and an editorial.[146])

Regimens used by Feedar et al. and Wood et al. appear typical of published PDC therapies for wound healing.

Representative PDC Regimen: Feedar et al. 1991[147]

(1) The wound bed was irrigated with saline solutions before and between treatments. Saline-soaked gauze sponges were applied on or in wounds.

(2) A 16 × 16 cm moistened electrode was applied ≥30.5 cm from the wound. A 7.5 × 7.5 cm saline-soaked gauze covered electrode was applied onto the wound.

(3) Stimulation was set for 35 mA at 128 Hz, with the negative electrode over the wound. Therapy was a minimum of 4 hours, with a maximum of 8 hours between treatment sessions.

(4) Some patients received surgical or whirlpool (WP) debridement as needed.

(5) The negative electrode was kept over the wound for 3 days after serosanguineous drainage.

(6) Thereafter, the polarity of active (wound) electrode was reversed every 3 days until the lesion decreased to stage II. (Polarity changed an average of 6 times in 28 days.)

(7) At the first polarity reversal, the pulse frequency was decreased to 64 Hz. When lesions reached stage II, the polarity was reversed daily.

Representative PDC Regimen: Wood et al. 1993[148]

(1) Stimulation was 600 µA with a 0.8 Hz pulse frequency administered from electrodes placed 2 cm on opposite sides of lesion.

(2) Stimulation was applied 3 times weekly.

[The investigators did not specify the duration of treatment sessions.]

HVPC studies generally used 100 to 250 V at 80 to 100 pulses per second (Hz). HVPC studies include Fitzgerald & Newsome,[149] Gogia et al.,[150] Griffin et al.,[151] Unger,[152,153] Kloth & Feedar,[154] and Feedar & Kloth.[155]

Regimens used by Griffin et al. and Kloth & Feedar appear typical of published HVPC therapies for wound healing.

Representative HVPC Regimen: Griffin et al. 1991[156]

(1) The ulcer site was packed with sterile 0.9% saline-soaked gauze. The active electrode was placed over the site and covered by wet gauze, aluminum foil, and plastic. The inactive (dispersive) electrode was placed on the medial thigh.

(2) The stimulator was initially set at 100 Hz frequency. The voltage intensity was gradually increased to 200 V or maximal voltage that did not produce visible muscular contraction, producing approximately 500 µA of total current.

(3) Daily treatment sessions were 1 hour and continued for 28 days or until the site healed. The polarity was not reversed.

(4) Ancillary care included (a) wound cleansing using Cara-Klenz, (b) Carrington gel topical medication, (c) dry dressings, (d) mechanical debridement if needed, (e) turning patients every 2 hours, and (f) continuing use of pressure-relieving devices.

Representative HVPC Regimen: Kloth & Feedar 1988[157]

(1) Before ES treatment, the ulceration site was debrided mechanically, with proteolytic enzyme ointment (Elase®) and collagenase enzyme ointment (Biozyme-C®). The site was packed with saline-soaked gauze to absorb enzymatic debridement, then flushed with saline solution before placement of electrodes.

(2) Electrical intensity was set at 100 V (below amount needed to produce visible muscular contraction) at 105 Hz frequency with 100 μs intraphase interval (from monophasic twin-pulsed generator). This produced a single-phase charge of 1.6 μC with a total-pulse charge of 342 μC/sec. The anode (positive electrode) was placed directly over wound in saline-soaked gauze; the cathode was placed 15 cm distal to anode.

(3) Daily sessions lasted 45 minutes and were continued 5 days per week for 4 to 16 weeks or until sites healed.

(4) Polarity (electrode placement) was maintained unless wounds exhibited growth (healing) plateau.

3.2.3 Alternating Current Applications

Some devices used AC delivered in a variety of waveforms. **Table 3.4** displays therapy synopses for AC stimulation for wound healing.

We classified published studies of AC stimulation for the treatment of wound healing into 2 sub-categories: (a) TENS and (b) biphasic pulsed.

Studies of TENS generally used small, portable devices capable of generating square-wave pulses at 80 to 90 Hz with 0.1 to 0.2 ms pulse widths. TENS studies include Lundeberg et al.,[158,159] Frantz,[160] Kjartansson & Lundeberg,[161] Kaada & Emru,[162] Alon et al.,[163] Barron et al.,[164] Kaada,[165] and Westerhof & Bos.[166]

Regimens used by Lundeberg et al. and Frantz are indicative of protocols reported in published TENS studies for wound healing.

Representative TENS Regimen: Lundeberg et al. 1992[167]

(1) Patients used an electrical nerve stimulation (ENS) unit capable of producing alternating constant current square-wave pulses (pulse width = 1 ms). Each ENS unit was applied just beyond ulcer surface area and was set to produce intensity-evoking paresthesia from the active (4 × 6 cm) electrode.

(2) Patients underwent 20-minute daily sessions for 12 weeks or until the site healed. They underwent treatment at a clinic for the first week, then used the unit at home for 11 weeks or until healing.

(3) Polarity was changed after each session.

Representative TENS Regimen: Frantz 1990[168]

(1) Conventional therapy was packing the ulcer with 0.9% normal saline gauze and changing the dressing TID.

(2) One set of surface electrodes was applied with the cathode between the 1st and 2nd metacarpal on one hand and the anode in a corresponding position on the other hand.

(3) The other set of surface electrodes was applied with the cathode placed immediately distal to ulceration and the anode placed immediately proximal to the ulcer.

(4) The TENS unit delivered 85 Hz (standard low-frequency) with 150 μs pulse width at a 30 mA amplitude.

(5) Sessions were 30 minutes TID.

(6) Patients underwent 2-hour turning schedules while laying on 4-inch foam mattresses.

Biphasic AC studies used 15 to 25 mA with 0.25 ms pulses at 40 Hz frequency. Biphasic AC studies include Stefanovska et al.[169] and Karba et al.[170]

Representative Biphasic AC Regimen: Stefanovska et al. 1993[171]

(1) A biphasic, charge-balanced AC stimulus was applied with a 0.25 ms pulse duration at 40 Hz. Four-second stimulation trains were rhythmically alternated with 4-second pauses. The AC amplitude was kept between 15 and 25 mA to prevent damage to newly formed tissue and to minimize tetanic contraction of stimulated tissues.

(2) Daily sessions lasted 2 hours and were continued until lesions healed.

3.2.4 Pulsed Electromagnetic Applications

Some electrical stimulators use generators which create energy in what is commonly referred to as the "radio frequency" or RF band (a few tens of megahertz {MHz}). They typically deliver energy by noncontacting means (e.g., coils) rather than by leads and surface electrodes typical of the three previous categories (DC, PC, and AC). We call this group of ES stimulators pulsed electromagnetic induction (PEMI). **Table 3.5** displays therapy synopses for PEMI stimulation for wound healing.

We classified published studies of PEMI stimulation for the treatment of wound healing into 2 sub-categories: (a) those using PEMF devices containing electromagnetic coils capable of generating a magnetic field and (b) those using PEE devices capable of generating a high peak wattage.[g] Both types of devices are applied externally on top of dressings; both types are also nonthermal. Neither uses electrodes wrapped in wet gauze.

PEMF studies generally used a low-level magnetic field that induced a low-level nonthermal electrical field. PEMF studies include Stiller et al.,[172] Todd et al.,[173] Ieran et al.,[174] and Jeran et al.[175] (Jeran et al. appears to be a preliminary report of results reported by Ieran et al.; Ieran and Jeran also appear to be different spellings of the same name.)

Representative PEMF Regimen: Stiller et al.[176]

(1) The device consisted of an electromagnetic transducer (attached to a generator powered by a 9 V battery) containing coils for generating magnetic fields. The transducer unit induced a low-level, nonthermal electrical field of 0.06 mV/cm, 3-part pulse (3.5 ms total width), and 25% duty cycle. It was capable of generating 22 Gauss.

(2) The device was applied externally (by velcro strapping) over existing wound dressing (elastic compression wrap) and used by patients at home.

(3) Patients were instructed to use the device 3 hr/day for 8 weeks or until the lesion healed.

(4) Ancillary treatment consisted of Duoderm® hydroactive dressing ± gentamicin ointment, mupirocin ointment + Vigilon® or nonadherent gauze, Elase® debridement ointment + gauze, or Unna boot beneath Ace® bandage compression wrap.

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g The acronym "PEE" was used in the Salzberg et al. 1995 study. The device is also known as pulsed radio frequency energy.

PEE Regimen:[h]

PEE studies used Diapulse® devices exclusively. These devices emit a nonthermal pulsed high-frequency high peak power electromagnetic energy delivered at 27.12 MHz, with a pulse repetition rate of 80 to 600 pulses/second, 65 µsec pulse width, and produce 273 to 975 W per pulse, with a 0.5% to 4.0% duty cycle. Energy is induced at the wound site by a 9″ drum-shaped treatment head placed in light contact with the dressing and tuned to resonance with the wound site. Recommended treatment consists of 30 minutes, twice daily, until the lesion is healed. As with PEMF devices, the device is applied externally over existing dressings. PEE studies include Salzberg et al.,[177] Tung et al.,[178] Itoh et al.,[179] and Goldin et al.,[180]. Therapies generally consisted of 30-minute sessions twice daily for 8 to 12 weeks or until the lesion healed.

3.2.5 Spinal Cord Stimulation Applications

Spinal cord stimulators are primarily designed to reduce intractable pain in patients with failed back syndrome and other chronically painful disorders. [See ECRI Technology Assessment "Spinal Cord (Dorsal Column) Stimulation for Chronic Intractable Pain."[181]] These devices significantly differ from the types of electrical stimulators previously mentioned for wound healing because spinal cord stimulators are (a) invasive and (b) not primarily intended to increase the rate of wound healing.

However, several case reports (Meglio et al.,[182] Richardson et al.,[183] and Cook et al.[184]) and 2 small case series (Graber et al.,[185] Jivegard et al.[186]) reported increased healing of ulcers in patients following implantation of epidural spinal cord stimulators.

Basic Procedure for Spinal Cord Stimulator Implantation (Percutaneous Epidural Type)[187]

(1) A Touhy needle is used to introduce the electrode into the epidural space at the appropriate spinal level for stimulation. The needle should be inserted at the most shallow angle possible (<40°) and close to the anatomical midline.

(2) A good epidural entry point is between the 1st and 2nd lumbar vertebrae. The process begins with a stab incision at the appropriate spinal level using a #11 blade, followed by insertion of the lead into the epidural space while ensuring electrode contact with the dura mater.

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h Diapulse refers to their device as a nonthermal pulsed high-frequency high peak power electromagnetic energy device (NT/PHF). This acronym does not appear in the literature.

(3) The lead is advanced (using fluoroscopy) into the area of the spinal cord to create a channel for subsequent insertion of active electrodes. Spinal cord leads are then bent and maneuvered into the desired position as needed.

(4) After the active electrodes are properly positioned, they can be connected to an external generator (for testing), an implanted receiver, or a totally implanted (inductively powered) pulse generator. The receiver or generator may then be inserted and anchored (sutured) to the appropriate site.

(5) SCS systems often use 4 (quadripolar) or 8 (octopolar) electrodes with an external or internal power source.

(6) "Multichannel" programmable SCS systems have been developed. These minimize the need for a clinician to surgically revise an implanted electrode's position and enable the patient to noninvasively select the best electrode orientation for pain relief. Patients may program amplitude, pulse width, frequency, wave type, electrode array, and polarity on an external transmitter to achieve the optimal pain relief.

(7) Patients may use these stimulators an average of 14 hours per day.

3.3 Safety

3.3.1 Reports from Published Studies

General contraindications include use in the presence of: metallic implants, neoplasms, osteomyelitis; or on patients with demand-type cardiac pacemakers.[188]

Direct Current Stimulators—No complications or adverse reactions were reported in any DC studies of wound healing.

Pulsed Current Stimulators—Minor complications included 7 cases of uncomfortable tingling, 1 case of excessive bleeding at the ulcer site, and 1 case of skin irritation were reported in 2 studies.[189,190] No other complications or adverse reactions reported in any other PC studies for wound healing.[191,192,193]

Alternating Current Stimulators—No complications or adverse reactions were reported in any AC study of wound healing. None of the studies specified any contraindications for therapy.

Pulsed Electromagnetic Induction Stimulators—No complications or adverse reactions were reported in any PEMF or PEE study of wound healing.[194,195,196,197]

Spinal Cord Stimulators[198]—Percutaneous SCS complications include a 5% to 11% infection rate, skin erosion, pain at the incision site, and cerebrospinal fluid fistula. [See ECRI Technology Assessment on "Spinal Cord (Dorsal Column) Stimulation for Intractable Chronic Pain."] The safety of these devices has not been established for young children or pregnant women. Spinal cord stimulators are contraindicated for patients who do not experience pain relief during preimplant percutaneous testing.

3.3.2 Contraindications and Warnings from Product Literature

There are several contraindications and warnings common to all types of stimulators evaluated in this assessment. These include not applying stimulation over the carotid sinus or on patients with demand-type pacemakers, advanced cardiac disease, epilepsy, osteomyelitis, or neoplasms. All stimulators may interfere with cardiac or fetal monitoring. In addition, neuromuscular stimulation is contraindicated in patients prone to seizures and following surgical procedures when muscle contraction may disrupt the healing process. Stimulation should not be delivered over the eyes, transcerebrally, or over the pharyngeal area. Pregnancy is considered a contraindication for neuromuscular

stimulation. Although some TENS units have been marketed to manage labor pain, most vendors note that the effects of using TENS units during pregnancy have not been determined. Caution is advised when delivering TENS therapy to patients taking narcotic medications.

3.3.3 ECRI Health Device Alerts Database

We searched our Health Device Alerts database using the following key words:

- (*Wound* or *ulcer* or *sore*) and (*heal* or *improve* or *reduce* or *current* or *treat*) and (*stimulator* or *electromagnetic* or *electrothermal* or *diathermal* or *TENS* or *neuromuscular* or *ultrasonic* or *transcutaneous*).

We found no reported patient injuries associated with ES devices for wound healing (excluding spinal column stimulators) as of December 14, 1995.[i]

[i] Despite the apparent lack of reported patient injuries in the medical literature and within the FDA databases, ECRI, through its accident and forensic investigations, is directly aware of several incidents of skin burns and adverse outcomes during such ES use for wound healing. However, in these very few cases, injury was the result of the healthcare practioner's inappropriate technique when using the device, sometimes combined with inappropriate use despite the presence of written contraindications for that use.

3.4 Manufacturers and Costs

This section lists devices that are (or may be) used for ES to promote wound healing. The published literature may not fully reflect the range of devices used and/or their manufacturer(s).

ECRI contacted many manufacturers of EC devices. A comprehensive list of devices is presented in **Table 3.6**.[j] Data presented in the table was based on information provided by the respective manufacturers.

We obtained the following information and specifications provided by device manufacturers and distributors:

- Manufacturer
- Model
- Waveforms
- Voltage
- Amperage
- Delivery Mode
- Frequency Range
- Pulse Width
- Number of Channels
- Programmability
- Intended Applications
- Price
- Type of Unit

Neuromuscular Stimulators—Specific applications claimed include

- increasing local blood circulation,

[j] This table does not include vendors of discontinued stimulators.

- reducing edema,
- accelerating metabolic activity,
- Preventing and/or retarding muscle atrophy,
- Relaxing muscle spasms or inhibiting spasticity,
- Maintaining and increasing range of motion,
- Strengthening muscles, and
- Preventing postoperative venous thrombosis.

Infrequent applications include accelerating wound healing, enhancing tissue repair, and gait training.

Pain Management Devices—Specific applications include

- relief from acute pain,
- relief from chronic pain, and
- relief from postoperative pain.

Types of Devices—The classification of devices reported in the product literature is inconsistent. Some electrical stimulators are recognized by the names of their inventors or by names designated by vendors (examples: Galvanic, faradic, diadynamic, high voltage, low voltage, low frequency, medium frequency, etc.). TENS (transcutaneous electrical nerve stimulation) has been used to refer to both a specific type of stimulator used for pain management and all devices that stimulate peripheral nerves transcutaneously through surface electrodes. Because of this inconsistency, we classified them into 2 groups: (a) electrical stimulators (first part of Table 3.6), which included combination ultrasound unit/electrical stimulators, and (b) pulsed electromagnetic energy devices (second part of Table 3.6). (Vendor classification of device and recommendations for intended use are reported in the "type of unit" and "indications" columns, respectively.) Devices cited in referenced articles are presented in the third part of Table 3.6.

Universal Medical Device Nomenclature System$^{\hat{O}}$ (UMDNS$^{\hat{O}}$)—We used ECRI's UMDNS to identify stimulators listed in the tables. The Universal Medical Device Nomenclature System (UMDNS) is an ECRI-developed and maintained system of classifying medical devices for indexing, storing, and retrieving device-related information. The scope of UMDNS covers all medical devices,

including capital equipment, implants, clinical laboratory equipment and reagents, and selected hospital furniture, systems, and test equipment.

UMDNS terms and the corresponding 5-digit codes are widely incorporated into publications, databases, information systems, and software used by government agencies, healthcare systems and facilities, medical information systems, hazard alerting systems, and other parties and other functions worldwide. UMDNS has also been incorporated into the U.S. National Library of Medicine's (NLM) Unified Medical Language System (UMLS), a long-term NLM research and development effort designed to facilitate the retrieval and integration of information from multiple machine-readable biomedical information sources. Links are being established between UMDNS and other biomedical vocabularies and classifications such as NLM MeSH, SNOMED, CPT, and ICD, and *HPCS*.

13762 Stimulators

Definition: Devices that generate and apply a current (stimulus) used to identify or evoke a response from nerves, muscles, tissues, or discrete areas of the central nervous system. Stimulators consist of an energy source, a delivery system (usually electrodes, lead wires, or a probe), an amplitude controller and/or circuit interrupter to prevent excessive energies from damaging the tissues. Stimulators permit control of specific duration, intensity, frequency, and waveform of the applied stimulus. Stimulators may be external, hard-wired percutaneous, transcutaneously coupled, or totally implantable. Implantable devices typically include an enclosure to prevent the biological environment from damaging the circuit components and vice versa.

13775 Stimulators, Neuromuscular

Definition: External stimulators that ameliorate muscle dysfunction through electrically-elicited muscle contraction. Neuromuscular stimulators may deliver low-intensity direct current, low-frequency pulsed current, high-voltage pulsed current, or a pulsed electromagnetic field.

16255 Stimulators, Neuromuscular, Therapeutic

Definition: Neuromuscular stimulators that activate muscle through stimulation of the intact peripheral nerve. Applications include delaying or reducing disuse atrophy, muscle re-education, and increasing range of motion.

16250 Stimulators, Neuromuscular, Functional

Definition: Neuromuscular stimulators that stimulate paralyzed muscle. These devices may enhance the function of a patient's paralyzed or weak muscles, eliminating the need for orthoses. This type of stimulation may also aid the

return of a functional sill such as walking or grasping, but does not treat the underlying dysfunction.

13782 Stimulators, Electroanalgesic, Transcutaneous Electrical Nerve

Definition: Stimulators used to manage acute and chronic pain. These devices block the transmission of pain impulses by delivering a series of electrical impulses to large-diameter sensory fibers. Transcutaneous electrical stimulation (TENS) units may be single or dual channel, use various types of electrodes, may be monophasic or biphasic, and may deliver a variety of waveforms. Applications include the management of postsurgical, posttraumatic, and labor-induced pain.

17908 Ultrasound Units/Neuromuscular Stimulators, Physical Therapy

Definition: Single units that combine therapeutic ultrasound with neuromuscular stimulation capabilities in which either modality can be used alone or in combination with the other.

Abbreviations Used in Table 3.6—
LIDC: Low-intensity Direct Current
MENS: Microcurrent Electrical Neuromuscular Stimulation
NMES: Neuromuscular Electrical Stimulator
PC: Pulsed Current[k]
TENS: Transcutaneous Electrical Nerve Stimulator

[k] Devices labelled or described by manufacturers as high-voltage pulsed galvanic are categorized as pulsed current (PC) and, when available, subcategorized as pulsed direct current (PDC) or high-voltage pulsed current (HVPC).

3.5 Tables

Table 3.1. Examples of Preclinical Studies Evaluating the Effects of Electrical Stimulation on Wound Healing

Study	Investigators' Conclusions
Carey & Lepley[199] (1962)	Cellular migration around positive pole after DC stimulation: dense infiltration with leukocytes and lymphocytes; predominant cell present was polymorphonuclear leukocyte
Assimacopoulos[200] (1968)	Improved healing of rabbit skin defects by electrical stimulation
Fenn[201] (1969)	PEE energy resolved hematomas faster than controls in rabbits
Barranco et al.[202] (1974)	DC inhibits growth of *S. aureus* in vitro
Wilson & Jagadeesh[203] (1975)	PEMF stimulation induced nerve-fiber regeneration across scars in rats
Konikoff[204] (1976)	DC current promoted soft-tissue healing in rabbits
Cheng et al.[205] (1982)	DC increases ATP (adenosine triphosphate) concentrations in tissue and stimulates amino acid incorporation into the proteins of rat skin
Alvarez et al.[206] (1983)	Improved epithelialization of superficial skin wounds in pig by DC current; suggests that proliferative and/or migratory capacity of epithelial and connective tissue cells involved in repair and regeneration can be affected by an electrical field
Raji & Bowden[207] (1983)	PEMF stimulation accelerated recovery of damaged nerves and reduced epi-, peri-, and intraneural fibrosis in rats
Foulds & Barker[208] (1983)	Human skin acts as battery; Identified negative electrical potentials from the stratum corneum with respect to the dermis at all sites examined; avg potential overall all sites and subjects was -23 mV ±9 mV (SD)
Korenstein et al.[209] (1984)	Pulsed ES caused changes in intracellular level of cAMP (cyclic adenosine monophosphate) and enhanced DNA synthesis in rat embryos
Young[210] (1984)	PEMF stimulation reduced Ca^{+2} accumulation in spinal cords of injured cats
Murray et al.[211] (1985)	PEMF increased production of collagen in fibroblasts (possibly by altering cAMP metabolism)
Jayakumar et al.[212] (1986)	PEMF reduced cerebral edema in rats
Bourguignon & Bourguignon[213] (1987)	HVPC produced increased rate of protein and DNA synthesis and migration of human fibroblasts in tissue culture
Kjartansson et al.[214] (1988)	Improved survival of ischemic musculocutaneous flaps by TENS stimulation in rats
Yen-Patton et al.[215] (1988)	PEMF produced 20% to 40% improvement in growth rate of partially denuded endothelial cells in vitro
Dunn et al.[216] (1988)	DC produced fibroblast ingrowth and collagen fiber alignment in vitro
Politis et al.[217] (1989)	DC on full-thickness grafts in rat skin and found that orienting the anode above the graft yielded significantly more healing than the cathode above the graft or no current at all
Kincaid et al.[218] (1989)	HVPC produced inhibition of *S. aureus*, *E. coli*, and *Pseudomonas aeruginosa*

Table 3.1. Examples of Preclinical Studies Evaluating the Effects of Electrical Stimulation on Wound Healing (continued)

Study	Investigators' Conclusions
Reger et al.[219] (1991)	Improved pressure-ulcer healing by AC or DC therapy in pigs
Akai et al.[220] (1991)	DC applied to severed rabbit ligament produced higher tensile stiffness and earlier changes of collagen types in newly formed tissues
Szuminsky et al.[221] (1994)	HVPC produced antimicrobial effects in vitro against *E. coli*, *Klebsiella*, *Pseudomona aeruginosa*, and *S. aureus*

DC = direct current; HVPC = high-voltage pulsed current; PEE = pulsed electromagnetic energy; PEMF = pulsed electromagnetic field; TENS = transcutaneous electrical nerve stimulator

Table 3.2. Synopses of Direct Current (DC) Stimulation Therapies for Wound Healing

Study	Type of Direct Current Stimulation	Therapy Synopsis
Katelaris et al.[222] (1987)	LIDC	20 µA current with cathode over ulceration; otherwise similar to Wolcott et al. [Device manufacturer not specified]
Carley & Wainapel[223] (1985)	LIDC	2 hr sessions BID of 300 to 700 µA with cathode initially over ulceration (with wet gauze) and regimen otherwise similar to Wolcott et al.; current density 30 to 110 µA/cm^2 [Device manufacturer not specified]
Akers & Gabrielson[224] (1984)	(Unspecified) DC	Not specified
Gault & Gatens[225] (1976)	LIDC	Regimen similar to Wolcott et al., except polarity reversed only once Device Manufacturers: Tri-tonics Laboratory, Inc. (Euless, TX); Prototype of Vitron Unit by Ritter Sybron Corp. (Rochester, NY)
Wolcott et al.[226] (1969)	LIDC	2 hr sessions (2 hrs on, 4 hrs off) TID of 600 to 800 µA with cathode initially over ulceration (with wet gauze) and anode proximal; electrodes switched (polarity reversed) after 3 days (if not infected) or until infection cleared + 3 days (if infected); polarity reversed if healing does not improve ("growth plateau") and/or every 24 hours [Device manufacturer not specified]
Assimacopoulos[227] (1968)	LIDC	50 to 100 µA at 0.25 to 0.80 V with negative electrode (cathode) over ulceration site and positive electrode (anode) lateral to lesion [Device manufacturer not specified]

TID = 3 times a day

Table 3.3. Synopses of Pulsed Current (PC) Stimulation Therapies for Wound Healing

Study	Type of Pulsed Current Stimulation	Therapy Synopsis
Wood et al.[228] (1993)	PDC	300 µA followed by 600 µA from electrodes placed on opposite sides of wound with current pulsed at 0.8 Hz Device Manufacturer: MEMS CS 600 (Harbor Medical Inc., Minneapolis, MN)
Fitzgerald & Newsome[229] (1993)	HVPC	100 to 120 V @ 80 to 100 Hz (100 µs interpulse interval); 1-hr session/day (20 minutes at negative polarity, 40 minutes positive polarity) 5 days/wk Device Manufacturer: PGS 200 Pulsed Galvanic Stimulator (Universal Technology Systems, Jacksonville, FL)
Gogia et al.[230] (1992)	HVPC	250 V (pulse width 5 to 8 µs) @ 100 Hz for 20 minute daily sessions; negative polarity (in wet gauze) directly over lesion (first 4 sessions), then polarity reversed (last 16 sessions) Device Manufacturer: HVGS (Chattanooga Corp., Chattanooga, TN)
Gentzkow et al.[231] (1991)	PDC	35 mA (from 6 V battery) pulsed at 128 Hz for 30-minute sessions BID; negative polarity (in wet gauze) directly over lesion, then polarity reversed every 3 days after site debrided; reduced to 64 Hz when ulcer decreased to stage II lesion; delivered charge of 0.89 Coulombs/tx (1.78 C/day) Device Manufacturer: Dermapulse® (Staodyn, Inc., Longmont, CO)
Griffin et al.[232] (1991)	HVPC	200 V intensity @ 100 Hz for 1-hr daily session for 20 days; negative polarity (in wet gauze) directly over lesion for duration (no polarity change); produced total current of 500 µA Device Manufacturer: Intelect 500 HVPC (Chattanooga Corp., Chattanooga, TN)
Feedar et al.[233] (1991)	PDC	35 mA @ 128 Hz (rectangular pulses of 29.2 mA and 132 µs duration) for 30-minute sessions BID with 4 to 8 hrs between sessions; treatment for 7 days/week; negative electrode on lesion; polarity reversed every 30-minute sessions BID 3 days after wound debrided up to 15 weeks Device Manufacturer: Vara/Pulse® (Staodynamics, Inc., Longmont, CO)
Mulder[234] (1991)	PDC	30, 35, or 40 mA (from 6 V battery) @ 128 Hz for 30-minute sessions BID with 4 to 8 hrs between sessions; negative (or positive) polarity (in wet gauze) directly over lesion; pulse width of 140 µs and charge/pulse of 4.2, 4.9, and 5.6 µC Device Manufacturer: Dermapulse® (Staodynamics, Inc., Longmont, CO)
Unger[235] (1991) [Abstract]	HVPC	150 V (750 mA peak current) @ 50 Hz; negative polarity (wrapped in tin foil) directly over wound; after 6 days, polarity reversed with 100 V intensity (500 mA peak current) @ 80 Hz [Device not specified]
Unger et al.[236] (1991) [Abstract]	HVPC	Same as Unger [Device not specified]

Table 3.3. Synopses of Pulsed Current (PC) Stimulation Therapies for Wound Healing (continued)

Study	Type of Pulsed Current Stimulation	Therapy Synopsis
Weiss et al.[237] (1989)	PDC	35 mA @ 128 Hz for 30-minute sessions BID with 4 to 8 hrs between sessions; treatment for 7 days/week; positive polarity on surgically induced wound Device Manufacturer: Vara/Pulse® (Staodynamics, Inc., Longmont, CO)
Kloth & Feedar[238] (1988)	HVPC	100 V @ 105 Hz (from monophasic twin-pulsed generator with 100 µs intraphase interval); results in single-phase charge at 1.6 µC with total-pulse charge of 342 µC/s; once daily 45-minute sessions, 5 days/wk for 4 to 16 wks; positive electrode (anode) on lesion for 3 days, then polarity reversed (cathode on wound) if healing plateau reached Device Manufacturer: DynaWave® Model 12 (DynaWave Corp., Geneva, IL)
Feedar & Kloth[239] (1985) [Abstract]	HVPC	100 V @ 105 Hz (100 µs intraphase interval); daily 45-minute sessions, 5 days/wk; negative electrode, then polarity reversed after 3 days Device Manufacturer: DynaWave® Model 12 (DynaWave Corp., Geneva, IL) [240]
Ross & Segal[241] (1981)	HVPC	[Voltage not specified] Negative polarity on wound site, 4 Hz pulses for 15 minutes, then polarity reversed with 80 Hz pulses Device Manufacturer: Galvanator Model 700 (Avra Tronics Corp., Greenvale, NY)
Thurman & Christian[242] (1971)	"High-frequency" DC*	Not specified

* Nomenclature used by investigators of study

Table 3.4. Synopses of Alternating Current (AC) Stimulation Therapies for Wound Healing

Study	Type of Alternating Current Stimulation	Therapy Synopsis
Stefanovska et al.[243] (1993)	Biphasic AC	Biphasic AC current of 15 to 25 mA with charge-balanced current stimuli with 0.25 ms pulse duration @ 40 Hz; 2 hr daily sessions [Device not specified]
Lundeberg et al.[244] (1992)	Electrical nerve stimulation (ENS) unit	AC (alternating constant-current square-wave pulses) of 1 ms pulse width @ 80 Hz applied just outside ulcer surface area—at current sufficient to produce paresthesia—for 20-minute sessions BID; polarity changed after each session Device Manufacturer: Delft Instruments, The Netherlands and/or Henley International, Houston, TX
Karba et al.[245] (1991)	Biphasic AC	Biphasic AC current of 15 to 25 mA with charge-balanced current stimuli with 0.25 ms pulse duration @ 40 Hz; amplitude adjusted for each individual patient; 60-minute daily sessions [Device not specified]
Frantz[246] (1990)	TENS	Constant square-wave pulses of 30 mA @ 85 Hz (150 µs pulse width); 1 set of electrodes on hands, other set proximal (anode) or distal (cathode) to lesions; applied for 30-minute sessions TID Device Manufacturer: Medtronic Eclipse Plus Model 7723 TENS
Kjartansson & Lundeberg[247] (1990)	Electrical nerve stimulation (ENS) unit	Monopolar square wave pulses with duration of 0.2 ms @ 90 Hz Device Manufacturer: TENS unit (Delta, U.K.)
Kaada & Emru[248] (1988)	TENS	Pocket stimulator delivering pulse trains (to electrodes in gauze around lesion) @ 2 Hz, 25 to 50 mA stimulation intensity, delivering constant square-wave pulses at 100 Hz internal frequency and 0.1 to 0.2 ms duration Device Manufacturer: Viking Single (Medi-Stim A/s, Oslo, Norway)
Lundeberg et al.[249] (1988)	Electrical nerve stimulation (ENS) unit	Alternating square-wave pulses 0.4 ms duration @ 80 Hz; stimulus intensity set to 3 times threshold in which tingling sensation felt by patient; 2 hr sessions BID Device Manufacturer: ENS unit (Enraf-Nonius, Netherlands)
Alon et al.[250] (1986) [Abstract]	TENS	Continuous mode @ 80 Hz; positive electrode (in sterile gauze) over ulcer site [Device not specified]
Barron et al.[251] (1985)	Percutaneous low-energy non-galvanic stimulator [TENS]	Modified biphasic square wave: 600 µA, 50 V @ 0.5 Hz administered percutaneously across ulcer surface; 3 sessions TID for 3 wks Device Manufacturer: Micro-Electro Medical Stimulation

Table 3.4. Synopses of Alternating Current (AC) Stimulation Therapies for Wound Healing (continued)

Study	Type of Alternating Current Stimulation	Therapy Synopsis
Kaada[252] (1983)	TENS	Constant square wave pulses of 15 to 30 mA (intensity increased until local contraction of adjacent muscles without producing pain), each stimulus consisting of bursts of 5 pulses with 100 Hz internal frequency; 30- to 45-minute sessions TID; 1 set of electrodes on hands, other set proximal (anode) or distal (cathode) to lesions; all applied from pocket stimulator [Device not specified]
Westerhof & Bos[253] (1983)	TENS	120 Hz, 250 µs pulse width, 0.5 sec pulse train envelope, 0.5 pulse train interval; 30-minute sessions TID Device Manufacturer: Bio-Medical Research P_8 unit

BID = two times a day; TID = three times a day

Table 3.5. Synopses of Pulsed Electromagnetic Induction (PEMI) Stimulation Therapies for Wound Healing

Study	Type of Electromagnetic Stimulation	Therapy Synopsis
Salzberg et al.[254] (1995)	PEE	Pulsed, nonthermal, high-frequency, high peak power electromagnetic energy delivered at 27.12 MHz, pulse repetition rates of 80 to 600 pulses/sec, 65 µs pulse width, 293 to 975 W per pulse peak, 0.5 to 3.9% duty cycle; treatment head placed in contact with wound site and tuned to resonance in area of wound; 30-minute sessions BID Device Manufacturer: Diapulse® (Diapulse Corp. of America, Great Neck, NY)
Tung et al.[255] (1995)	PEE	Same device parameters as Salzberg et al.; applied in case reports Device Manufacturer: Diapulse® (Diapulse Corp. of America, Great Neck, NY)
Stiller et al.[256] (1992)	PEMF	Electromagnetic transducer (attached to signal generator 9 V battery) containing coils for magnetic focusing strapped over wound dressing with elasticized Velcro strap; induces low level, nonthermal electrical field of approx. 0.06 mV/cm; has 3-part pulse of 3.5 ms total width, 25% duty cycle, 22 Gauss; applied (at home) 3 hrs/day on top of dressing for 8 to 12 wks (or healing) Device Manufacturer: PELUT* System (Geomed, Inc.)
Todd et al.[257] (1991)	PEMF	Active coils in Helmholtz arrangement; ulcer placed between coils connected to magnetic field generator; field strength = 60, intensity = 5 Hz; 15-minute sessions performed twice/week for 5 wks after initial 2 wks on standard ulcer therapy [Device not specified]
Itoh et al.[258] (1991)	PEMF	Same device parameters as Salzberg et al.; applied directly through dressings at 600 pulses/sec and 6 peak power; 30-minute sessions BID (8 hour separation between sessions) until healed Device Manufacturer: Diapulse® (Diapulse Corp. of America, Great Neck, NY)
Ieran et al.[259] (1990)	PEMF	Stimulators supplied electromagnetic coils with a single pulse of electrical current generating magnetic field of 2.8 mT @ 75 Hz and 1.3 ms pulse width; patients instructed to use stimulators at home 3-4 hrs/day for 90 days or until healed Device Manufacturer: Dermagen, Igea (Carpi, Italy)
Jeran et al.[260] (1987)	PEMF	Stimulation parameters in electromagnetic coils: maximum magnetic field = 2.7 mT, 75 Hz, 1.3 ms pulse width; patients instructed to use stimulators at home 4 hrs/day for 90 days or until healed Device Manufacturer: Dermagen, Igea (Carpi, Italy)

Table 3.5. Synopses of Pulsed Electromagnetic Induction (PEMI) Stimulation Therapies for Wound Healing (continued)

Study	Type of Electromagnetic Stimulation	Therapy Synopsis
Goldin et al.[261] (1981)	Pulsed "radio energy"	Peak output of 975 W @ 400 pulses/sec, 65 µs average pulse duration, mean energy output with 3 cm depth penetration; 30-minute application to graft donor site at time of premedication and 6 hours postoperatively Device Manufacturer: Diapulse® (Diapulse Corp. of America, Great Neck, NY)

* PELUT = pulsed electromagnetic limb ulcer therapy
BID = 2 times a day

Table 3.6. Manufacturers, Models, and Device Specifications of Electrical Stimulators

(Data in this table was based on information from respective manufacturers.)

Manufacturer	Model	Waveforms	Voltage, Volts	Amperage	Delivery Modes	Frequency Range, Hz.	Pulse Width, microseconds	No. of Channels	Programmable	Intended Application	Price	Type of Unit
Electrical Stimulators												
3M Health Care	Dual Channel TENS 6880[262]	Biphasic		60 mA peak (1000 Ohm load)	Pulsed, burst	2-140	25-250	2	No	Pain management		TENS
3M Health Care	Dual Channel TENS 6820[263]	Biphasic		80 mA peak (500 Ohm load)	Pulsed, burst	2-170	24-250	2	No	Pain management		TENS
Advance	Araddin[264]			0-10 mA (1000 Ohm load)	Pulsed	40	100	1	No			TENS
Avra Tronics	Galvanator 770[265]	Monophasic	0-500		Pulsed	4-80		1	No	Neuromuscular stimulation		PC, NMES
American Imex	A-TENS[266]	Biphasic	0-100	80 mA peak (500 Ohm load)	Pulsed, burst, pulse width modulation	2-180	40-250	2	No	Pain management		TENS
American Imex	Easy TENS[267]	Biphasic	0-100	80 mA peak (500 Ohm load)	Pulsed, burst	2,110	100	2	No	Pain management	$520	TENS
American Imex	MES iF[268]	Biphasic, interferential	60 peak	10-600 microamps	Pulsed, interferential beat wave	0-1000		2	No	Pain management		Microcurrent, medium freq.
American Imex	Premier TENS[269]	Biphasic	0-68	80 mA peak (500 Ohm load)	Pulsed, burst, pulse width modulation	2-160	40-250	2	No	Pain management	$595	TENS
American Imex	Ultima Xs[270]	Biphasic	60 peak	10-600 microamps	Pulsed	0.5 and 100		2	No	Pain management	$795	Microcurrent
Amrex	Synchrosonic U/HVG50[271]	Monophasic, biphasic	0-500	0-10 mA	Constant, pulsed	1-160	30	2	No	Pain management, neuromuscular stimulation	$3295	PC, LIDC, NMES, ultrasound

Table 3.6. Manufacturers, Models, and Device Specifications of Electrical Stimulators (continued)

Manufacturer	Model	Waveforms	Voltage, Volts	Amperage	Delivery Modes	Frequency Range, Hz.	Pulse Width, microseconds	No. of Channels	Programmable	Intended Application	Price	Type of Unit
Amrex	Synchrosonic US/50[272]	Low volt, biphasic, asymmetrical	100 peak (1K Ohm load); 28 peak (100 Ohm load)		Pulsed	1-80	200 (at 50% V max)	1	No	Pain management	$1850	Low voltage, ultrasound
Amrex	Synchrosonic US/54[273]	Low volt, biphasic, asymmetrical	110 peak (1K Ohm load); 28 peak (100 Ohm load)		Pulsed	1-80	200 (at 50% V max)	2	No	Pain management	$2100	Low voltage, ultrasound
Amrex	Synchrosonic US/752[274]	Biphasic	0-500		Pulsed	1-160	10, 20, 30	2	No	Pain management, neuromuscular stimulation	$2695	PC, ultrasound
Biomedical Life Systems	BioMed Plus[275]	Biphasic	120	0-98 mA peak	Pulsed, burst, pulse width modulation	2-200	50-250	2	No	Pain management		TENS
Biomedical Life Systems	EMS 2000[276]	Biphasic	120 max	0-98 mA	Pulsed, interrupted	2-80	300	2	No	Neuromuscular stimulation		NMES
Biomedical Life Systems	Gentle Touch[277]	Biphasic		0-80 mA	Pulsed, burst	14, 120	150	2		Pain management		TENS
Biomedical Life Systems	MFIII	Biphasic		0-50 mA	Pulsed	2-200, 8000-12000	20-250, 5-40	2	No	Pain management		TENS
Biomedical Life Systems	Systems 2000[278]	Biphasic	120	0-80 mA peak	Pulsed, burst, pulse rate/width modulation	2-120	50-250	2	No	Pain management		TENS
Biomedical Life Systems	Systems Plus[279]	Biphasic	120 peak	0-80 mA peak	Pulsed, burst, pulse rate/width modulation	2-120	50-250	2	No	Pain management		TENS
Biorem	Compact 100[280]	Monophasic, biphasic, interferential		0-100 mA	Continuous, pulsed, interferential beat wave, modulated Kotz current, interrupted	4-400, 4000-4250 (interfer)	50-200	2	Yes	Neuromuscular Stimulation		TENS, Kotz, medium frequency, PC, NMES

Table 3.6. Manufacturers, Models, and Device Specifications of Electrical Stimulators (continued)

Manufacturer	Model	Waveforms	Voltage, Volts	Amperage	Delivery Modes	Frequency Range, Hz.	Pulse Width, microseconds	No. of Channels	Programmable	Intended Application	Price	Type of Unit
Biorem	Ergon[281]	Biphasic	0-160 (1000 Ohm load)		Modulated Kotz current, interrupted	2500		8	Yes	Neuromuscular stimulation		Kotz, medium frequency
Biorem	Expert[282]	Monophasic, biphasic, interferential		0-100 mA	Continuous, pulsed, interferential beat wave, modulated Kotz current, interrupted	4-400, 4000-4250 (interfer)	50-200	2	Yes	Neuromuscular stimulation		TENS, Kotz, medium frequency, PC, NMES
Biorem	Expert Mini[283]	Monophasic, biphasic, interferential		0-100 mA	Continuous, pulsed, interferential beat wave, modulated Kotz current, interrupted	4-400, 4000-4250 (interfer)	50-200	2	Yes	Neuromuscular stimulation		TENS, Kotz, medium frequency, PC, NMES
Biorem	Expert Plus[284]	Monophasic, biphasic, interferential		0-80 mA	Continuous, pulsed, interferential beat wave, modulated Kotz current, interrupted	4-400, 4000-4250 (interfer)	50-200	2	Yes	Neuromuscular stimulation		TENS, Kotz, medium frequency, PC, NMES
Bloomex Intl	BX-400C[285]	Biphasic	80 peak (1000 Ohm load)		Pulsed, interrupted	90	250	4	No	Pain management, neuromuscular stimulation		NMES, low voltage
Bloomex Intl	BX-600C[286]	Monophasic, biphasic	55 peak (1000 Ohm load)		Pulsed, interrupted	4-190	30-250	4	No	Pain management, neuromuscular stimulation		NMES, low voltage
Bloomex Intl	BX-1000[287]	Monophasic, biphasic	70 peak (1000 Ohm load)		Pulsed, interrupted	4-120	20-340	10	Yes	Neuromuscular stimulation		NMES, LIDC
Bloomex Intl	BX-200SC[288]	Biphasic	80 peak (1000 Ohm load)		Pulsed, interrupted	1-180	50-300	2	No	Pain management, neuromuscular stimulation		NMES
Brudermueller	DoloTENS 1[289]	Biphasic		0-60 mA	Pulsed	2-150	50-250	2	No	Pain management	DM 325	TENS
Brudermueller	DoloTENS 2[290]	Biphasic		0-60 mA	Pulsed, burst	2-150	50-250	2	No	Pain management	DM 545	TENS

Table 3.6. Manufacturers, Models, and Device Specifications of Electrical Stimulators (continued)

Manufacturer	Model	Waveforms	Voltage, Volts	Amperage	Delivery Modes	Frequency Range, Hz.	Pulse Width, microseconds	No. of Channels	Programmable	Intended Application	Price	Type of Unit
Brudermueller	DoloTENS EMS[291]	Biphasic		0-60 mA	Pulsed, burst	2-150	50-250	2	No	Pain management	DM 595	TENS
Brudermueller	Medimoll 1000[292]	Biphasic		0-60 mA	Pulsed	2-100	50-250	1	No	Pain management	DM 395	TENS
Brudermueller	Medimoll 2000[293]	Biphasic		0-60 mA	Pulsed, burst	2-100	50-250	2	No	Pain management	DM 595	TENS
Carin	Interferential 94[294]	Biphasic, interferential			Pulsed, interrupted, interferential beat wave	1,000-10,000		2	Yes	Pain management, neuromuscular stimulation		NMES, medium frequency
Carin	Megasonic 90[295]	Monophasic, biphasic		75 mA peak (3000 Ohm load)	Pulsed, burst, interrupted			1	Yes	Pain management, neuromuscular stimulation		PC, NMES
Carin	Megasonic 212P[296]	Biphasic		60 mA	Pulsed	10-100	20-220	2	No	Pain management		TENS, ultrasound
Carin	Megasonic 313[297]	Monophasic, biphasic		90 mA (3000 Ohm load)	Pulsed, burst	1-200, 1000-5000	20-500	6	Yes	Pain management, neuromuscular stimulation		NMES
Cefar	Birth[298]	Biphasic		0-60 mA	Pulsed, burst	1.5, 50-120	180	2	No	Relief of labor pain		TENS
Cefar	Dual[299]	Biphasic		0-60 mA	Pulsed, burst	1.7, 10-100	180	2	No	Pain management		TENS
Befar	Dumo[300]	Biphasic		0-60 mA	Pulsed, burst, pulse width modulation	1.5, 50-120	50-170	2	No	Pain management		TENS
Cefar	Easy[301]	Biphasic		0-60 mA	Pulsed, burst	1.5 and 80	180	1	No	Pain management		TENS
Cefar	Mini[302]	Biphasic		0-60 mA	Pulsed, burst	1.5, 10-100	180	1	No	Pain management		TENS
Cefar	Must[303]	Biphasic		0-60 mA	Pulsed, interrupted	20-120	200	2	No	Neuromuscular stimulation		NMES, TENS
Cefar	Step[304]	Biphasic		0-60 mA	Triggered, pulsed	40-110	180	1	No	Assistance in walking		Peroneal nerve stimulator

Table 3.6. Manufacturers, Models, and Device Specifications of Electrical Stimulators (continued)

Manufacturer	Model	Waveforms	Voltage, Volts	Amperage	Delivery Modes	Frequency Range, Hz.	Pulse Width, microseconds	No. of Channels	Programmable	Intended Application	Price	Type of Unit
T.H. Charters	Electro BLOC[305]	Monophasic			Burst, modulated			2	No	Pain management	$895	PC
T.H. Charters	Exer-Stim[306]	Biphasic	90 peak	60 mA peak (1000 Ohm load)	Pulsed, interrupted	50	350	1	No	Neuromuscular stimulation, pain management		TENS, NMES
T.H. Charters	Exer-Stim 2[307]	Biphasic	150 peak	75 mA peak (1000 Ohm load)	Pulsed, interrupted	45	300	2	No	Neuromuscular stimulation, Pain management		NMES
T.H. Charters	Mini-1[308]	Biphasic		0-55 mA (1000 Ohm load)	Pulsed, interrupted, pulse rate modulation	70, 50-100	240	1	No	Pain management	$395	TENS
T.H. Charters	Myopulse[309]	Biphasic	120 peak	85 mA peak (1000 Ohm load)	Pulsed	0.8	2000	1	No	Neuromuscular stimulation		NMES
T.H. Charters	Biphasico-Pulser 2+[310]	Biphasic		10-60 mA (1000 Ohm load)	Pulsed, interrupted, pulse rate modulation	0.7-100	30-250	2	No	Pain management	$495	TENS
Chattanooga Group	Forte ES450[311]	Monophasic, biphasic, interferential, Russian		10-1000 microamps peak, 0-200 mA peak	Pulsed, burst, interferential beat wave, interrupted	0.1-1000, 2000-5000 (Interfer, Russian)	20-300	4	Yes	Neuromuscular stimulation		PC, microcurrent, medium frequency
Chattanooga Group	Intelect 150[312]	Monophasic	0-500	0-2500 mA peak	Pulsed, interrupted	1-128		1	No	Neuromuscular stimulation		NMES, PC (HVPC)
Chattanooga Group	Intelect 500S[313]	Monophasic	0-500	0-2500 mA peak	Pulsed, interrupted	1-120		1	No	Neuromuscular stimulation		NMES, PC
Citronix	MS-77[314]	Biphasic		0-90 mA (1000 Ohm load)	Pulsed	3-130	60-140	2	No	Pain management	$350	TENS
Comfort Technologies	Comfort-SD[315]	Biphasic	0-80 (500 Ohm load)		Pulsed, burst, pulse rate/width modulation	2-150	50-250	2	No	Pain management		TENS

Table 3.6. Manufacturers, Models, and Device Specifications of Electrical Stimulators (continued)

Manufacturer	Model	Waveforms	Voltage, Volts	Amperage	Delivery Modes	Frequency Range, Hz.	Pulse Width, microseconds	No. of Channels	Programmable	Intended Application	Price	Type of Unit
Comfort Technologies	Comfort-Stim[316]	Biphasic	0-80 (500 Ohm load)		Pulsed, burst, modulated	2-150	50-250	2	No	Pain management		TENS
Comfort Technologies	Comtech[317]	Biphasic	0-80 (500 Ohm load)		Pulsed	2-150	50-250	2	No	Pain management		TENS
Comfort Technologies	Micro II[318]	Biphasic			Pulsed	0.5, 8, 80		2	No	Pain management		TENS, microcurrent
Comfort Technologies	Myomed-EMS[319]	Biphasic			Pulsed, interrupted	65	200	4	No	Neuromuscular stimulation		NMES
Comfort Technologies	Myotech[320]	Biphasic		0-68 mA	Pulsed, interrupted	5, 30, 100	250	2	No	Neuromuscular stimulation		NMES
Danmeter	Automove AM 706[321]	Biphasic		0-60 mA	Pulsed, Triggered	20-100	200	1	No	EMG controlled electrical stimulation		NMES
Danmeter	Elpha 2000[322]	Monophasic		0-60 mA	Pulsed, burst, interrupted, pulse width modulation	10-150	50-250	2	No	Pain management, neuromuscular stimulation		NMES, TENS
Danmeter	TS 6000[323]	Monophasic, biphasic	150 peak	0-60 mA (2500 Ohm load)	Pulsed, burst, interrupted	10-100	50-250	6	No	Pain management, neuromuscular stimulation, wound healing		TENS, HVPG, NMES
Diter	DI-83[324]	Monophasic	0-500 (3,000 Ohm load)	1.2 mA (at 500 V and 80 Hz)	Pulsed	5-100		1	No	Pain management, neuromuscular stimulation		TENS, HVPG
Diter	DTU-30 Sport[325]	Monophasic, biphasic		50 mA (1000 Ohm load)	Pulsed, interrupted	1-100	100-1000	2	No	Pain management		TENS, ultrasound
Diter	Interference DIT-83 S[326]	Interferential		50 mA (1000 Ohm load)	Interferential beat wave	4000-4200		2	Yes	Pain management		TENS, medium frequency

Table 3.6. Manufacturers, Models, and Device Specifications of Electrical Stimulators (continued)

Manufacturer	Model	Waveforms	Voltage, Volts	Amperage	Delivery Modes	Frequency Range, Hz.	Pulse Width, microseconds	No. of Channels	Programmable	Intended Application	Price	Type of Unit
Diter	Interference DIT-940[327]	Interferential		50 mA (1000 Ohm load)	Interferential beat wave	4000-4200		2	Yes	Pain management		TENS, medium frequency
Dynatronics	Dynatron 400[328]	Biphasic, interferential			Pulsed, interferential beat wave	0-10, 80-150		4	Yes	Pain management, treatment of edema, increasing circulation		Interferential
Dynatronics	Dynatron 500plus[329]	Monophasic, biphasic, interferential, Russian			Pulsed, interrupted, interferential beat wave	0-10, 80-150		4	Yes	Pain management, neuromuscular stimulation		NMES, MENS, microcurrent
Dynatronics	Dynatron 800[330]	Monophasic, biphasic, interferential, Russian			Pulsed, interrupted, interferential beat wave	0-10, 80-150		4	Yes	Pain management, neuromuscular stimulation		TENS, medium frequency, ultrasound
Dynatronics	Dynatron 850[331]	Monophasic, biphasic, interferential, Russian			Pulsed, interrupted, interferential beat wave				No	Pain management		TENS, microcurrent, medium frequency, ultrasound
Dynawave	Dynalator[332]	Monophasic	0-500		Pulsed, pulse rate modulation	10-100		1	No	Pain management, facilitating optimal healing		TENS, HVPG, ultrasound
Dynawave	Dynawave Model 12[333]	Monophasic	0-500	Microamp	Pulsed, interrupted	1-105	100	2	No	Neuromuscular stimulation		PC (HVPC), microcurrent, NMES
NH Eastwood & Son	Mini-Tens 2600[334]	Biphasic		0-50 mA (1000 Ohm load)	Pulsed	15-150	100	1	No	Pain management		TENS

Table 3.6. Manufacturers, Models, and Device Specifications of Electrical Stimulators (continued)

Manufacturer	Model	Waveforms	Voltage, Volts	Amperage	Delivery Modes	Frequency Range, Hz.	Pulse Width, microseconds	No. of Channels	Programmable	Intended Application	Price	Type of Unit
NH Eastwood & Son	Mini-Tens 2800[335]	Biphasic		0-50 mA (1000 Ohm load)	Pulsed, burst	15-150	50, 100	1	No	Pain management		TENS
NH Eastwood & Son	Mini-Tens 4600[336]	Biphasic		0-50 mA (1000 Ohm load)	Pulsed	15-150	100	2	No	Pain management		TENS
NH Eastwood & Son	Mini-Tens 4800[337]	Biphasic		0-50 mA (1000 Ohm load)	Pulsed, burst	15-150	50, 100	2	No	Pain management		TENS
NH Eastwood & Son	Mini-Tens 4900[338]	Biphasic		0-50 mA (1000 Ohm load)	Pulsed, burst, pulse width modulation	15-150	100, 50-100	2	No	Pain management		TENS
Electro Therapeutics Devices	Accu-O-Matic VM2[339]	Monophasic, biphasic (“Tsunami”)	55 peak	20-600 microamps	Pulsed	0.8-320		1	No	Pain management, tissue repair		TENS, microcurrent
Electro Therapeutics Devices	Myostim EX[340]	Biphasic		0-140 mA	Pulsed	1-200	100-200	2	No	Pain management	$105	TENS
Electro Therapeutics Devices	TENSaid III[341]	Biphasic		0-90 mA	Pulsed, burst, modulated	1-200	100-200	2	No	Pain management	$215	TENS
Electromedical Products	Alpha-Stim 100[342]	Biphasic		0-600 microamps	Pulsed, interrupted	0.5, 1.5, 100	100,000-500,000	2	No	Pain management		TENS
Electro-Med Health Industries	Model 300[343]	Monophasic	0-330		Pulsed, interrupted	1-100	100	1	No	Neuromuscular stimulation		PC, NMES
Electro-Med Health Industries	EGS 100-2S[344]	Monophasic	0-500		Pulsed	1-120	65-75	1	No	Neuromuscular stimulation		PC, NMES
Electro-Med Health Industries	EGS 100SL[345]	Monophasic	0-500		Pulsed, interrupted	1-120	120	1	No	Neuromuscular stimulation		Microcurrent, PC
Electro-Med Health Industries	VersaStim 380[346]	Biphasic	240 peak	0-200 mA (1000 Ohm load)	Pulsed, burst	1000-4500		1	Yes	Neuromuscular stimulation		NMES, medium frequency

Table 3.6. Manufacturers, Models, and Device Specifications of Electrical Stimulators (continued)

Manufacturer	Model	Waveforms	Voltage, Volts	Amperage	Delivery Modes	Frequency Range, Hz.	Pulse Width, microseconds	No. of Channels	Programmable	Intended Application	Price	Type of Unit
Electro-Medical Supplies	EMS 950[347]	interferential		130 mA peak (500 Ohm load)	Interferential beat wave	2000, 4000		1	No	Neuromuscular stimulation		Medium frequency
Electro-Medical Supplies	Medi-Link[348]	Monophasic, biphasic, interferential, Russian	0-125	0-140 mA peak	Pulsed, burst, interrupted, interferential beat wave	1-250, 2000-4000		1	No	Pain management		Medium frequency, ultrasound
Elmed	HVG 500[349]	Monophasic	0-500		Pulsed, interrupted	5-200	45	1	No	Pain management, neuromuscular stimulation		TENS, PC, NMES
Empi	ComfortPulse[350]	Biphasic		0-60 mA (100-1000 Ohm load)	Pulsed, burst	1-125, 5000	30-250	2	No	Pain management		TENS, medium Frequency
Empi	Dynex IV[351]	Biphasic		0-60 mA (0-1500 Ohm load)	Pulsed, burst, modulated	2-110	40-250	2	No	Pain management		TENS
Empi	Eclipse+[352]	Biphasic		0-60 mA (200-1200 Ohm load)	Pulsed, burst, pulse rate/width/amplitude modulation	2-125	30-250	2	No	Pain management	$665	TENS
Empi	Epix XL[353]	Biphasic		0-60 mA	Pulsed, burst	2-150	0-400	2	No	Pain management, increasing circulation		TENS, PC
Empi	Focus[354]	Biphasic		0-100 mA (1000 Ohm load)	Pulsed, interrupted	25, 35, 50	300 max	1	No	Neuromuscular stimulation		NMES
Empi	Respond Select[355]	Biphasic		0-100 mA (1000 Ohm load)	Pulsed, interrupted	1-80	300	2	Yes	Neuromuscular stimulation		NMES

Table 3.6. Manufacturers, Models, and Device Specifications of Electrical Stimulators (continued)

Manufacturer	Model	Waveforms	Voltage, Volts	Amperage	Delivery Modes	Frequency Range, Hz.	Pulse Width, microseconds	No. of Channels	Programmable	Intended Application	Price	Type of Unit
Excel	Ultra III[356]	Monophasic, biphasic, interferential, Russian			Pulsed, interferential beat wave	0.1-100, 2500-5000	40-160	2	Yes	Pain management		TENS, microcurrent, medium frequency, ultrasound
Futuremed	Mega-TENS[357]	Biphasic		0-80 mA	Pulsed, burst, modulated	2-150	5-25	2	No	Pain management		TENS
General Physiotherapy	Porta-Puls II[358]	Biphasic		0-80 mA	Pulsed, interrupted	5, 30, 100		2	No	Neuromuscular stimulation		NMES
Globalcare/Bay Medical	Elite[359]	Biphasic		0-70 mA	Pulsed, modulated		40-260	2	No	Pain management		TENS
Globalcare/Bay Medical	Gold[360]	Biphasic		0-70 mA	Pulsed, modulated		40-260	2	No	Pain management		TENS, PC
Globalcare/Bay Medical	Micro II Stimulation System[361]	Biphasic		60-6000 microamps	Pulsed			2	No	Pain management		TENS
Globalcare/Bay Medical	MicroTENS[362]	Biphasic		60-6000 microamps	Pulsed			2	No	Pain management		TENS
Globalcare/Bay Medical	Sigma[363]	Biphasic		0-80 mA	Pulsed		40-260	2	No	Pain management		TENS
Globalcare/Bay Medical	Supreme[364]	Biphasic		0-70 mA	Pulsed, modulated		40-260	2	No	Pain management		TENS
Globalcare/Bay Medical	T x 3[365]	Biphasic		0-80 mA	Pulsed, modulated		40-260	2	No	Pain management		TENS
Henley	EMS 8100[366]	Biphasic		0-80 mA	Pulsed, interrupted	20-100	60-800	2	No	Pain management	$829	TENS
Henley	Isowave 3300[367]	Biphasic			Pulsed	1-160	40-200	2	No	Pain management	$695	TENS
Henley	Omega T100[368]	Biphasic		0-70 mA (500 Ohm load)	Pulsed	2-120	40-200	2	No	Pain management	$495	TENS
Henley	Omega T200[369]	Biphasic		0-70 mA (500 Ohm load)	Pulsed, burst, pulse rate/width modulation	2-120	40-200	2	No	Pain management	$595	TENS

Table 3.6. Manufacturers, Models, and Device Specifications of Electrical Stimulators (continued)

Manufacturer	Model	Waveforms	Voltage, Volts	Amperage	Delivery Modes	Frequency Range, Hz.	Pulse Width, microseconds	No. of Channels	Programmable	Intended Application	Price	Type of Unit
Henley	Orion[370]	Biphasic		0-150 mA (1200-1500 Ohm load)	Pulsed, burst, modulated	2-100	20	2	No	Pain management	$595	TENS
Henley	TTS-2500[371]	Biphasic		0-60 (1000 Ohm load)	Pulsed, pulse rate modulation	2-110	20-150	2	No	Pain management	$589	TENS
Henley	TTS-2700[372]	Biphasic		0-60 (1000 Ohm load)	Pulsed, pulse rate/width modulation	3-85	40-200	2	No	Pain management	$649	TENS
Henley	Teammate Tri-Stim[373]	Monophasic, biphasic	0-330 (Monophasic)	1-100 mA (Biphasic)	Pulsed, interrupted	1-100	50-300	2	Yes	Neuromuscular stimulation		NMES
ITO	TENS 120Z[374,375]	Biphasic	40 peak (500 Ohm load)	0-80 mA (500 Ohm load)	Pulsed, burst, interrupted	2-200	50-200	2	No	Pain management, increasing circulation		TENS
ITO	TENS 240Z[376,377]	Monophasic, biphasic		0-90 mA (500 Ohm load)	Pulsed, burst	1-125	70-350	2	No	Pain management		TENS
JACE Systems	PGS-900[378]	Monophasic	0-330		Pulsed, interrupted	1-100		1	No	Neuromuscular stimulation		NMES
Lindquist	Model 370[379]	Monophasic, biphasic	500 (Biphasic)	30 mA (Monophasic)	Pulsed, continuous			1	No	Neuromuscular stimulation, denervated muscle stimulation		NMES
Lindquist	Chronowave[380]	Monophasic, biphasic		0-30 mA (Monophasic), 0-100 mA (Biphasic)	Pulsed, continuous, interrupted	1-120		1	No	Neuromuscular stimulation, denervated muscle stimulation		NMES
Lindquist	miniSound 600[381]					1-100			No	Pain management		NMES, ultrasound
Mason	T.E.N.S. Unit[382]	Biphasic		0-80 mA	Pulsed, burst, modulated	1-120	50-260	2	No	Pain management		TENS

Table 3.6. Manufacturers, Models, and Device Specifications of Electrical Stimulators (continued)

Manufacturer	Model	Waveforms	Voltage, Volts	Amperage	Delivery Modes	Frequency Range, Hz.	Pulse Width, microseconds	No. of Channels	Programmable	Intended Application	Price	Type of Unit
Medical Devices	FasTENS[383]	Biphasic		0-80 mA (500 Ohm load)	Pulsed	60	0-600	1	No	Pain management	$125	TENS
Medical Devices	FasTENS 30[384]	Biphasic	12	0-70 mA (500 Ohm load)	Burst	60	0-600	1	No	Pain management	$125	TENS
Medical Devices	GV II[385]	Monophasic	0-350	0-700 mA	Pulsed, interrupted	1-100	5	1	No	Neuromuscular stimulation		PC
Medical Devices	IF II[386]	Biphasic, interferential		0-50 mA	Pulsed, interferential beat wave	4000		1	No	Pain management		Medium frequency
Medical Devices	Matrix I[387]	Biphasic	0-30	0-60 mA	Pulsed, burst, pulse rate/width modulation	2-160	0-400	2	No	Pain management		TENS
Medical Devices	MC II[388]	Monophasic, biphasic, interferential		0-800 microamps, 0-60 mA	Pulsed, interferential beat wave	0.1-1000, 2500	200	2	No	Pain management		TENS, Medium frequency
Medical Devices	MediMOD[389]	Biphasic		0-70 mA	Pulsed, burst, pulse rate/width modulation	2-120	40-200	2	No	Pain management		TENS
Medical Devices	Mentor 159[390]	Biphasic		0-60 mA	Pulsed, burst	2.5-110	60-200	2	No	Pain management	$500	TENS
Medical Devices	Mentor 259[391]	Biphasic		0-60 mA	Pulsed, burst, pulse rate/width modulation	2.5-145	36-200	2	No	Pain management	$590	TENS
Medical Devices	Ultrapac II SX[392]	Biphasic		0-70 mA (500 Ohm load)	Pulsed, burst, pulse rate/width modulation	2-120	40-250	2	No	Pain management	$575	TENS
Medical Devices	Ultrapac II SX Plus[393]	Biphasic		0-100 mA	Pulsed, burst, pulse rate/width modulation	2-120	40-250	2	No	Pain management		TENS
Mettler Electronics	Sonicator Plus[394]	Monophasic	0-500	0-2500 mA	Pulsed	0-120		2	Yes	Pain management		PC, ultrasound
Mettler Electronics	SysStim 206[395]	Monophasic, biphasic	0-102	30 mA peak (Continuous), 100 mA peak (Pulsed)	Pulsed, continuous	1-83	500-1500	1	No	Neuromuscular stimulation		NMES

Table 3.6. Manufacturers, Models, and Device Specifications of Electrical Stimulators (continued)

Manufacturer	Model	Waveforms	Voltage, Volts	Amperage	Delivery Modes	Frequency Range, Hz.	Pulse Width, microseconds	No. of Channels	Programmable	Intended Application	Price	Type of Unit
Mettler Electronics	SysStim 206A[396]	Monophasic, biphasic	0-102	0-30 mA (continuous), 0-200 mA (Pulsed) (500 Ohm load)	Pulsed, continuous, interrupted	1-83	500-1500	2	No	Neuromuscular stimulation		NMES
Mettler Electronics	SysStim 207A[397]	Monophasic, biphasic, Russian	0-102	0-30 mA (continuous), 0-200 mA (Pulsed) (500 Ohm load)	Pulsed, continuous, interrupted	1-120, 2500	500-1500	2	No	Neuromuscular stimulation		NMES, medium frequency
Mettler Electronics	SysStim 220[398]	Biphasic, interferential		0-60 mA	Pulsed, interferential beat wave, interrupted	4000		2	No	Neuromuscular stimulation, pain management		NMES, medium frequency
OMS Medical Supplies	TX-3 TENS[399]	Biphasic	0-40 (500 Ohm load)	0-80 mA (500 Ohm load)	Pulsed, burst	2-120	50-250	2	No	Pain management		TENS
OMS Medical Supplies	Dr Pulse[400]	Biphasic	0-60 (500 Ohm load)	0-120 mA (500 Ohm load)	Pulsed	1.5-27	250	1	No	Pain management		TENS
OMS Medical Supplies	HP-707[401]	Monophasic	0-30 (500 Ohm load)	0-60 mA (500 Ohm load)	Pulsed	2	80	1	No	Trigger point treatment		TENS
OMS Medical Supplies	Mstim-2000[402]	Biphasic	0-30 (500 Ohm load)	0-60 mA (500 Ohm load)	Pulsed, interrupted	2-100	230	2	No	Neuromuscular stimulation		NMES
Preston	Health Pulse[403]	Biphasic	0-55	0-130 mA peak	Pulsed	0-100		1 or 2	No	Pain management	$130, $160	TENS
Preston	Portamax[404]	Monophasic	0-500		Pulsed, interrupted	1-140		1	No	Neuromuscular stimulation	$1395	PC
Preston	Ultramax III[405]	Monophasic	0-500	1.0 mA (at 500 V, 140 Hz)	Pulsed, interrupted	1-140		1	No	Neuromuscular stimulation	$2195	PC

Table 3.6. Manufacturers, Models, and Device Specifications of Electrical Stimulators (continued)

Manufacturer	Model	Waveforms	Voltage, Volts	Amperage	Delivery Modes	Frequency Range, Hz.	Pulse Width, microseconds	No. of Channels	Programmable	Intended Application	Price	Type of Unit
PTI	Omnistim 500[406]	Monophasic, biphasic, interferential, Russian	0-250		Pulsed, burst, interrupted, interferential beat wave	0.1-999, 2000-5000 (Interfer)		2	No	Pain management, neuromuscular stimulation, treatment of edema		TENS, PC, NMES
PTI	Omnisound 2500C[407]	Monophasic, biphasic, interferential, Russian			Pulsed, burst, interrupted interferential beat wave	0.1-999, 2000-5000	30-500	2	No	Pain management		PC, medium frequency, ultrasound
Rich-Mar	HV II SP[408]	Monophasic			Pulsed, interrupted	2-120			No	Pain management		PC, ultrasound
Rich-Mar	VI[409]	Biphasic			Pulsed, interrupted				No	Pain management		NMES, ultrasound
Rich-Mar	VI HV[410]	Monophasic			Pulsed, interrupted	5-80			No	Pain management		PC, ultrasound
Rich-Mar	Theratouch 3.3[411]	Monophasic, biphasic, interferential, Russian			Pulsed, interferential beat wave			4	No	Pain management, neuromuscular stimulation		TENS, NMES, microcurrent, medium frequency
Rich-Mar	Theratouch 4.7[412]	Monophasic, biphasic, interferential, Russian			Pulsed, interferential beat wave			4	No	Pain management, neuromuscular stimulation		TENS, NMES, microcurrent, medium frequency
Rich-Mar	III	Biphasic	21		Pulsed, interrupted	1-60		2	No	Neuromuscular stimulation		NMES
Rich-Mar	III-G	Monophasic, biphasic	21	0-40 mA (monophasic)	Pulsed, interrupted	1-60	800, 1400 (monophasic)	2	No	Denervated muscle stimulation, neuromuscular stimulation		NMES

Table 3.6. Manufacturers, Models, and Device Specifications of Electrical Stimulators (continued)

Manufacturer	Model	Waveforms	Voltage, Volts	Amperage	Delivery Modes	Frequency Range, Hz.	Pulse Width, microseconds	No. of Channels	Programmable	Intended Application	Price	Type of Unit
Sale & Service, S.L.	3002 TENS[413]	Biphasic	0-180	0-80 mA peak (500 Ohm load)	Pulsed	2-130	100-200	2	No	Pain management		TENS
ST-Electromedicina	Sarria ST-110[414]	Monophasic, biphasic	270 max	70 mA peak (3500 Ohm load)	Pulsed			4	No	Pain management, neuromuscular stimulation		TENS, NMES
ST-Electromedicina	Sarria ST-120[415]	Monophasic, biphasic	270 max	70 mA peak (3500 Ohm load)	Pulsed			4	Yes	Pain management, neuromuscular stimulation		TENS, NMES
Staodyn	Dermapulse[416]	Monophasic		0-42 mA peak	Pulsed	64, 128	140	4	No	Wound management, accelerated healing		PC (PDC)
Staodyn	EMS+2[417]	Monophasic, biphasic		0-100 mA (0-500 Ohm load)	Pulsed, interrupted,	4-80	5-300	2	No	Neuromuscular stimulation		NMES
Staodyn	Maxima II[418,419]	Biphasic	75	0-80 mA peak (500 Ohm load)	Pulsed, burst, pulse rate/width modulation	2-150	50-250	2	No	Pain management	$645	TENS
Staodyn	Maxima III[420,421,422]	Biphasic	130	0-100 mA (1300 Ohm load)	Pulsed, interrupted	2-160	50-400	2	No	Pain management	$665	TENS
Staodyn	Nuwave[423,424]	Biphasic	100	100 mA peak (500 Ohm load)	Pulsed	278	60	2	No	Pain management	$795	TENS
Staodyn	Tuwave[425]	Biphasic, triphasic	100 peak (2000 Ohm load)	100 mA peak (500 Ohm load)	Pulsed	278, 222	60	2	No	Pain management, treatment of edema, increasing circulation		PC, TENS
Titan Electronics	Compact-TENS[426]	Biphasic		0-60 mA (1000 Ohm load)	Pulsed, pulse rate/width modulation	1-200	30-300	2	No	Pain management		TENS
Titan Electronics	TiCi-EL[427]	Biphasic	0-50 (1000 Ohm load)	0-50 mA (1000 Ohm load)	Pulsed	100	100	1	No	Management of menstrual pain		TENS

Table 3.6. Manufacturers, Models, and Device Specifications of Electrical Stimulators (continued)

Manufacturer	Model	Waveforms	Voltage, Volts	Amperage	Delivery Modes	Frequency Range, Hz.	Pulse Width, microseconds	No. of Channels	Programmable	Intended Application	Price	Type of Unit
Ultraschall Dr. Born GmbH	M 200[428]	Monophasic	0-500 (10000 Ohm load)		Pulsed	2-150			No	Pain management		PC, ultrasound
Universal Technology Systems	PGS-3000[429]	Monophasic	330		Pulsed	1-100		1	No	Neuromuscular stimulation		NMES, PC
Verimed	Veristim II[430]	Biphasic	80 (1000 Ohm load)		Pulsed	10-100	10-350	1	No	Neuromuscular stimulation		NMES
Verimed	Phyaction 780[431]	Monophasic, biphasic, interferential, Russian		140 mA peak (500 Ohm load)	Pulsed, burst, interrupted, interferential beat wave	1-500, 4000 (Interfer), 2500 (Russian)		2	Yes	Pain management, neuromuscular stimulation		TENS, NMES
Pulsed Electro-magnetic Induction												
Manufacturer	Model	Field Strength	Generator Frequency	Pulse Duration	Programmable	Intended Application	**Price**					
Biorem	Maxima[432]	1-50 Gauss	1-100 Hz		Yes	Increase circulation, reduce inflammation						
Biorem	Micra[433]	48 Gauss	1-50 Hz		Yes	Increase circulation, reduce inflammation						
Diapulse	D103 [434]	293-975 W (radiated energy)	27.12 MHz	65 microseconds	Yes	Wound treatment						

Table 3.6. Manufacturers, Models, and Device Specifications of Electrical Stimulators (continued)

Manufacturer	Model	Waveforms	Voltage, Volts	Amperage	Delivery Modes	Frequency Range, Hz.	Pulse Width, microseconds	No. of Channels	Programmable	Intended Application	Price	Type of Unit
Electropharmacology	sofPulse[435]		80-600	65 microseconds	No	Pain management, treatment of edema						
Devices Cited in Referenced Articles												
Avra Tronics	Galvanator 770[436]	Monophasic	0-500		Pulsed	4-80		1	No	Neuromuscular stimulation		PC, NMES
Chattanooga Group	Intelect 500S[437]	Monophasic	0-500	0-2500 mA peak	Pulsed, interrupted	1-120		1	No	Neuromuscular stimulation		NMES, PC (HVPC)
Dynawave	Dynawave Model 12[438]	Monophasic	0-500	Microamp	Pulsed, interrupted	1-105		2	No	Neuromuscular stimulation		Microcurrent, NMES
Empi	Eclipse+[439]	Biphasic		0-60 mA (200-1200 Ohm load)	Pulsed, burst, pulse rate/width/amplitude modulation	2-125	30-250	2	No	Pain management	$665	TENS
Henley	EMS 8100[440]	Biphasic		0-80 mA	Pulsed, interrupted	20-100	60-800	2	No	Pain management	$829	TENS
Staodyn	Dermapulse[441]	Monophasic		0-42 mA peak	Pulsed	64, 128	140	4	No	Wound Management, Accelerated healing		PC (PDC)
Universal Technology Systems	PGS-3000[442]	Monophasic	330		Pulsed	1-100		1	No	Neuromuscular stimulation		NMES, PC

Table 3.6. Manufacturers, Models, and Device Specifications of Electrical Stimulators (continued)

Manufacturer	Model	Waveforms	Voltage, Volts	Amperage	Delivery Modes	Frequency Range, Hz.	Pulse Width, microseconds	No. of Channels	Programmable	Intended Application	Price	Type of Unit
Pulsed Electro-magnetic Energy												
Manufacturer	**Model**	**Radiated Energy**	**Generator Frequency**	**Pulse Duration**	**Programmable**	**Intended Application**	**Price**					
Diapulse	D103 [443]	293-975 W	27.12 MHz	65 microseconds	Yes	Wound treatment						

4.0 Quality of Electrical Stimulation Studies for Chronic Wound Healing

Our analysis of studies of electrical stimulation for the treatment of chronic wounds consisted of

- an analysis of the quality of the ES studies (section 4);
- a description of ES study procedures and outcomes (as reported by investigators) in evidence tables (section 5);
- a quantitative analysis and meta-analyses of healing rates and complete wound healing within ES studies (section 6);
- a comparative analysis of the quality of controlled ES studies with controlled studies of alternative therapies (section 7); and
- a comparative analysis of healing rate and complete wound healing of ES studies with outcomes reported in alternative therapies (section 8).

Our analysis of ES literature quality consisted of the following:

- Step 1: literature search (section 4.1) and collection of appropriate articles
- Step 2: an overall description of possible confounding factors that may arise from flaws in patient selection, randomization, or concomitant therapy that may lead to potentially biased outcomes (section 4.2)
- Step 3: a description of weaknesses in outcome reporting possibly leading to erroneous conclusions (section 4.2)
- Step 4: an assessment of the quality of individual ES studies (section 4.3)

4.1 Databases and Search Strategies for Electrical Stimulation Studies

ECRI searched the following databases:

- Ageline (1966 through December 1995)
- Biosis Previews (1969 through December 1995)
- Catline (1985 through December 28, 1995)
- Ei Compendex Plus (1970 through December 1995)
- Current Contents (January 1994 through January 4, 1996)
- Diogenes (1976 through January 4, 1996)
- Dirline (1985 through December 1995)
- Embase (1974 through November 11, 1995)
- Federal Research in Progress (January 1996; updated monthly)
- Health Care Standards (1990 through January 4, 1996)
- Health Device Alerts (1977 through January 4, 1996)
- Health Devices Sourcebook (January 1995; updated monthly)
- Health Planning and Administration (1975 through December 19, 1995)
- Health Services/Technology Assessment Research (1985 through December 19, 1995)
- INSPEC (1969 through December 1995)
- International Health Technology Assessment (1990 through January 4, 1996)
- MEDLINE (1966 through December 19, 1995)
- Nursing and Allied Health (1984 through December 19, 1995)

We also identified relevant literature by hand searching through

- journals,
- bibliographies of articles reviewed,
- material provided by experts contacted, and
- material provided by manufacturers contacted.

Our search strategies for identifying ES studies of chronic wound healing within these databases used the following subject areas (and keywords in parentheses):

- Chronic wounds, ulcers *(wounds; decubitus ulcer; skin ulcer; varicose ulcer; stasis ulcer; venous ulcer; pressure ulcer; pressure sore; diabetic foot; foot ulcer; leg ulcer; bedsore; ischemic ulcer; ischemia; soft tissue)*
- Wound healing *(wound healing; ulcer healing)*
- Electric stimulation *(electric stimulation; electric stimulation therapy; electrostimulation; electrostimulation therapy; pulsed electromagnetic frequency {PEMF}; low-intensity direct current {LIDC}; diathermy; electrocoagulation; monophasic; biphasic; radiowave; shortwave; diapulse; electromagnetics; electromagnetic therapy; electromagnetic energy; electromagnetic radiation; electromagnetic fields; electricity; electrotherapy; transcutaneous electric nerve stimulation; TENS; stimulators; equipment safety; equipment failure)*
- Randomized/controlled trials *(clinical trials; clinical trials, phase I; clinical trials, phase II; clinical trials, phase III; clinical trials, phase IV; randomized controlled trials; controlled clinical trials; multicenter studies; random allocation; single-blind method; double-blind method; placebos; mask; random; control; blind)*

[See section 7.1 for search strategies used for alternative therapies.]

A search of these databases yielded 41 studies of ES for the treatment of chronic wounds. They included

- 6 studies using DC stimulation (2 randomized controlled trials {RCTs}, 1 comparative, 2 case series {with embedded RCTs}, and 1 case report);

- 14 studies using PC stimulation (9 RCTs, 2 case series, and 3 case reports);
- 9 studies using AC or TENS stimulation (2 RCTs, 6 case series {1 with a very preliminary RCT}, and 1 case report);
- 7 studies using PEE devices (5 RCTs, 1 case series, and 1 case report); and
- 5 studies using implanted SCS (2 case series, 3 case reports) + 1 background article (on SCS for amputations).

These studies form the basis of our qualitative and quantitative analyses.

We also identified 8 background studies of ES for wound or soft tissue healing including DC for healing of grafts following burn injuries;[444] PC for evaluation of transcutaneous oxygen levels in spinal cord injury patients;[445] TENS for the prevention of amputations,[446] and for improved healing postoperative healing[447] or for skin flaps;[448] PEE for the healing of donor sites for grafts[449] or soft tissue injuries;[450] and SCS for improving limb salvage in patients with inoperable severe leg ischemia.[451]

Our only exclusion criteria was that these studies not explicitly state that they primarily used patients with lesions of less than 30-day duration. (Our definition of chronic was duration ≥30 days.)

Throughout our analyses, the terms “lesion,” “wound,” and “ulcer” are used interchangeably.

In addition we searched the literature for published studies of cost effectiveness of ES for wound healing. In this search we used the previously identified subject areas and keywords related to chronic wounds, wound healing and electrical stimulation in conjunction with the following keywords:

- Economics (*economics; costs and cost analysis; cost allocation; cost-benefit analysis; cost control; cost savings; cost of illness; health care costs; direct service costs; drug costs; employer health costs; health expenditures; capital expenditures; economics, hospital; hospital charges; hospital costs; economics, medical; fees and charges)*

The searches did not yield any relevant cost-effectiveness studies.

4.2 Possible Confounding Factors in Wound Healing Studies

Any investigator conducting a study on wound healing faces a daunting challenge—demonstrating that any observed effect (improvement in healing) is due exclusively to the therapeutic modality (e.g., dressing, ointment, device). This means that investigators must design studies that eliminate, or at least address, potential confounding factors. Failure to do so may compromise outcomes and lead investigators to erroneously conclude that the modality under study improves healing when it actually does not—or does not improve healing when it actually does. Investigators must also choose one or more outcome measures that are not intrinsically flawed and that adequately quantify the healing process. Therefore, any study of wound healing should answer the following basic questions:

- What is the study designed to measure?
- Is the study adequately designed?
- Does the study have a sufficiently large statistical power to detect which a difference in healing between ≥2 therapies?
- Does the study design eliminate confounding factors such as patient heterogeneity, differences in concomitant therapy, or variations within the modality being evaluated?
- Are the outcome measure(s) chosen intrinsically flawed, biased, or inappropriate to assess wound healing?

4.2.1 Study Types

Investigators may choose from many study designs including randomized controlled trials (RCTs), comparative controlled trials, case controlled, crossover, case series, and case reports.

A case report is an anecdotal presentation that cannot quantify the effect of a therapeutic modality. A case series is also inadequate because wounds may heal with little or no intervention, and any summary statistic may only be measuring outcomes for the particular sample of patients, not the effect of the therapeutic modality. For example, suppose investigators used the same modality to treat 2 sets of patients with leg ulcers—except that 1 group of patients had poor circulation and the other had excellent circulation. In this case, healing outcomes would probably differ because of heterogeneity in the sample population—not the treatment effect. A comparative controlled trial is an improvement, but again, differences in outcomes between groups of patients may be due to differences in patients rather than treatment.

An RCT is the optimal study design to evaluate wound healing because individuals are assigned to a treatment group by chance. This design maximizes the chances that any significant differences in outcome measurements are ascribable to treatment and minimizes the chances that the differences are due to characteristics of patients in the study.

RCTs for wound healing may control for treatment effect or patient selection.

In one type of RCT, a patient with similar bilateral lesions undergoes therapy A on one lesion and therapy B on the other lesion. This design controls for patient selection, but *attempts* to control for treatment effect. The advantage of this design is that there is no possible bias in patient selection. However, the investigator must conclusively demonstrate the effect of the therapy on one lesion is localized and does not affect healing of the other lesion. This is very difficult to prove. Also, it is difficult to blind investigators to treatment, which could lead to bias.

In the other design, investigators randomly allocate patients with similar lesions to different treatment groups. This design controls for treatment effect, but *attempts* to control for patient selection. The advantage of this design is that there is no bias in effect. However, even treatment groups with apparently randomly assigned patients may differ significantly from each other in 1 or more important patient characteristics. This can pose a problem in studies using only a few patients. Generally, this type of RCT is considered to be the "gold standard" for study design. It is used in most ES studies.

RCTs may be nonblind, single-blind, or double-blind. In a nonblind study, both patients and clinicians know which treatment group the patient has been assigned. (For example, in a study comparing ES and whirlpool therapy for wound healing, patients and clinicians are aware which therapy the patient receives.) Such RCTs may be biased by patients and/or clinicians. In a single-blind study, patients do not know which treatment they receive. (For example, in a study comparing ES device and a sham ES device, the patient may not be aware which therapy he receives, but the clinician knows.) Such RCTs may be unconsciously biased by the clinician. In a double-blind study, patients *and clinicians* do not know which treatment the patient receives. Such RCTs are unlikely to be biased by patients or clinicians, but are difficult to conduct. For some therapies, it may be technically and/or ethically infeasible to perform single- or double-blind studies.

An RCT of ES for wound healing may be designed to answer 1 or more of the following questions:

- Is ES therapy significantly different from no therapy at all for wound healing?

- Is ES therapy significantly different from conventional or standard therapy for wound healing?

- Is ES with conventional therapy significantly different from conventional therapy alone?

- Is ES therapy significantly different from the best available conventional therapy?

These are important distinctions. An RCT demonstrating that ES is significantly better than no therapy at all (e.g., ES versus a sham unit) does not show that it is as effective as standard therapy.

An RCT for wound healing must have a sufficient follow-up duration, particularly if it measures the percentage of patients who completely heal. The remodeling phase does not begin until at least 3 weeks after injury.[452] [See section 2.1.] Therefore, a study measuring the number of patients healed with only a 3-week follow-up may yield substantially different results than studies with 12- or 16-week follow-up durations.

An RCT should also have sufficient statistical power to demonstrate whether the investigators can detect the hypothesized effect on healing. If the study size is too small, there is probably insufficient power to ascertain whether the effect size is significant (i.e., reaches a specified *p* level). For example, a study of 10 patients (5 ES, 5 placebo) has insufficient statistical power to determine whether a 20% healing rate among patients receiving ES for 8 weeks is significantly greater than the 0% observed among patients receiving placebo. The same study using 200 patients would have sufficient power.

4.2.2 Confounding Sources

Outcomes of wound healing studies may be confounded by several types of confounding factors:

- Lack of homogeneity of study groups

- Failure to account for systemic or local medical conditions that can interrupt or alter wound healing

- Inconsistencies in regimen of primary wound therapy,

- Inconsistencies in concomitant wound therapy

Differences Between Study Groups—Designing proper RCTs to test a therapeutic modality for chronic wounds is difficult because of differences between patients.[453] In an RCT, one wants to compare the outcomes of groups of patients that have similar characteristics entering the study. For example, if an RCT (with 2 groups of patients) yields significantly different outcomes and there is no (statistically) significant difference between the mean ages of patients in the groups, then one can be reasonably certain that the outcomes are not confounded by the age of the patients.[1] On the other hand, if an RCT (with 2 groups of patients) yields significantly different outcomes and the mean ages of patients in the groups significantly differ, then the outcomes may be correlated to differences in patient ages, not therapy. Differences between patients also compromise case series outcomes.

Relevant patient characteristics include age, gender, and presence of underlying systemic medical conditions (e.g., diabetes mellitus, rheumatoid arthritis). Lesion characteristics include type of wound (e.g., venous, decubitus, diabetic), duration of wound, previous therapies, stage of wound, initial size of wound (e.g., surface area, volume), vascularization (perfusion) around wound site, and infection status.

Medical Conditions Affecting Wound Healing—Outcomes of wound healing studies can be confounded if investigators do not account for systemic medical conditions and local wound conditions that can severely impede or arrest wound healing. Potential factors include obesity, inadequate perfusion to the wound site, anemia, interstitial edema, repeated trauma at site, the presence of foreign bodies, infection, nutritional deficiencies (e.g., proteins, vitamins {A, B, C}, and trace elements {Zn, Fe, Cu}), smoking, radiation exposure, and medications (e.g., exogenous steroids).[454] Diseases predisposing patients to chronic wounds include diabetes mellitus (leading to atherosclerosis, neuropathy, multiple disorders of the immune system, and metabolic abnormalities), chronic venous stasis ulceration, inherited disorders of wound healing (Ehlers-Danlos syndrome {inability to produce normal collagen}, epidermolysis bullosa {inherited failure of adhesion of epidermis, dermis, and basement membrane of skin}, and Marfan's syndrome {abnormalities in collagen maturation and cross-linking}), connective tissue disorders (e.g., rheumatoid arthritis, osteoarthritis, scleroderma), hematologic disorders (e.g., sickle cell disease, thalassemia, myeloma, cryoglobulinemia, myeloid metaplasia, macroglobulinemia), lymphedema, malignancies, inflammatory bowel disease, and ulcerative necrobiosis lipoidica.[455]

Inconsistencies in Primary Therapeutic Modality—If patients are not treated uniformly, then it is difficult to determine how the treatment affects outcome. For example, if a study of TENS therapy for chronic venous leg ulcerations permitted patients to undergo therapy from 1 to 14 hours per day,

[1] Assuming that the outcome measurement is not flawed.

the outcomes would be compromised (unless reported per subject and regimen). Patient compliance also potentially confounds outcomes. [See section 5 for critique of individual ES study regimen flaws.]

Inconsistencies in Concomitant Wound Therapy—Patients undergoing ES for wound healing often undergo a concomitant standard (or minimal) therapy (e.g., saline-soaked gauze). Concomitant therapy may include debridement (e.g., mechanical/surgical, enzymatic), use of topical and/or cleansing agents, applications of dressings, use of pressure-relieving devices or regimens, and administration of topical or systemic antibiotics. In an RCT, if one group of patients receives a conventional therapy and another group receives ES with a similar concomitant therapy, then any significant difference in outcomes between the groups may be attributed to ES therapy (assuming patient groups do not otherwise differ). On the other hand, if some patients within a treatment group receive different types of dressings and/or debridement agents and/or topical agents, then outcomes may be biased. ES wound healing studies that do not maintain uniform concomitant therapies for patients may not accurately reflect the effect on healing by electrical stimulation.

4.2.3 Outcome Measures

Investigators can measure the surface area, depth, volume, or clinical appearance (e.g., granulation tissue, exudate) of an ulceration at any given time.

Surface Area—Measurement techniques include planimetry, direct tracing, and stereophotogrammetry.[456] These methods generally employ photographing or tracing a wound and using a computer and/or digitized scanner to directly calculate the surface area. Surface area is the most frequently recorded measurements of wounds. Healing rates may be small, so accurate measurements are essential. If a wound was exactly circular, one could calculate the surface area based on a single accurate measure of the diameter (area = $p \times (d/2)^2$). If a wound was exactly rectangular, one could calculate the surface area based on 2 accurate measurements, length and width (area = length × width). If a wound was exactly oval shaped, one could also calculate the surface area. However, wounds are rarely exact geometric shapes. Multiplying the length times the width of a wound often leads to inaccurate estimations of the surface area. Such systematic errors can lead to erroneous healing rates. Accurate planimetry is essential to properly measure surface area and calculate healing rates.

Volume—Ulcerations have 3 dimensions; ulcer depths vary. Surface area only measures 2 dimensions. Therefore, volume is a better measure of wound size than surface area. For example, if two wounds of 5 cm^2 surface area each undergo the same therapy and heal in 8 weeks, then the average (surface area) healing rate may be expressed as 62.5 mm^2/week. If one lesion is 1 mm deep and

the other is 4 mm deep, then the volumetric healing rates substantially differ (62.5 mm^3/week versus 250 mm^3/week). Calculating the volume of a wound by linear measurements creates inaccuracies. Wounds are not precisely cylindrical (volume = $p \times (d/2)^2 \times$ depth) or cubic solids (volume = length × width × depth). Using such formula can overestimate wound size by ≥20%.[457] Accurate volumetric assessment often requires clinical intervention such as filling the lesion with sterile saline and measuring the volume or temporarily molding substances such as Jeltrate (mixture of diatomaceous earth, potassium alginate, calcium sulfate, potassium titanium fluoride, magnesium oxide, tetrasodium pyrophosphate, and spearmint oil) into the wound and measuring the volume.[458] Although some wound healing studies have reported ulcer depths, few, unfortunately, have reported ulcer volume.

Types of Reported Outcomes—The efficacy of any therapy for wound healing is based on how rapidly it promotes healing and the percentage of patients who are likely to heal. Investigators have described different outcomes, including:

- time required for all lesions to heal,
- the percentage of lesions healed during a specified period of time (e.g., 4 weeks, 8 weeks),
- mean (± some measure of variance[m]) time for complete healing of lesions,
- mean (± some measure of variance) healing (or reduction) expressed as a percentage of surface area and/or volume of all lesions a specified period of time,
- healing rate (± some measure of variance) = total surface area or volume healed divided by a specified time,
- linear healing rate (± some measure of variance) = average of total surface area or volume healed at different times (e.g., 70 mm^2 healed at 2 weeks and 150 mm^2 healed at 5 weeks = average of 32.5 mm^2 healed/week),
- exponentially modeled healing rate (theta)[see section 6],
- mean (± some measure of variance) of treatment time and percentage of lesions healed,

[m] Measures of variance include standard deviation {SD}, standard error {SE}, 95% confidence interval {CI}, or variance itself.

- mean (± some measure of variance) of treatment time and percentage of total surface or volume healed, and

- subjective (clinically-based) grading system accounting for development of granulation tissue, rating of excellent/good/poor healing, etc.

Studies expressing outcomes for each subject provide the best data for analysis. Those providing means and some index of variance are also useful; those failing to provide variances are rarely useful.

Although outcomes reported in wound healing studies are often idiosyncratic and difficult to compare and contrast, they can be classified into several types:

- objective expressions of complete healing,

- objective expressions of the healing rate, and

- subjective assessments describing the healing process.

4.2.3.1 Objective Outcomes: Percentage of Patients Completely Healed

Many wound healing studies report the number (and/or percentage) of patients healed at given time intervals. One might assume that this is a straightforward, simple measurement of a therapy to promote healing. Unfortunately, the number (percentage) of patients healed is a flawed outcome measure because it depends on study follow-up duration and initial wound size.[459]

Problems with Percentage (or Number) of Patients Totally Healed—We illustrate by the following theoretical example. Suppose we have a 2-group, properly randomized, double-blind RCT: 15 patients in group A receive an experimental therapy and 15 patients in group B receive standard therapy. The surface areas of the lesions at the beginning of the study (i.e., initial size) are as follows:

Group A = 14 cm^2, 14 cm^2, 14 cm^2, 14 cm^2, 14 cm^2, 10 cm^2, 10 cm^2, 10 cm^2, 10 cm^2, 10 cm^2, 6 cm^2, 6 cm^2, 6 cm^2, 6 cm^2, 6 cm^2

(n = 15 patients)

Group B = 12 cm^2, 12 cm^2, 12 cm^2, 12 cm^2, 12 cm^2, 10 cm^2, 10 cm^2, 10 cm^2, 10 cm^2, 10 cm^2, 8 cm^2, 8 cm^2, 8 cm^2, 8 cm^2, 8 cm^2

(n = 15 patients)

Further assume that patients in both groups are similar, that there are no known systemic and local medical conditions which could interrupt wound healing, and that there are no inconsistencies in either the experimental or concomitant wound therapies. Group A mean surface area and standard error (SE) is 10.0 ±0.9 cm^2 (95% CI = 8.1 to 11.9 cm^2); group B mean and SE is 10.0 ±0.4 cm^2 (95% CI = 9.1 to 10.9 cm^2). There is no significant difference between these groups.

If the experimental and standard therapies both had a linear healing rate of 1 cm^2 per week, then after 6 weeks, the percentage of patients healed would be 33% for group A (5 of 15 healed) and 0% for group B. We would detect significantly different percentages of patients healed based exclusively on initial wound size. If the healing rate in the experimental group was 14 cm^2/6 weeks and the rate in the control group was 12 cm^2/6 weeks, we would observe 100% healing at 6 weeks for both groups. If the healing rate in the experimental group was 1 cm^2/week and was 2 cm^2/week in the control group, but the follow-up was only 3 weeks, we would observe 0% healing in both groups and erroneously conclude that there was no effect.

In this example, we have shown that a double-blind RCT using the percentage (or number) of healed patients is flawed by dependence on initial wound size and follow-up duration.

Wound healing investigators have considered the percentage of patients healed an important measure of wound healing, because of concerns that a therapy might only "partially" heal lesions—failing to completely heal them. Possible causes of arrested wound healing include inadequate perfusion to the wound site, blood dyscrasias (e.g., anemia), edema, repeated trauma, foreign body, infection, excessive necrotic tissue at wound site, nutritional deficiencies, metabolic disorders steroids, and topical agents inhibiting cell growth.[460] If a wound is healing with a therapy, then appears to stop, it seems more likely that this is due to a physiologic cause rather than a deficiency in the therapy.

4.2.3.2 Objective Outcomes: Healing Rates

Most wound healing studies expressed healing as a rate, usually the percentage of ulcer healed per week.

Many other studies expressed the healing rate as the percentage difference between the initial size of a lesion and the final size divided by the time interval.

For example, if after 5 weeks, lesions were an average of 40% of their initial size, then the healing rate was:

(100% initial size - 40%) ÷ 5 weeks = 12%/week.

This healing rate means little unless we know the initial size of a lesion. One might ask "12% of what?" Without knowing initial lesion size, 12% healing per week could represent 1 cm^2 per week or 10 cm^2 per week. Unfortunately, many wound healing studies neglected to specify initial lesion size.

Many studies provided the initial mean wound size, often with some measure of variance. They often provided healing rates as percentages of lesion healed or in cm^2 healed from initial to final lesion size. In some studies, healing rates were obtained empirically at selected intervals between initial and final lesion sizes and averaged to yield a mean healing rate. Such healing rates assume that healing is linear. There is no evidence that this is true. We examined healing rate curves of ES and conventional therapy RCTs and the relationship often visually appears as an exponential decay. Pierard and Pierard-Franchimont[461] recently concluded that chronic leg ulcers heal at uniform, nonlinear rates, following a proportional change process.

We used an exponential decay model to express healing rates for wound healing. [See Section 6 for explanation of the normalized healing rate (?).]

Wound healing rates are generally good measures of the healing process. Unfortunately, the results of nearly all wound healing studies are expressed in healing rates by surface area. These rates may substantially differ from volumetric healing rates which more accurately represent true healing.

4.2.3.3 Subjective Outcomes

Subjective, clinically-based rating systems score the development of granulation tissue, the degree of exudate, patient discomfort, and healing. Such rating systems qualitatively describe the healing process. However, they are not standardized and do not present a quantitative measure suitable for comparison with other wound healing studies.

4.3 Quality of Individual Electrical Stimulation Studies of Wound Healing

We evaluated the quality of ES studies for wound healing by study design, sources of confounding, and outcome measures. (Case reports and background studies were excluded.)

For study design, each trial was evaluated to determine the following:

- Type of study
- Whether randomization process was specified (if an RCT)
- Blinding of patients, or patients and clinicians
- Study size

For differences between study groups, each trial was evaluated to determine whether it accounted for the following:

- Patient age and whether it was specified by subject, group (without some measure of variance), or group with some measure of variance
- Gender
- Type of wound (venous, decubitus, mixed)
- Duration of wounds and whether these were specified by subject group (without variance), or group with variance
- Stage or grading of wounds
- Anatomical location of wounds
- Infective status of wounds

For medical conditions affecting wound healing, each trial was evaluated to determine whether it accounted for the following:

- Presence of peripheral arterial or peripheral vascular disease and/or performed pre-therapy vascular perfusion testing
- Presence of rheumatoid arthritis
- Exogenous steroid use by patients

- Nutritional status of patients

For inconsistencies in concomitant wound therapy, each trial was evaluated to determine whether it accounted for possible confounding by the following:

- Debridement
- Use of topical and/or cleansing agents
- Use of dressings
- Use of pressure devices or turning therapy (if applicable)
- Use of topical or systemic antibiotics

For outcome measures, each trial was evaluated to determine whether it

- specified initial wound size by surface area and/or volume, and
- specified initial wound size by subject, group (without some measure of variance), or group with some measure of variance.

Quality assessments for individual ES studies are presented by stimulation type in **Table 4.1** (Direct Current), **Table 4.2** (Pulsed Current), **Table 4.3** (Alternating Current), and **Table 4.4** (Pulsed Electromagnetic Induction).

Summaries of flaws and/or deficiencies in ES controlled studies by stimulation type are presented in sections 4.3.1 through 4.3.4. [See section 5 for more details of individual studies.]

4.3.1 Direct Current Controlled Studies

(1) Katelaris et al. (1987)[462]—A controlled study in which patients were not randomly assigned for LIDC with povidone solution versus povidone solution alone, and LIDC with normal saline dressing versus saline alone for venous lesions

- Small study (average 6 patients per treatment group)
- Duration of lesions not specified
- Lesion size expressed in surface area alone
- No vascular perfusion testing before therapy

- Did not specify whether patients with infected lesions, with peripheral arterial disease, or with rheumatoid arthritis were included or excluded from study
- Did not specify steroid use or nutritional status of patients

(2) Carley & Wainapel (1985)[463]—RCT of LIDC therapy versus control (saline-soaked gauze) for unspecified lesions

- Did not specify lesion type (e.g., venous, decubitus, diabetic) and therefore may have examined several types of ulcers
- Randomization method not specified
- Lesion size expressed in surface area alone
- No vascular perfusion testing before therapy
- Did not specify whether patients with infected lesions, with peripheral arterial or venous disease, or with rheumatoid arthritis were included or excluded from study
- Did not specify steroid use or nutritional status of patients
- Possibly confounded by dressings used in concomitant therapy

(3) Akers & Gabrielson (1984)[464]—Comparative (nonrandomized) controlled study of DC with whirlpool (WP) versus DC alone versus WP alone for decubitus lesions

- Small study (average <5 patients per treatment group)
- Did not specify number of patients per treatment group
- Did not specify important patient and lesion characteristics: patient age, gender, anatomical location and duration of lesions, stage of lesions
- Did not provide initial or final size of lesions, so not possible to determine healing rate
- No vascular perfusion testing before therapy
- Did not specify whether patients with infected lesions, with peripheral arterial or venous disease, with diabetes, or with rheumatoid arthritis were included or excluded from study

- Did not specify steroid use or nutritional status of patients

4.3.2 Pulsed Current Controlled Studies

(1) Wood et al. (1993)[465]—Double-blind RCT of PDC versus sham (placebo) unit for decubitus lesions

- Randomization method not specified
- Lesion expressed in surface area; can only determine crude approximation of volume (surface area multiplied by depth)
- No vascular perfusion testing before therapy
- Did not specify whether patients with infected lesions, with peripheral arterial or venous disease, with diabetes, or with rheumatoid arthritis were included or excluded from study
- Did not adequately specify nutritional status of patients

(2) Gogia et al. (1992)[466]—RCT of HVPC with WP versus WP alone for lesions of mixed etiology

- Small study (6 patients per treatment group)
- Mixed etiology including diabetic, venous, and decubitus
- Heterogeneous sample population
- Randomization method not specified
- Lesion expressed in surface area alone
- No vascular perfusion testing before therapy
- Did not specify whether patients with infected lesions, with peripheral arterial disease, or with rheumatoid arthritis were included or excluded from study
- Did not adequately specify nutritional status of patients
- Possibly confounded by inclusion of diabetic patients in study

- Possibly confounded by debridement therapy used in study

(3) Gentzkow et al. (1991)[467]—Double-blind RCT of PDC versus sham (placebo) unit for decubitus lesions

- Randomization method not specified
- Lesion expressed in surface area alone
- No vascular perfusion testing before therapy
- Did not specify whether patients with infected lesions, with peripheral arterial or venous disease, with diabetes, or with rheumatoid arthritis were included or excluded from study
- Did not adequately specify nutritional status of patients
- Possibly confounded by debridement and/or whirlpool (cleansing) therapy used in study

(4) Griffin et al. (1991)[468]—Single-blind RCT of HVPC versus sham (placebo) unit for decubitus lesions

- Small study (<10 patients per treatment group)
- Randomization method not specified
- Did not specify gender of patients
- No vascular perfusion testing before therapy
- Did not specify whether patients with infected lesions, with peripheral arterial or venous disease, with diabetes, or with rheumatoid arthritis were included or excluded from study
- Did not specify steroid use or nutritional status of patients

(5) Feedar et al. (1991)[469]—Double-blind RCT of PDC versus sham (placebo) unit for lesions of mixed etiology

- Mixed etiology including decubitus, surgical, vascular, and traumatic
- Heterogeneous sample population
- Randomization method not specified

- Lesion expressed in surface area alone
- Systematic inaccuracies in measurement of surface area because determined as product of length x width
- No vascular perfusion testing before therapy
- Did not specify whether patients with infected lesions or with rheumatoid arthritis were included or excluded from study
- Did not adequately specify nutritional status of patients
- Possibly confounded by debridement and/or whirlpool (cleansing) therapy used in study

(6) Mulder (1991)[470]—Double-blind RCT of PDC versus sham (placebo) unit for lesions of mixed etiology. This study is an apparent duplication of the study by Feedar et al. (1991). Any discrepancies in the quality assessment between this article and Feedar et al. are due to reporting inconsistencies in the Mulder article.

(7) Unger et al. (1991)[471]; Abstract—Double-blind RCT of HVPC versus sham (placebo) unit for decubitus lesions

- Small study (<10 patients per treatment group)
- Insufficient data for determining homogeneity of study population
- Did not specify important patient and lesion characteristics: patient age, gender, anatomical location or duration of lesions, stage of lesions
- Did not provide initial or final size of lesions, so not possible to determine healing rates
- No vascular perfusion testing before therapy
- Did not specify whether patients with infected lesions, with peripheral arterial or venous disease, with diabetes, or with rheumatoid arthritis were included or excluded from study
- Did not specify steroid use or nutritional status of patients
- Did not specify any concomitant therapy (e.g., debridement, use of topical or cleansing agents, dressings, antibiotics)

(8) Kloth & Feedar (1988)[472]—Single-blind RCT of HVPC versus sham (placebo) unit for decubitus lesions

- Small study (<10 patients per treatment group)
- Differences in patient characteristics
- Lesion expressed in surface area alone
- No vascular perfusion testing before therapy
- Did not specify whether patients with infected lesions or with rheumatoid arthritis were included or excluded from study
- Did not specify steroid use or nutritional status of patients
- Possibly confounded by inclusion of patients with peripheral vascular disease or diabetes in study
- Possibly confounded by debridement therapy used in study

(9) Feedar & Kloth (1985)[473]**; Abstract**—Single-blind RCT of HVPC versus sham (placebo) unit for decubitus lesions

- Small study (≤5 patients per treatment group)
- Randomization method not specified
- Did not specify important patient and lesion characteristics: patient age, gender, anatomical location and duration of lesions
- Did not provide initial or final size of lesions, so not possible to determine healing rates
- No vascular perfusion testing before therapy
- Did not specify whether patients with infected lesions, with peripheral arterial or venous disease, with diabetes, or with rheumatoid arthritis were included or excluded from study
- Did not specify steroid use or nutritional status of patients
- Possibly confounded by debridement therapy used in study

4.3.3 Alternating Current and TENS Controlled Studies

(1) Stefanovska et al. (1993)[474]—RCT of Biphasic AC versus LIDC versus conventional therapy for decubitus lesions

- Randomization method not specified
- Stage of lesions not specified
- Lesions expressed in surface area alone
- No vascular perfusion testing before therapy
- Did not specify whether patients with infected lesions, with diabetes, or with rheumatoid arthritis were included or excluded from study
- Did not specify steroid use or nutritional status of patients
- Did not specify any concomitant therapy (e.g., debridement, use of topical or cleansing agents, dressings, antibiotics)

(2) Lundeberg et al. (1992)[475]—Double-blind RCT of TENS versus sham (placebo) unit for diabetic ulcerations

- Did not specify patient age or duration of lesions
- Lesions expressed in surface area alone
- Did not specify whether patients with infected lesions were included or excluded from study
- Did not specify steroid use or nutritional status of patients

4.3.4 Pulsed Electromagnetic Induction Controlled Studies

(1) Salzberg et al. (1995)[476]—Double-blind RCT of PEE device versus sham (placebo) unit for decubitus ulcers

- Randomization method not specified
- Did not specify patient age, anatomical location of lesions, or duration of lesions

- Lesions expressed in surface areas alone
- No vascular perfusion testing before therapy
- Did not specify whether patients with peripheral arterial or venous disease, with diabetes, or with rheumatoid arthritis were included or excluded from study
- Did not specify steroid use of patients

(2) Stiller et al. (1992)[477]—Double-blind RCT of PEMF device versus sham (placebo) unit for venous ulcers

- Lesions expressed in surface areas alone
- Did not specify whether patients with infected lesions or with rheumatoid arthritis were included or excluded from study
- Did not specify steroid use of patients
- Possibly confounded by debridement therapy, use of dressings, and antibiotic therapy

(3) Todd et al. (1991)[478]—Double-blind RCT of PEMF versus sham (placebo) unit for venous ulcers

- Small study (≤10 patients per treatment group)
- Randomization method not specified
- Lesion expressed in surface area alone
- Did not specify whether patients with diabetes or with rheumatoid arthritis were included or excluded from study
- Did not specify steroid use or nutritional status of patients

(4) Ieran et al. (1990)[479]—Double-blind RCT of PEMF versus sham (placebo) unit for venous ulcers

- Lesions expressed in surface area alone
- Did not specify whether patients with infected lesions or with rheumatoid arthritis were included or excluded from study
- Did not specify nutritional status of patients

- Possibly confounded by inclusion of patients with diabetes in study
- Possibly confounded by antibiotic therapy used in study

(5) Jeran et al. (1987)[480]—Double-blind RCT of PEMF versus sham (placebo) unit for venous ulcers

- Randomization method not specified
- Did not specify patient age or gender
- Lesions expressed in surface area alone
- No vascular perfusion testing before therapy
- Did not specify whether patients with peripheral arterial disease, with diabetes, or with rheumatoid arthritis were included or excluded from study
- Did not specify steroid use or nutritional status of patients
- Possibly confounded by inclusion of infected lesions in study
- Possibly confounded by antibiotic therapy used in study

4.3.5 ES Study Quality: General Findings

All of the controlled trials of ES for the treatment of wound healing have flaws. However, these may or may not be typical for all RCTs for wound healing. See section 7 for a comparison of the quality of ES studies with non-ES studies for wound healing.

4.4 Tables

Table 4.1. Assessment of Quality of Direct Current Stimulation Studies of Wound Healing

Study Specified...	Katelaris[481]	Carley[482]	Akers[483]	Gault[484]	Wolcott[485]
Stimulation Type	LIDC	LIDC	DC	LIDC	LIDC
Wound	Venous	Not specified	Decubitus	Mixed	Mixed
Homogeneous	Yes	?	Yes	No	No
N (Patients or Lesions)	24	30	14	100	75
Study Type	Controlled	RCT	Comparative controlled	Case series*	Case series*
Randomization	Not specified	No	—	—	—
Patients Blinded	No	No	—	—	—
Clinicians Blinded	No	No	—	—	—
Patient Age	By group	By group + variance	No	No	By group
Gender	Yes	Yes	No	No	No
Location of Lesions	Yes	No	No	No	No
Duration of Lesions	No	By group + variance	No	No	No
Stage of Lesions	No	No	No	No	No
Specified Previous Therapy	No	No	No	No	No
Size of Lesions	Surface area	Surface area	No	No	Volume
Initial Size of Lesions	By group	By group + variance	No	No	No
Pre-tx Vascular Perfusion Performed	No	No	No	No	No

Table 4.1. Assessment of Quality of Direct Current Stimulation Studies of Wound Healing (continued)

Study Specified...	Katelaris[481]	Carley[482]	Akers[483]	Gault[484]	Wolcott[485]
Inclusion criteria considered:					
Infection	No	No	No	Yes	No
PAD/PVD	No	No	No	Yes	Yes
Diabetes	No	No	No	Yes	No
Rheumatoid Arthritis	No	No	No	No	Yes
Steroids	No	No	No	No	No
Nutrition	No	No	Yes	Yes	Yes
Possible confounding by:					
Infection	No	No	No	No	No
PAD/PVD	No	No	No	Yes	Yes
Diabetes	No	No	No	Yes	No
Rheumatoid Arthritis	No	No	No	No	Yes
Steroids	No	No	No	No	No
Nutrition	No	No	No	No	No
Specified use of:					
Debridement	No	No	No	Yes	No
Topical/Cleansing Agents	Yes	Yes	Yes	Yes	No
Dressings	Yes	Yes	No	Yes	Yes
Pressure Devices	NA	No	No	NA	NA
Antibiotics	No	No	No	No	No
Possible confounding by:					
Debridement	No	No	No	Uncertain	No
Topical/Cleansing Agents	No	No	No	No	No
Dressings	No	Yes	No	No	No
Pressure Devices	No	No	No	No	No
Antibiotics	No	No	No	No	No

* Embedded RCT (study comparing bilateral lesions on same patient) not applicable to quality assessment
Group + variance = study specified some measure of variance
Excluded: Fakhri & Amin[486] (background study)
Assimacopoulos[487] (case report)

Table 4.2. Assessment of Quality of Pulsed Current Stimulation Studies of Wound Healing

Study Specified...	Wood[488]	Gogia[489]	Gentzkow[490]	Griffin[491]	Feedar[492]	Mulder[493]	Unger, Eddy[494] [Abstract]	Kloth[495]	Feedar[496] [Abstract]
Stimulation Type	PDC	HVPC	PDC	HVPC	PDC	PDC	HVPC	HVPC	HVPC
Wound	Decubitus	Mixed	Decubitus	Decubitus	Mixed	Mixed	Decubitus	Decubitus	Decubitus
Homogeneous	Yes	No	Yes	Yes	No	No	?	No	Yes
N (Patients or Lesions)	74	12	40	17	50	50	17	16	8
Study Type	Double-blind RCT	RCT	Double-blind RCT	Single-blind RCT	Double-blind RCT	Double-blind RCT	Double-blind RCT	Single-blind RCT	Single-blind RCT
Randomization	No	No	No	No	No	No	No	Yes	No
Patients Blinded	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Clinicians Blinded	Yes	No	Yes	No	Yes	Yes	Yes	?	?
Patient Age	By subject	By group	By group + variance	By group	By group + variance	No	No	By subject	No
Gender	Yes	Yes	Yes	No	Yes	No	No	Yes	No
Location of Lesions	Yes	Yes	Yes	Yes	Yes	No	No	No	No
Duration of Lesions	By subject	By group	By group	By group	By group	By group	No	By group	No
Stage of Lesions	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes
Specified Previous Therapy	No	No	No	No	No	No	No	Yes	No
Size of Lesions	Surface area + volume	Surface area	Surface area	Surface area	Surface area	Surface area	No	Surface area	No
Initial Size of Lesions	By subject	By group	By group + variance	By group	By subject	By group	No	By subject	No
Pre-tx Vascular Perfusion Performed	No	No	No	No	No	No	No	No	No

Table 4.2. Assessment of Quality of Pulsed Current Stimulation Studies of Wound Healing (continued)

Study Specified...	Wood[488]	Gogia[489]	Gentzkow[490]	Griffin[491]	Feedar[492]	Mulder[493]	Unger, Eddy[494] [Abstract]	Kloth[495]	Feedar[496] [Abstract]
Inclusion criteria considered:									
Infection	No	No	No	No	No	No	No	No	No
PAD/PVD	No	No	No	No	Yes	Yes	No	Yes	No
Diabetes	No	Yes	No	No	Yes	Yes	No	Yes	No
Rheumatoid Arthritis	No	No	No	No	No	No	No	No	No
Steroids	No	No	No	No	Yes	Yes	No	No	No
Nutrition	Yes	Yes	Yes	No	No	No	No	No	No
	No	No	No	No	No	No	No	No	No
Possible confounding by:									
Infection	No	No	No	No	No	Yes	No	Yes	No
PAD/PVD	No	Yes	No	No	No	No	No	Yes	No
Diabetes	No	No	No	No	No	No	No	No	No
Rheumatoid Arthritis	No	No	No	No	No	No	No	No	No
Steroids	No	No	No	No	No	No	No	No	No
Nutrition	No	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes
Specified use of:									
Debridement	No	No	Yes	Yes	Yes	Yes	No	Yes	No
Topical/Cleansing Agents	No	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes
Dressings	Yes	No	No	Yes	No	No	No	No	No
Pressure Device	No	No	No	No	No	No	No	No	No
Antibiotics	No	Yes	Yes	Yes	Yes	No	No	Yes	Uncertain
Possible confounding by:									
Debridement	No	No	Yes	No	Yes	No	No	No	No
Topical/Cleansing Agents	No	No	No	No	No	No	No	No	No
Dressing	No	No	No	No	No	No	No	No	No
Pressure Device	No	No	No	No	No	No	No	No	No
Antibiotics	No	No	No	No	No	No	No	No	No

Group + variance = study specified some measure of variance

Excluded:

Fitzgerald & Newsome[497] (case report)

Weiss et al.[498] (background study)

Unger[499] (abstract on wounds?)

Table 4.2. Assessment of Quality of Pulsed Current Stimulation Studies of Wound Healing (continued)

Mawson et al.[500] (background study)
Ross & Segal[501] (case report)
Thurman & Christian[502] (case report)

Table 4.3. Assessment of Quality of Alternating Current Stimulation Studies of Wound Healing

Study Specified...	Stefanovska[503]	Lundeberg[504]	Karba[505]	Frantz[506]	Kaada[507]	Alon[508] [Abstract]	Barron[509]
Stimulation Type	Biphasic AC	(T)ENS	Biphasic AC	TENS	TENS	TENS	TENS
Wound	Decubitus	Diabetic	Decubitus + Vascular + Surgical	Decubitus	Leper (tuberculoid + leperomatous)	Diabetic	Decubitus
Homogeneous	Yes	Yes	No	Yes	Yes	Yes	Yes
N (Patients or Lesions)	150	64	63	4	32	15	6
Study Type	RCT	Double-blind RCT	Case series	Case series (Pilot study)	Case series	Case series	Case series
Randomization	No	Yes	—	—	—	—	—
Patients Blinded	?	Yes	—	—	—	—	—
Clinicians Blinded	No	Yes	—	—	—	—	—
Patient Age	By group + variance	No	No	By group	By subject	By group	By subject
Gender	Yes	Yes	No	Yes	Yes	Yes	Yes
Location of Lesions	Yes	Yes	No	Yes	Yes	Yes	Yes
Duration of Lesions	By group + variance	No	By group + variance	By group	By subject	By group	By subject
Stage of Lesions	No	No	No	No	No	No	No
Specified Previous Therapy	No	No	Yes	No	Yes	No	Yes
Size of Lesions	Surface area	Surface area	Surface area	Surface area + circumference	Surface area + volume	Surface area	Surface area
Initial Size of Lesions	By group + variance	By group + variance	By group + variance	By subject	By subject	No	By subject
Pre-tx Vascular Perfusion Performed	No	Yes	No	No	No	No	No

Table 4.3. Assessment of Quality of Alternating Current Stimulation Studies of Wound Healing (continued)

Study Specified...	Stefanovska[503]	Lundeberg[504]	Karba[505]	Frantz[506]	Kaada[507]	Alon[508] [Abstract]	Barron[509]
Inclusion criteria considered:							
Infection							
PAD/PVD							
Diabetes	No	No	No	Yes	No	No	Yes
Rheumatoid Arthritis	Yes	Yes	Yes	No	Yes	No	No
Steroids	No	Yes	Yes	No	Yes	Yes	No
Nutrition	No	Yes	No	No	No	No	No
	No	No	No	No	No	No	No
	No	No	No	Yes	No	No	No
Possible confounding by:							
Infection	No	No	No	No	No	No	No
PAD/PVD	No	No	No	No	No	No	No
Diabetes	No	No	No	No	No	No	No
Rheumatoid Arthritis	No	No	No	No	No	No	No
Steroids	No	No	No	No	No	No	No
Nutrition	No	No	No	No	No	No	No
Specified use of:							
Debridement	No	No	No	No	No	No	No
Topical/Cleansing Agents	No	Yes	No	No	Yes	No	No
Dressings	No	Yes	No	Yes	Yes	Yes	No
Pressure Devices	No	NA	No	No	NA	No	No
Antibiotics	No	No	No	No	No	No	No
Possible confounding by:							
Debridement	No	No	No	No	No	No	No
Topical/Cleansing Agents	No	No	No	No	No	No	No
Dressings	No	No	No	Yes	No	No	No
Pressure Devices	No	No	No	No	No	No	No
Antibiotics	No	No	No	No	No	No	No

Group + variance = study specified some measure of variance
Excluded: Finsen et al.[510] (background study)
Lundeberg et al.[511] (background study)

Table 4.3. Assessment of Quality of Alternating Current Stimulation Studies of Wound Healing (continued)

Kjartansson et al.[512] (background study)
Kaada[513] (case report)
Westerhof & Bos[514] (case report)

Table 4.4. Assessment of Quality of Pulsed Electromagnetic Induction Studies of Wound Healing

Study Specified...	Salzberg[515]	Stiller[516]	Todd[517]	Itoh[518]	Ieran[519]	Jeran[520]
Stimulation Type	PEE	PEMF	PEMF	PEE	PEMF	PEMF
Wound	Decubitus	Venous	Venous	Decubitus	Venous	Venous
Homogeneous	Yes	Yes	Yes	Yes	No	Yes
N (Patients or Lesions)	20	31	19	22	37	21
Study Type	Double-blind RCT	Double-blind RCT	Double-blind RCT	Case series	Double-blind RCT	Double-blind RCT
Randomization	No	Yes	No	—	Yes	No
Patients Blinded	Yes	Yes	Yes	—	Yes	Yes
Clinicians Blinded	Yes	Yes	Yes	—	Yes	Yes
Patient Age	By group	By group	By group	By subject	By group	No
Gender	No	Yes	Yes	Yes	Yes	No
Location of Lesions	No	Yes	Yes	Yes	Yes	Yes
Duration of Lesions	No	By group + variance	By group	By group	By group	Yes
Stage of Lesions	Yes	No	No	Yes	No	No
Specified Previous Therapy	No	Yes	No	Yes	No	No
Size of Lesions	Surface area	Surface area	Surface area	Surface area	Surface area	Surface area
Initial Size of Lesions	By subject	By group + variance	By group	By subject	By group	By group
Pre-tx Vascular Perfusion Performed	No	Yes	Yes	No	Yes	No

Table 4.4. Assessment of Quality of Pulsed Electromagnetic Induction Studies of Wound Healing (continued)

Study Specified...	Salzberg[515]	Stiller[516]	Todd[517]	Itoh[518]	Ieran[519]	Jeran[520]
Inclusion criteria considered:						
Infection	Yes	No	Yes	No	No	Yes
PAD/PVD	No	Yes	No	No	Yes	No
Diabetes	No	Yes	No	No	Yes	No
Rheumatoid Arthritis	No	No	No	No	No	No
Steroids	No	No	No	No	Yes	No
Nutrition	Yes	Yes	No	Yes	No	No
Possible confounding by:						
Infection	No	No	No	No	No	Yes
PAD/PVD	No	No	No	No	No	No
Diabetes	No	No	No	No	Yes	No
Rheumatoid Arthritis	No	No	No	No	No	No
Steroids	No	No	No	No	No	No
Nutrition	No	No	No	No	No	No
Specified use of:						
Debridement	No	Yes	No	No	No	No
Topical/Cleansing Agents	No	Yes	Yes	Yes	No	No
Dressings	Yes	Yes	Yes	Yes	No	No
Pressure Devices	No	NA	NA	Yes	NA	NA
Antibiotics	No	Yes	Yes	Yes	Yes	Yes
Possible confounding by:						
Debridement	No	Yes	No	No	No	No
Topical/Cleansing Agents	No	No	No	Yes	No	No
Dressings	No	Yes	No	Yes	No	No
Pressure Devices	No	No	No	Yes	No	No
Antibiotics	No	Yes	No	Yes	Uncertain	Uncertain

Group + variance = study specified some measure of variance

Excluded: Wilson[521] (background study)
Tung et al.[522] (case report)
Goldin et al.[523] (background study)

5.0 Electrical Stimulation Study Descriptions and Outcomes

The second part of our analysis of ES for the treatment of wound healing consists of basic study descriptions and outcomes as reported by investigators.

ECRI's analysis included all published studies of ES for the treatment of chronic wound healing. We defined a chronic wound as a (non-burn-induced) lesion of ≥ 30 days duration. [See section 4.1.] Many studies did not specify wound duration. (The absence of lesion duration data is specified in **Tables 4.1** through **4.4.**) [See section 4.3.]

Published studies were categorized as

- direct current (DC) stimulators,
- pulsed current (PC) stimulators,
- alternating current (AC), including TENS, stimulators,
- pulsed electromagnetic induction (PEMI) stimulators, and
- spinal cord stimulators (SCS).

Studies within each category were classified as

- uncontrolled (case series or case reports), or
- controlled (randomized controlled {RCT}, case-controlled, or comparative controlled).

Properly designed RCTs are the most important type of studies for evaluating wound healing therapies because they determine whether differences between 2 or more treatments are due to the treatments—without confounding by patient heterogeneity. [See section 4.2.1.] Uncontrolled studies, on the other hand, either report outcomes from case reports or outcomes that may reflect characteristics of the patients being studied—not the effect of therapy. [Uncontrolled ES studies of wound healing presented in the following sections cannot be used to quantitate efficacy. We present them merely as background studies.]

5.1 Direct Current Studies

Outcomes of DCS of wound healing (as reported by study investigators) are presented in **Table 5.1**. Studies in sections 5.1.1 and 5.1.2 are presented in chronological order.

5.1.1 Uncontrolled Studies

Assimacopoulos[524] conducted the first clinical study (case reports) of low intensity direct current (LIDC) on 3 patients with chronic venous ulcers. Each patient received between 50 and 100 µA and 0.25 to 0.80 V with the negative electrode (cathode) over the ulceration site and the positive electrode (anode) placed on the lateral thigh. All ulcers completely healed 32, 40, and 42 days after therapy.

Wolcott et al.[525] treated 83 ischemic ulcers (including paraplegic, venous stasis, and peripheral arteriosclerotic etiology) on 67 patients with LIDC. Before ES therapy, nonviable tissue surrounding the lesions was debrided and scrubbed with antibacterial detergent. Details of this ES protocol are discussed in section 3.2. Briefly, it consisted of giving patients three 2-hour sessions of 600 to 800 µA daily (2 hours therapy on and 4 hours off) and switching electrode polarity after 3 days for noninfected ulcers or, if infected, 3 days after the infection healed. Fresh gauze was placed in the site daily with cleansing and adjustments in current flow as deemed appropriate. (The investigators did not specify specific current adjustments, which could affect outcomes, making it difficult for subsequent investigators to reproduce them.) When there was no apparent improvement ("growth plateau"), electrode polarity was switched every 24 hours until sites completely healed. Lesion size was assessed before therapy and at weekly intervals afterward by measuring the volume of normal saline needed to fill the wound. Therapy was discontinued after 16 weeks or if the wound healed. The study consisted of 2 parts: a case series evaluation of 75 ischemic lesions, and an "embedded" RCT[n] using 8 patients with contralateral lesions. In the case series evaluation, 53 paraplegic lesions had an 80.5% mean decrease in volume (9.3% weekly decrease) in a mean of 8.7 weeks; 15 arteriosclerotic lesions had an 82.2% volume decrease (14.0% weekly decrease) in 5.9 weeks; and venous stasis ulcers had an 85.0% volume decrease (14.4% weekly decrease) in 5.9 weeks. Forty percent of the ulcerations healed, but the investigators did not specify the time required for them to heal. The weighted mean decrease of ulcer volume was 81.8% during a mean of 7.7 weeks, which the investigators presented as a mean (linear) healing rate of 13.4% per week. There was insufficient data presented to verify whether healing was, indeed, linear. These healing rate outcomes as reported are not useful for

[n] Patients with bilateral lesions (within a case series) treated by ES on one lesion and a non-ES therapy (control therapy) on the contralateral lesion.

comparison with other therapies because the investigators did not specify initial wound sizes. [See sections 4 and 6.]

Gault and Gatens[526] treated 76 patients who had 106 ischemic lesions (including sequelae of quadriplegia, paraplegia, cerebral vascular accident brain tumor, cardiac disease, peripheral vascular disease, burns, diabetes, tuberculosis, fractures, and amputations) using a similar LIDC regimen to Wolcott et al., except that they reversed the polarity only once. The investigators did not specify whether they measured lesion volume and/or surface area. The study consisted of 2 parts: a case series evaluation of 100 ischemic lesions, and an embedded RCT using 6 patients with contralateral lesions. In the case series evaluation, 100 ulcers were treated over a range of 3 days to 24 weeks. After a mean of 4.7 weeks, 80.5% of the ulcers treated had healed. The mean healing rate was 28.4% per week. Outcomes reported by these investigators cannot be readily compared with other therapies because the investigators combined outcomes of different types of ischemic ulcers (e.g., vascular, diabetic) and did not specify initial lesion size for normalization.

Fakhri & Amin[527] used a Baghdad elastoplast device (1 cm wide aluminum foil sandwiched between 2 cm wide lint and 3 cm wide adhesive plaster) delivering 10 to 20 mA current and 10 to 25 V on 20 patients with full-, mixed-, or partial-thickness burns that had failed to respond to conventional therapy. The reported regimen was an indeterminate treatment setting and duration twice weekly. The investigators reported that all burn sites healed in 2 weeks to 4 months. They provided no data on initial lesion size.

5.1.2 Controlled Studies

Wolcott et al.[528] randomized some of the patients from the case series [see section 5.1.1], using 8 patients (6 paraplegics, 1 with chronic varicosities, 1 with rheumatoid arthritis) with contralateral lesions in an “embedded RCT.” Patients underwent LIDC therapy on 1 lesion and saline-soaked gauze therapy on the other. Three-quarters of LIDC-treated lesions healed after 15.4 weeks compared to none of the conventionally treated. All patients had greater healing of 1 lesion (volumetric measurement) by LIDC than by conventional therapy. The weekly healing rate (volumetric decrease in lesion size per week) was 27.0% for LIDC therapy compared to 5.0% for controls. This study suffers from 2 major weaknesses. First, because the investigators did not specify initial lesion sizes, we cannot be certain that bilateral lesions on patients were the same size. Substantial differences in lesion size, even on the same patient, can lead to substantially different healing rates expressed as percentages [see section 4]. Second, the investigators did not demonstrate that the effect of LIDC is localized to the treatment site and has no effect on the contralateral lesions. This may confound outcomes.

Gault and Gatens[529] also randomized 6 patients from their case series) [see section 5.1.1] with contralateral lesions. Patients underwent LIDC therapy on one lesion and conventional therapy on the other lesion. After a mean of 4 weeks, the mean percentage of lesion healed was 74.0% for LIDC-treated lesions and 27.3% for conventionally treated lesions. The mean healing ratio (percentage of lesion healed per week) was 30.0% for LIDC- and 14.7% for conventionally-treated lesions. This study suffers from 4 major weaknesses. First, the investigators did not specify initial lesion size. Second, they did not specify whether lesion size was measured by surface area and/or volume. Healing rates by surface area may substantially differ from healing rates by volume. Third, they did not demonstrate that the effect of stimulation is localized to the treatment site. Fourth, they did not specify the type of ulcer (e.g., venous, decubitus, diabetic), which also influences the percentage of patients healing and healing rates.

Akers & Gabrielson[530] conducted a controlled comparison among patients with decubitus ulcers undergoing high-voltage direct current (galvanic) stimulation (DC) with whirlpool (WP) therapy twice daily, DC alone, and WP once daily. The investigators found no significant difference between the healing rates of these therapies. However, this study has several weaknesses. First, the investigators did not specify treatment regimen or ES parameters. Second, they did not specify the number of patients in each treatment group. Third, they did not provide any patient characteristics (e.g., age) or lesion data (e.g., duration, stage). Fourth, they did not specify initial lesion sizes.

In an RCT, Carley & Wainapel[531] treated 15 patients who had unspecified lesions by a regimen similar to Wolcott et al. (2-hour daily sessions of 300 to 700 μA twice daily) and 15 by conventional therapy. They matched patients in each treatment group by age, diagnosis, wound size, and wound etiology. They reported patients undergoing LIDC healed 1.5 to 2.5 times faster than those treated conventionally. Wounds were significantly smaller by LIDC therapy than conventional therapy after 3 weeks (LIDC = 1.11 ±0.42 cm^3 {SD}, control = 2.62 ±0.98 cm^3;, 4 weeks (LIDC = 0.69 ±0.26 cm^3, control = 2.48 ±0.85 cm^3); and 5 weeks (LIDC = 0.50 ±0.20 cm^3, control = 2.16 ±0.88 cm^3). This study suffers from 3 flaws. First, the most important shortcoming is that the investigators did not specify the types of lesions treated. We cannot determine whether these outcomes pertain to venous, decubitus, and/or diabetic ulcerations. Second, the follow-up duration is only 5 weeks. [See section 4.2.1.] From data provided, we cannot determine whether LIDC-treated wounds completely heal faster than controls. Third, the outcomes may be confounded because of differences in concomitant therapy. Some patients received saline-damped gauze whereas others received ". . . various absorption gels daily. . . ." The investigators did not demonstrate that these differences did not bias outcomes from the LIDC- and/or conventionally treated groups.

Katelaris et al.[532] conducted a comparative (nonrandomized) controlled trial on 24 patients with venous leg ulcers. Four patients received LIDC with povidone-iodine soaked gauze, 11 received povidone-iodine therapy alone, 5 received LIDC with saline-soaked gauze, and 4 received saline-soaked gauze alone. LIDC therapy was 20 μA current using a regimen similar to Wolcott et al. The investigators observed no significant difference in healing between the groups. LIDC with povidone-treated patients healed in 85.3 ±7.2 days (mean ± SE) compared to 49.2 ±4.3 days for those treated by povidone alone; LIDC with saline-treated patients healed in 45.9 ±6.4 days compared to 46.1 ±7.2 days. This study has 2 flaws. First and foremost, the sample size is very small. The study suffers from lack of statistical power. Three of the 4 treatment groups have ≤5 patients. This study would not be able to detect any significant difference between groups unless there was a huge effect size. Second, patients were apparently not randomly assigned to groups.

5.2 Pulsed Current Studies

Outcomes of PC studies of wound healing (reported by study investigators) are presented in **Table 5.2**. Studies in sections 5.2.1 and 5.2.2 are presented in chronological order.

5.2.1 Uncontrolled Studies

Thurman & Christian[533] treated a diabetic patient who had a draining abscess to a "high frequency" direct current once or twice daily for 4 weeks. The lesion healed within 4 months.

Ross & Segal[534] reported treating 2 patients following foot surgery with HVPC (negative polarity at wound site, 4 Hz pulses for 15 minutes, then reversed polarity with 80 Hz pulses). Patients reported minimal postoperative pain and swelling.

Weiss et al.[535] treated donor skin graft sites of 4 patients with pulsed current stimulation (peak current = 35 mA, frequency = 128 Hz, pulse width = 150 μs) with positive polarity for two 30-minute sessions for a week. They observed reduced scar thickness and hypertrophic scar formation.

Unger[536] reported treating 223 wounds (average duration 2.4 months) with HVPC (150 V or 750 mA peak current at 50 Hz, negative polarity initially over wound for 6 days). They reported 200 wounds (89.7%) healed in a mean healing time of 10.85 weeks (54.25 days). However, the investigators did not specify wound type and omitted important specifics of the regimen (length of treatment sessions, number of session per day, duration of treatment).

Fitzgerald & Newsome[537] treated a quadriplegic patient who had a large wound overlying the thoracic spine to monophasic HVPC (100 to 200 V, 80 to 100 Hz) for daily 1-hour sessions (switching polarity after 20 minutes). The ulcer healed after 10 weeks.

Mawson et al.[538] found that HVPC (75 V, 10 Hz) increased the typically low levels of sacral transcutaneous oxygen tension in patients with spinal cord injuries.

5.2.2 Controlled Studies

In a single-blind RCT, Feedar & Kloth[539] treated patients who had stage IV decubitus ulcers to HVPC (100 V, 105 Hz, 100 μs intraphase interval, polarity reversed after 3 days) or a sham device for daily 45-minute sessions (5 sessions per week, 4 to 16 weeks). Five patients underwent HVPC therapy; 3 received placebo therapy. All HVPC patients healed (in a mean of 7.3 weeks).

HVPC-therapy wounds decreased a mean of 25.3% per week whereas placebo-therapy wounds increased a mean of 13.8% per week (in a mean of 10.6 weeks). The investigators did not provide initial lesion sizes.

In a subsequently published study,[540] Kloth & Feedar used the same therapeutic regimen on 16 patients with stage IV decubitus ulcers (9 HVPC, 7 sham). All HVPC-therapy lesions had healed after 16 weeks, but none of the placebo-therapy lesions had healed after 17 weeks. The mean (and SD) healing rate of HVPC-treated wounds decreased 44.8% ±22.6% per week compared to an 11.6% ±18.6% increase per week for placebo-treated wounds. This study has 2 flaws. First, lesion etiologies of the study groups are dissimilar (heterogeneous). The primary diagnoses of the treatment group includes 3 patients with diabetes, 2 with cerebrovascular accidents, 2 with peripheral vascular disease, 1 with a pilonidal cyst, and 1 with a lower extremity fracture; primary diagnoses of the control group include 1 patient with diabetes, 2 with cerebrovascular accidents, 0 with peripheral vascular disease, 1 with a pilonidal cyst, 0 with a lower extremity fracture, 1 with a stasis ulcer, 1 with anemia, and 1 with senile dementia. Adequate perfusion and nutrition are essential for wound healing. The differences between these groups includes patients with substantially different levels of perfusion and nutrition (e.g., diabetes, peripheral vascular disease, anemia), which can affect wound healing. Such heterogeneity in conjunction with small study groups may confound outcomes. Second, some patients underwent additional debridement by Biozyme-C®. Unless we know which patients (or at least the proportional number) in each group who received Biozyme-C debridement, the outcome may be confounded by this inconsistency in concomitant therapy.

Unger et al.[541] performed a double-blind RCT on patients with pressure ulcers. Nine patients received the same HVPC therapy specified by Unger in section 5.2.1; 8 patients underwent placebo-therapy with a sham device. Eight HVPC-treated patients (88.9%) healed, whereas 3 placebo-treated patients (37.5%) healed. HVPC-treated wounds healed in an average of 51.2 days compared to 77.0 days for those treated by sham devices. This study has several weaknesses. (Some of these shortcomings may be reporting omissions because this was an abstract.) First, the study is small and therefore has low statistical power. Second, the study did not provide sufficient patient and lesion characteristic data to ascertain whether these groups are similar (homogeneous). The investigators did not specify lesion stage which can affect healing rates and percentage of patients who completely heal. Third, the study did not provide initial lesion size. Fourth, the investigators did not specify any elements of concomitant therapy (e.g., debridement, dressings). Unless one knows that the concomitant therapy did not vary within or between treatment groups, one cannot be certain that inconsistencies in this therapy did not confound outcomes.

In a double-blind RCT, Feedar et al.[542] treated 50 patients who had stages II through IV decubitus ulcerations of mixed etiologies. Twenty-six patients

(22 stage III, 4 stage IV) received PDC therapy (30-minute sessions BID of 35 mA at 128 Hz every day for 4 to 16 weeks, polarity reversed every 3 days after wound debrided); 24 patients (2 stage II, 17 stage III, 5 stage IV) received sham-therapy. The frequency was reduced to 64 Hz when stage III or IV lesions improved to stage II. After 4 weeks, none of the patients had healed in either group. The investigators reported a significantly greater reduction in the percentage of wound size after 4 weeks with PDC therapy (43.9% of original size) than sham therapy (67.2%). PDC-treated lesions healed an average of 14%/week compared to 8.25%/week for sham-treated lesions. Mulder[543] also reported outcomes from this study, noting that, after 4 weeks, 38.5% of PDC-treated lesions exhibited excellent healing (<25% of their original size) versus 20.8% for sham-treated, 53.8% exhibited good healing (50% to 75% of original size) versus 33.3%, and 7.7% exhibited poor healing (≥75% of original size) versus 45.8%. Fourteen patients in the sham group "crossed over" to PDC; 6 (42.9%) of these completely healed. This study has many potential shortcomings. First, the study groups combined patients with acute duration lesions (<1 month) with long-standing lesions (>12 months). Although the percentages of these patients do not significantly differ among the groups, combining these patients makes it difficult to interpret outcomes. Second, the groups combined patients with different etiologies: decubitus (65% of PDC group, 75% of control group); postoperative (23% of PDC, 13% of controls); vascular (0% of PDC, 4% of controls); and traumatic (12% of PDC, 8% of controls). These may not confound the outcomes, but unless outcomes are provided separately for these different types of lesions, the results may be difficult to interpret. Third, the investigators expressed surface area of lesions as the product of length multiplied by width. As stated previously [see section 4], length times width is an accurate measurement of surface area only if the wound is exactly rectangular. This introduces a systematic error in all outcome measurements. Fourth, the investigators changed the pulse rate from 128 Hz to 64 Hz when lesions improved to stage II. However, they did not provide individual patient or summary data for these changes in ES therapy. Without such data, it is difficult to interpret whether the change in frequency altered the healing rate or confounded PDC outcomes. Fifth, the follow-up duration of most patients in the study was too short. Only 12 patients (46%) of the PDC group were followed for at least 8 weeks. Six patients of the 14 patients followed for <8 weeks had lesions ≤20% of their original size, indicating that a longer follow-up time might have yielded substantially different total healing rates. Sixth, some patients received surgical or whirlpool debridement. Although 10% of both patient groups received debridement, this therapy was not consistent because surgical debridement may have been used predominantly in one group compared to whirlpool debridement. This could confound outcomes.

In a single-blind RCT, Griffin et al.[544] treated 17 patients who had grade II through IV decubitus ulcers. Eight patients (2 grade II, 5 grade III, 1 grade IV) received HVPC therapy (1 hr daily sessions of 200 V at 100 Hz for 20 days, no polarity reversal) and 9 patients (2 grade II, 6 grade III, 1 grade IV) received

sham therapy.[o] After 20 days, 3 HVPC lesions (37.5%, including 2 grade II and 1 grade III) and 2 sham-therapy lesions (22.2%, both grade II) had healed. This study had 3 major shortcomings. First, study groups were small. There is insufficient statistical power for concluding the efficacy of HVPC for grade II decubitus lesions, much less more severe ulcerations. Second, the follow-up duration is short. The last phase of healing does not normally begin until 3 weeks after injury. The follow-up time is probably inadequate to observe complete healing of grade II lesions, let alone more severe lesions extending through subcutaneous tissue. Third, the investigators only provided the median initial lesion size. A median[p] is often an inadequate measure of distribution, especially in nonnormal distributions (e.g., bimodal).

In a double-blind RCT, Gentzkow et al.[545] treated 21 patients who had decubitus ulcers. Twenty-one stage IV patients received an PDC therapy nearly identical to Feedar et al. (1991); 19 patients (1 stage III, 18 stage IV) received sham-therapy. The investigators reported a significantly greater healing in the percentage of wound size after 4 weeks with PDC therapy (49.8%) than by sham therapy (23.4%). PDC-treated lesions healed an average of 12.5%/week compared to 5.8%/week for sham-treated lesions. Fifteen patients in the sham group "crossed over" to PDC; after 4 weeks of stimulation, the percentage of surface area healed was 47.9%, significantly greater than with previous sham therapy. This study had outcomes and shortcomings similar to Feedar et al. (1991). First, the study groups combined patients having acute duration lesions (<1 month) with long-standing lesions (>12 months), which makes it difficult to generalize outcomes. Second, the investigators expressed surface area of lesions as the product of length multiplied by width, introducing a systematic error in all outcome measurements. Third, the investigators changed the pulse rate from 128 Hz to 64 Hz when lesions sufficiently improved without providing individual patient or summary data for these changes. Fourth, the investigators reported on the percentage of ulcers healed at 1, 2, 3, and 4 weeks after initiating therapy and found significant differences between PDC and sham therapy at 1, 2, and 4 weeks. However, it appears that they used repeated t-tests between these intervals. If so, this is invalid. A more proper test would have been an analysis of variance (ANOVA) to reduce the risk of finding a statistically significant result that was due to chance.

In an RCT, Gogia et al.[546] treated 12 patients who had stage III lesions (full-thickness skin loss) of mixed etiologies on the leg or foot. Six patients (3 diabetic, 2 decubitus, 1 venous stasis) received HVPC therapy (daily 20-minute sessions of 250 V at 100 Hz for 20 days, negative polarity for 4 days, positive polarity for

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[o] Grade II: a break in or blistering of the epidermis, surrounded by erythema and induration; Grade III: a shallow, irregular defect extending through the dermis to the subcutaneous fat junction; Grade IV: ulcer extending through the full thickness of the skin into the subcutaneous tissue, fascia, or muscle.

[p] Medians are often reported when data are highly variable.

16 days) and 6 patients (2 diabetic, 3 decubitus, 1 venous stasis) received whirlpool therapy. After 20 days, 37.4% of HVPC-treated lesions had healed compared to 27.2% for control lesions. The healing rates did not significantly differ. This study has several weaknesses. First, these study groups are small, so this study has little statistical power. Second, lesion etiologies are heterogeneous. Patients in these groups have substantially different degrees of tissue perfusion. (Diabetics would be expected to have worse tissue perfusion than patients with venous stasis ulcerations.) Although there is no significant difference between the types of patients in each treatment group, such differences can confound interpretation of outcomes, particularly in studies with such small sample sizes. Third, the investigators did not provide a measure of variance for interpreting healing rates. Fourth, the follow-up time was only 20 days, which is inadequate to observe complete healing. Fifth, some patients had debridement, which may confound outcomes by inconsistencies in concomitant therapy.

In a double-blind RCT, Wood et al.[547] treated 78 patients who had stage II or III decubitus ulcerations. Forty-three patients underwent PDC therapy (300 µA followed by 600 µA at 0.8 Hz, 3 times weekly, initial negative polarity) and 31 patients received sham therapy. Three patients (2 PDC and 1 sham therapy) were lost to follow-up. After 8 weeks, 25 (58%) of the PDC-treated ulcers healed compared to one (3%) of the sham-treated ulcers. Seventy-three percent of PDC ulcers decreased 80% within 8 weeks compared to 13% of sham-treated ulcers. Surface area and ulcer depth healing rates were significantly greater with PDC therapy than sham therapy. The major flaw of this study was that the investigators did not specify the duration of each treatment session.

5.3 Alternating Current (and TENS) Studies

Outcomes of alternating current studies of wound healing (reported by study investigators) are presented in **Table 5.3**. Studies in sections 5.3.1 and 5.3.2 are presented in chronological order.

5.3.1 Uncontrolled Studies

Westerhof & Bos[548] treated a patient who had severe (trigeminal) neurotrophic facial ulcers with 30-minute sessions of TENS therapy TID (sufficient energy to cause vigorous contractions, 120 Hz, 250 µs pulse width, 0.5 sec pulse train interval). The ulcerations healed after 6 weeks of therapy.

Kaada[549] treated 10 patients who had ulcers of mixed etiology (traumatic neuropathy, arteriosclerosis, venous stasis ulcers, thrombophlebitis, decubitus ulcers, and scleroderma) to TENS therapy. Patients used a pocket stimulator to apply trains of 5 pulses (15 to 30 mA at 100 Hz internal frequency, 0.1 to 0.2 ms duration) for 30- to 45-minute sessions TID. Seven of the lesions healed after 22 weeks.

Barron et al.[550] treated 6 patients who had decubitus ulcers with a "percutaneous low-energy nongalvanic stimulator." The stimulation was a modified biphasic square wave of 600 µA, 50 V at 0.5 Hz administered percutaneously by electrodes positioned 2 cm from the edge of the ulcer. Patients underwent sessions TID (of unspecified duration) for 3 weeks. Two patients (22.2%) completely healed and 3 others nearly healed (remaining surface area <0.1 cm^2).

In an abstract, Alon et al.[551] reported treating 15 patients who had diabetic foot ulcers with "high voltage TENS" therapy. Patients underwent stimulation by 200 V, 80 Hz, 5 to 10 µs pulse durations for 1-hour sessions TID. Twelve patients (80%) healed in a mean of 11.1 weeks.

Kaada & Emru[552] treated 32 patients suffering from leprosy with TENS therapy. Patients used a pocket stimulator to apply trains of 5 pulses (25 mA at 100 Hz internal frequency, 0.1 to 0.2 ms duration) for 30-minute sessions, BID, 5 to 6 days per week. Fifty-nine percent of the patients healed after 12 weeks of therapy; all of those who completed therapy healed in a mean of 5.2 weeks. The mean healing index was 1.0 cm^3 per week and was 3 times greater in patients with tuberculous leprosy than those with the lepromatous type.

Frantz[553] treated 4 patients who had decubitus ulcers with 30 minutes of TENS therapy TID (30 mA at 85 Hz, constant square-wave pulses, 150 µs pulse width, 1 set of electrodes on hands and other set with anode proximal and cathode distal to lesion). After 4 weeks, 1 lesion had healed.

Karba et al.[554] treated 32 patients who had vascular wounds (diabetes or peripheral vascular disease), 14 patients with decubitus ulcers, and 17 patients with posttraumatic wounds with a biphasic, asymmetrical alternating current of 15 to 25 mA (4 second trains at 40 Hz repetition, 0.25 ms pulse duration) for 1-hour daily sessions. Forty-nine wounds (77.8%) healed in the rehabilitation center and an additional 11 (17.4%) healed 2 to 3 weeks after discharge. All decubitus lesions had healed after 5.5 weeks; 90.6% of all vascular lesions had healed after 10 weeks. The investigators calculated the healing rate based on an exponential model. Healing was described by a normalized healing rate, theta (?), which is normalized to the initial wound size. [See section 6.] Theta is calculated as follows:

$$? = \ln[(S_0/S)] \div t$$

where S_0 is the initial wound size, S is the size of the wound at a given time `t,' and t is the time (usually expressed in weeks). Theta describes the rate of wound healing. Values of ? >0 implies that the wound is healing; greater positive values of ? imply faster healing. Values of ? <0 imply that the wound, in fact, is growing larger; greater negative values of ? imply increased wound deterioration. At ? = 0, the wound is neither healing nor deteriorating. The investigators observed that the healing rates depended on the type of wound. The normalized healing rates were ? = 1.02 ±0.26 (SE) per week for post-traumatic lesions, ? = 0.83 ±0.33 per week for decubitus ulcers, and 0.47 ±0.09 per week for vascular lesions.

5.3.2 Controlled Studies

Finsen et al.[555] treated 51 patients who were scheduled to undergo a Syme's, below-knee, or through-knee amputation for ischemic changes due to diabetes or arteriosclerosis. Patients either underwent TENS stimulation, sham TENS therapy, or sham TENS therapy and chlorpromazine. The investigators reported fewer re-amputations and more rapid stump healing among below-knee amputees who had received active TENS, and that sham therapy decreased pain. However, this study did not directly address wound healing.

In a single-blind randomized trial, Lundeberg et al.[556] treated 24 patients who had recently undergone reconstructive surgery for breast cancer with TENS therapy or sham stimulation. The investigators primarily evaluated blood flow to the postoperative skin flaps and did not specify the rate of wound healing. In a subsequent randomized crossover trial on 20 patients, Kjartansson & Lundeberg[557] observed that local blood flow and capillary refill significantly increased in skin flaps treated by TENS therapy. The study did not directly address wound healing.

Frantz[558] reported preliminary findings in an ongoing RCT employing TENS therapy described in section 5.3.1. However, the report only included 3 patients, which is insufficient for analysis or critique.

In a double-blind RCT, Lundeberg et al.[559] treated 64 patients who had diabetic leg ulcers. Thirty-two patients received TENS therapy (AC constant current square-wave pulses applied outside the ulcer surface at sufficient intensity to evoke paresthesia, 1 ms pulse width at 80 Hz, 20-minute sessions BID) and 32 patients received sham therapy. The polarity was changed after each session. After 4 weeks, 12% of TENS lesions had healed compared to 7% of those treated by sham units. After 8 weeks, 25% of TENS-treated lesions had healed compared to 11% of sham treated. After 12 months, 42% of TENS-treated had healed compared to 15% of sham treated. The only shortcoming of this study was that it did not describe the diabetic population in the study (e.g., insulin-dependent versus non-insulin-dependent), which could affect outcomes.

In an RCT, Stefanovska et al.[560] treated 150 patients who had decubitus ulcers with AC, DC, or conventional therapy. Eighty-two patients received biphasic AC therapy similar to Karba et al.[see section 5.3.1], except that sessions were 2 hours daily; 18 patients received LIDC therapy (600 μA for two hours daily); 50 control patients received conventional therapy. The investigators reported normalized healing rates (expressed in percent per day) of ? = 5.43% ±4.4% (SD) per day for AC-treated ulcers, ? = 3.11% ±3.83% for LIDC-treated ulcers, and 2.21% ±3.27% for controls. They stated that AC current produced a significantly greater rate of normalized wound healing than controls. This study has several shortcomings. First, the investigators did not specify the stage of decubitus ulcers in the study. Without knowing the number or type of ulcer stages in each treatment group, the outcomes may be confounded. For example, if the AC group consisted primarily of stage II lesions and the control group consisted primarily of stage IV lesions, we would expect slow healing rates in the control group. Second, the investigators did not specify the “conventional therapy” used on the control group. Without knowing the regimen, the therapy may not reflect accepted standards of care. Third, they did not specify what type of concomitant therapy was administered to patients in the AC and LIDC groups. This could potentially confound outcomes.

5.4 Pulsed Electromagnetic Induction Studies

Outcomes of pulsed electromagnetic induction (PEMI) studies of wound healing (as reported by study investigators) are presented in **Table 5.4**. Studies in sections 5.4.1 and 5.4.2 are presented in chronological order.

5.4.1 Uncontrolled Studies

Itoh et al.[561] treated 22 patients who had stages II and III decubitus ulcers of mixed etiology (cerebrovascular accident, multiple sclerosis, spinal cord injury, and diabetes) with pulsed, nonthermal, high-frequency, high peak power electromagnetic energy (27.12 MHz, 80 to 600 pulses/sec, 65 μs pulse width, 293 to 975 W/pulse peak) administered from a device placed on the surface of the wound dressing. Patients underwent 30-minute sessions BID until lesions healed. All 9 stage II patients healed after 6 weeks of therapy; all 13 stage III patients healed after 22 weeks of therapy. However, the patient groups were heterogeneous (e.g., diabetic and nondiabetic). Concomitant therapy variations included cleansing agents (e.g., hydrogen peroxide, normal saline, povidone-iodine) and dressings (e.g., Bacitracin ointment, povidone iodine wet-to-dry, acetic acid wet-to-dry, Vaseline gel, Silvadene, hydrogen peroxide wet-to-dry).

Tung et al.[562] treat 4 four patients who had stage IV decubitus ulcers (including 1 diabetic) with PEE therapy using a regimen similar to Itoh et al. All ulcers healed regardless of size.

5.4.2 Controlled Studies

In a double-blind RCT, Wilson[563] treated 40 patients who had soft tissue injuries around the ankle. Twenty patients received PEE therapy (up to 975 W emission for 65 μs at 27.12 MHz, 1-hour daily sessions for 3 days); 20 patients received sham therapy. The investigators observed significantly reduced swelling disability and pain in patients treated by PEE. However, this study did not address healing of lesions.

In a double-blind RCT, Goldin et al.[564] treated the donor sites of 67 patients who underwent medium-thickness split-skin grafting. Twenty-nine donor sites received PEE therapy (25.3 W mean energy output, one 30-minute session preoperatively and one 30-minute session 6 hours postoperatively); 38 patients received sham therapy. The investigators observed that 1 week postoperatively, ≥90% of the lesions had healed in 17 PEE-treated sites (58.6%) compared to 11 (29.0%) sham-treated sites. However, this study did not address *chronic* wound healing.

In a double-blind RCT, Jeran et al.[565] treated 21 patients who had venous ulcers. Eleven patients (with 11 ulcers) received PEMF therapy (2.7 mT magnetic field at 75 Hz, 1.3 ms pulse width); 10 patients (with 11 ulcers) received sham therapy. Patients were instructed to use the stimulators at home for 3 to 4 hours a day for 90 days or until complete healing. The investigators reported that 10 ulcers (90.9%) in the PEMF-treated group had healed in a mean of 71 days whereas 5 (45.5%) in the sham-treated group had healed in a mean of 78 days. In the follow-up published study 3 years later, Ieran et al.[566] reported treating 18 patients with PEMF and 19 with sham therapy. After 90 days of therapy, significantly more PEMF-treated patients completely healed (12 patients, 66.6%) than sham treated (6 patients, 31.5%). One year after the start of therapy, significantly more PEMF-treated patients had healed (16 patients, 88.8%) than sham treated (8 patients, 42.1%). PEMF-treated lesions completely healed in an average of 71 days compared to 76 days for sham-treated lesions. Patient compliance was objectively monitored and did not significantly differ between the groups. This study has several weaknesses. First, the investigators included patients with diabetes (27.8% of experimental group, 10.5% of control group), which can confound outcomes. Second, the investigators did not provide a measure of the initial ulcer sizes for all patients in the study. This may affect outcomes, particularly if the differences between initial wound sizes in groups significantly (or nearly significantly) differed. Third, the investigators reported that ". . . oral and local antibiotic therapy was always given concomitantly . . . ." This may be a source of confusion. If the same antibiotics were administered to all patients in a group for prophylaxis, then this is not a source of confounding. If, however, the antibiotics were used to combat ongoing infections, then use of the same agents against different and/or resistant organisms is itself a source of confounding because some patients will benefit from antibiotic therapy whereas others will not.

In a double-blind RCT, Todd et al.[567] treated 19 patients who had chronic venous ulcers. Ten patients received PEMF therapy ("field strength set at 60" [sic] at 5 Hz intensity, 15-minute sessions twice weekly for 5 weeks); 9 received sham therapy. The investigators found no difference between the healing rates of the 2 groups. There are 3 major shortcomings in this study. First, the number of patients in each group was small (≤10 patients); the study has little statistical power. Second, the investigators provided no measures of variance. Without such measurements, it is not possible to verify whether there was any significant difference between treatment groups. Third, the follow-up period was too brief to adequately determine the number of patients who completely healed.

In a double-blind RCT, Stiller et al.[568] treated 31 patients who had chronic venous ulcers. Eighteen patients received PEMF therapy (0.06 mV/cm, 22 Gauss, 3.5 ms total width pulse, applied 3 hours per day at home on top of dressing for 8 to 12 weeks); 13 received sham therapy. After 8 weeks, the wound surface area healed was significantly greater in PEMF-treated lesions than sham-treated lesions. PEMF-treated lesions decreased a mean of 47.1% whereas the

sham-treated lesions increased 48.7%. This study has several flaws. First, both active and placebo groups used 6 different types of dressings and topical agents (Duoderm® dressing, gentamicin ointment and Duoderm dressing, mupirocin ointment and Vigilon®, mupirocin ointment and nonadherent gauze, Elase® debridement ointment and gauze, and Unna boot). Although there appeared to be no significant difference in use of these concomitant therapies between treatment groups, the investigators are combining different types of conventional therapies, which may have different effects on healing. This may introduce confounding. In addition, one is left to wonder what does constitute conventional therapy in such a heterogeneous treatment group. Second, the investigators did not specify how they monitored patient compliance (proper utilization of the devices at home), which can lead to biased outcomes. Third, the investigators did not specify whether variances reported in their study were standard error or standard deviation. This can lead to confusion in interpreting outcomes.

In a double-blind RCT, Salzberg et al.[569] treated 30 patients who had decubitus ulcers (20 stage II and 10 stage III). Patients received PEE therapy (10 stage II, 5 stage III) by the same regimen described in Itoh et al.[see section 5.4-1] or sham therapy (10 stage II, 5 stage III) for 12 weeks or until lesions healed. Nine of ten stage II PEE-treated patients healed within 3 weeks[q] whereas all stage II sham-treated patients required ≥3 weeks. (All sham-treated patients healed in 11.9 weeks.) The median percentage of stage II patients who healed at 1 week was significantly greater for the PEE-treated group than the sham-treated group. PEE-treated patients required a median of 13.0 days for complete healing compared to 31.5 days for sham treated. Among patients with stage III ulcerations, three (60%) of the PEE-treated healed whereas none of the sham treated healed after 12 weeks. This study has 1 main flaw: it described lesion surface area as the product of its length and width. This introduces a systematic error throughout outcome measures.

[q] One patient died of unrelated causes.

5.5 Spinal Cord Stimulation Studies

Outcomes of implanted SCS studies of wound healing (reported by study investigators) are presented in **Table 5.5**. Studies in sections 5.5.1 are presented in chronological order.

5.5.1 Uncontrolled Studies

Cook et al.[570] treated a patient who had a foot ulcer due to obliterative arterial disease by epidural spinal cord stimulation. The site healed after 8 weeks of stimulation.

Richardson et al.[571] reported complete healing of a decubitus ulcer in a patient suffering from paraplegia after therapy with implanted epidural lumbar electrodes (1.0 to 1.5 V, 33 to 50 Hz, 200 μs pulse duration).

Meglio et al.[572] reported complete healing of a trophic foot ulcer in a patient suffering from arteriosclerosis after 9 months of therapy with an epidural spinal cord stimulator (electrode tips at T-7 and T-8 spinal levels, bipolar stimulation, 60 Hz, 0.5 msec, 1 to 2 hours nightly).

Graber & Lifson[573] treated 9 patients suffering from limb-threatening ischemia to implanted spinal cord stimulation. None of the patients completely healed and ulcer healing was “erratic.”

Jivegard et al.[574] treated 32 patients (25 arteriosclerotic disease, 7 diabetic) with spinal cord stimulation (voltage sufficient to induce paresthesia, 100 Hz, 0.2 msec pulse width, treatment duration at patient discretion). Half of the patients had ischemic skin ulcers. (The investigators did not specify which patients.) One year after therapy, 47% of the arteriosclerotic patients with lesions had complete healing, and 1 of the diabetic patients with skin lesions had complete healing.

5.5.2 Controlled Study

In an RCT, Jivegard et al.[575] studied the effect of SCS on limb salvage in 51 patients (41 arteriosclerotic, 10 diabetic) with inoperable severe leg ischemia. Twenty-five patients received SCS and peroral analgesic therapy; 26 received peroral analgesic therapy alone. After 18 months follow-up, the limb salvage rates did not significantly differ (62% for SCS, 45% for controls). This study did not directly report wound healing outcomes.

5.6 Ongoing Studies

We identified 4 ongoing studies in a search of Federal Research in Progress[576]: 2 studies of TENS for pressure ulcers, 1 study of PEMF for pressure ulcers in patients with spinal cord injuries, and 1 study of pulsed radio frequency diathermy for pressure ulcers in patients with spinal cord injuries. [See Table 5.6.] All ongoing trial protocols are randomized and controlled.

5.7 Tables

Table 5.1. Outcomes Reported by Investigators in Direct Current Studies of Wound Healing

Study	Electrical Stimulation	Study Type	Number of Patients or Ulcers	% Patients Healed	Other Reported Outcomes
Katelaris et al.[577] (1987)	LIDC	Comparative controlled	14 povidone vs. 4 LIDC + povidone; 4 saline; 4 saline + LIDC	Not available	Healing times (mean days ±SE): povidone = 49.2 ±4.3 (SE); povidone + LIDC = 85.3 ±7.2; saline = 46.1 ±7.2; saline + LIDC = 45.9 ±6.4; no significant differences between groups
Carley & Wainapel[578] (1985)	LIDC	RCT	15 LIDC ulcers vs. 15 control: TYPE NOT SPECIFIED	Not available	Sizes (mean cm^3 ±SD)— Initial: LIDC = 4.74 ±1.39, control = 3.92 ±1.24; 3rd week: LIDC = 1.11 ±0.42, control = 2.62 ±0.98; 4th week: LIDC = 0.69 ±0.26, control = 2.48 ±0.85; 5th week: LIDC = 0.50 ±0.20, control = 2.16 ±0.88; LIDC therapy significantly better than control for weeks 3 to 5 weeks
Akers & Gabrielson[579] (1984)	DC	Comparative controlled	14 decubitus ulcers: DC vs. DC + WP vs. WP	Not available	Correlation coefficient (*r*) for wound healing for patients receiving HVDC = 0.957; *r* <0.5 for patients receiving WP alone or WP + HVDC; no significant difference between groups
Gault & Gatens[580] (1976)	LIDC	Case series	100 ulcers (mixed)	48%*	Mean healing ratio = 28.4%/week; Mean % of lesion area healed = 80.5%; Mean treatment time = 4.7 weeks
		"Embedded" RCT#	Contralateral lesions on 6 patients: 6 LIDC + 6 control ulcers	50%*	Mean healing ratio: LIDC = 30.0%, control = 14.7%; Mean % lesion area healing: LIDC = 74.0%, control = 27.3%; Mean treatment time: LIDC = 4 weeks, control = 4 weeks

Table 5.1. Outcomes Reported by Investigators in Direct Current Studies of Wound Healing (continued)

Study	Electrical Stimulation	Study Type	Number of Patients or Ulcers	% Patients Healed	Other Reported Outcomes
Wolcott et al.[581] (1969)	LIDC	Case series	75 ulcers (mixed)	40%*	Paraplegics (N = 53): 9.3% weekly healing rate, 80.5% overall mean % volume decrease; Peripheral arteriosclerotic (N = 15): 14.4% weekly healing rate, 82.2% overall mean volume decrease; Venous stasis (N = 5): 14.4% weekly healing rate; 85.0% overall mean volume decrease; Others (N = 2): 100% weekly and overall healing
		"Embedded" RCT#	Contralateral lesions on 8 patients: 8 LIDC + 8 control ulcers	75% LIDC @ 15.4 weeks; 0% control @ 15.4 weeks	Weekly healing rates (% volume decrease/week): LIDC ulcers = 27.0%, control = 5.0%
Assimacopoulos[582] (1968)	LIDC	Case report	3 venous ulcer patients	100% @ 6 weeks	—

WP = whirlpool

* Precise duration for healing not specified.

\# "Embedded" RCT = patients with bilateral lesions (within a case series) treated by ES on one lesion and a control therapy (non-ES) on the contralateral lesion.

Excluded: Fakhri & Amin[583] (study of burn patients)

Table 5.2. Outcomes Reported by Investigators in Pulsed Current Studies of Wound Healing

Study	Electrical Stimulation	Study Type	Number of Patients or Ulcers	% Patients Healed	Other Reported Outcomes
Wood et al.[584] (1993)	PDC	Double-blind RCT	Stage II/III decubitus ulcers: 43 PDC + 31 sham	@ 8 wks: 56.1% PDC vs. 4.0% sham	73% of PDC ulcers decreased 80% within 8 wks vs. 13% of sham; 0% PDC ulcers increased in size vs. 30% of sham; significant decrease of mean surface area of PDC ulcers compared to controls at 4 to 8 weeks
Fitzgerald & Newsome[585] (1993)	HVPC	Case report	1 quadriplegic with decubitus ulcer	Healed in 10 weeks	—
Gogia et al.[586] (1993)	HVPC	RCT	Mixed ulcer/lesions: 6 HVPC vs. 6 WP	Not available	Rate of surface area healing @ 20 days: 34.7% HVPC vs. 27.2% control; rate of wound depth healing @ 20 days: 30.3% HVPC vs. 56.8% control; observed no increased healing rate of lower leg/foot ulcers
Gentzkow et al.[587] (1991)	PDC	Double-blind RCT	Stage III/IV decubitus ulcers: 21 PDC vs. 19 sham	41% of PDC in average of 11.8 weeks	% of ulceration healed @ 4 wks significantly different: 49.8 ±30.9% SD for PDC, 23.4 ±47.4% SD for sham
Griffin et al.[588] (1991)	HVPC	Single-blind RCT	Grade II-IV decubitus ulcers: 8 HVPC vs. 9 sham	@ 20 days: 37.5% HVPC vs. 22.2% sham	After 20 days— Grade II ulcer healing: 2/2 HVPC vs. 2/2 sham Grade III ulcer healing: 1/5 HVPC vs. 0/6 sham Grade IV ulcer healing: none for HVPC or sham
Feedar et al.[589] (1991)	PDC	Double-blind RCT	Mixed etiology ulcers: 26 PDC vs. 24 sham	@ 4 weeks: 0% PDC vs. 0% sham	Significantly greater reduction in % wound size after 4 wks: 43.9% decrease in PDC vs. 67.2% decrease in sham Average healing rate: 14%/wk PDC vs. 8.25%/wk sham
Mulder[590] (1991)	PDC	Double-blind RCT	Mixed etiology ulcers: 26 PDC vs. 24 sham	Not available	@ 4 wks—Excellent healing (<25% of original size): 38.5% PDC vs. 20.8% sham; Good healing (50% to 75% of original size): 53.8% PDC vs. 33.3% sham; Poor healing (≥75% of original size): 7.7% PDC vs. 45.8% sham

Table 5.2. Outcomes Reported by Investigators in Pulsed Current Studies of Wound Healing (continued)

Study	Electrical Stimulation	Study Type	Number of Patients or Ulcers	% Patients Healed	Other Reported Outcomes
Unger et al.[591] (1991)[Abstract]	HVPC	Double-blind RCT	Decubitus ulcers: 9 HVPC vs. 8 sham	88.9% HVPC vs. 37.5% sham[unspecified time period]	Average time for healing: HVPC = 51.2 days, sham = 77.0 days Average wound area healed: HVPC = 4.60 cm^2, sham = 1.19 cm^2
Unger[592] (1991) [Abstract]	HVPC	Case series	223 (unspecified type) wounds	89.7% healed (mean 10.9 weeks)	—
Kloth & Feedar[593] (1988)	HVPC	Single-blind RCT	Stage IV decubitus ulcers: 9 HVPC vs. 7 sham	100% HVPC @ 16 weeks; 0% sham @ 17 weeks	Healing rate: HVPC = 44.8 ±22.6%/wk (SD), sham = -11.6 ±18.6%/wk
Feedar & Kloth[594] (1985)[Abstract]	HVPC	Single-blind RCT	Stage IV decubitus ulcers: 5 HVPC vs. 3 sham	100% HVPC (mean 7.3 weeks)	Average healing rate: HVPC = 25.3%/wk, sham = -13.8%/wk
Thurman & Christian[595] (1971)	"High frequency" DC	Case report	Diabetic foot ulcer	100% @ 16 weeks	—

Excluded: Ross & Segal[596]: study evaluating postoperative swelling and edema
Weiss et al.[597]: study evaluating healing at donor sites for skin grafting
Mawson et al.[598]: study evaluating sacral transcutaneous oxygen tension in patients with spinal cord injuries

Table 5.3. Outcomes Reported by Investigators in Alternating Current and TENS Studies of Wound Healing

Study	Electrical Stimulation	Study Type	Number of Patients or Ulcers	% Patients Healed	Other Reported Outcomes
Stefanovska et al.[599] (1993)	AC	RCT	Decubitus ulcers: 82 AC vs. 18 LIDC vs. 50 control	Not available	Theta (?) values in %/day: ?(AC) = 5.43 ±4.4% (SD); ?(LIDC) = 3.11 ±3.83%; ?(control) = 2.21 ±3.27% Normalized healing rates for AC significantly greater than control; pulsed current significantly greater than control
Lundeberg et al.[600] (1992)	(T)ENS	Double-blind RCT	Diabetic ulcers: 32 TENS vs. 32 sham	@ 12 weeks: 42% TENS vs. 15% sham	Percentage of ulcers healed at: 2 weeks—0% TENS, 4% sham 4 weeks—12% TENS, 7% sham 8 weeks—25% TENS, 11% sham 12 weeks—42% TENS, 15% sham
Karba et al.[601] (1991)	AC	Case series	Lesions: 82 vascular, 14 decubitus, 17 posttraumatic	95% of all wounds healed (unspecified time)	Complete healing: Vascular lesions = 90.6% healed by 10 weeks, Decubitus lesions = 100% healed by 5.5 weeks Theta (?) values (per week): ?(vascular) = 0.47 ±0.09 (SE), ?(decubitus) = 0.83 ±0.33, ?(post-traumatic) = 1.02 ±0.26
Frantz[602] (1990)	TENS	Case series (pilot study)	Decubitus ulcers: 4 TENS	25% healed @ 4 weeks	—
Kaada & Emru[603] (1988)	TENS	Case series	Lepromatous lesions: 32 TENS	59% healed @ 12 weeks	Mean healing time = 5.2 weeks Mean healing index = 1.0 cm^3/week Mean healing index in tuberculoid type 3 times higher than lepromatous type
Alon et al.[604] (1986)[Abstract]	TENS	Case series	Diabetic foot ulcers: 15 TENS	80% healed (mean 11.1 weeks)	No significant correlation between pre-existing duration of ulcers and healing time; no significant correlation between initial ulcer size and healing time
Barron et al.[605] (1985)	TENS	Case series	Decubitus ulcers: 6 TENS	22.2% healed @ 3 weeks	Significant difference between means of initial lesion size and final reported sizes

Table 5.3. Outcomes Reported by Investigators in Alternating Current and TENS Studies of Wound Healing (continued)

Study	Electrical Stimulation	Study Type	Number of Patients or Ulcers	% Patients Healed	Other Reported Outcomes
Kaada[606] (1983)	TENS	Case report	Mixed lesions/ulcerations: 10 TENS	70% healed @ 22 weeks	—
Westerhof & Bos[607] (1983)	TENS	Case report	Neurotrophic facial ulcers: TENS	Healed @ 6 weeks	—

Excluded: Lundeberg et al. 1988[608]: study of circulation in reconstructive skin flaps
Kjartansson & Lundeberg 1990[609]: study of circulation in reconstructive skin flaps
Finsen et al. 1988[610]: study of prevention of repeated lower extremity amputation

Table 5.4. Outcomes Reported by Investigators in Pulsed Electromagnetic Induction Studies of Wound Healing

Study	Electrical Stimulation	Study Type	Number of Patients or Ulcers	% Patients Healed	Other Reported Outcomes
Salzberg et al.[611] (1995)	PEE	Double-blind RCT	Stage II decubitus ulcers: 10 PEE vs. 10 sham	PEE: 90% @ 3 wks; sham: 100% @ 11.9 wks	Median % patients healed at 1 wk significantly greater for PEE than sham; PEE healed in median of 13.0 days vs. 31.5 days for sham
			Stage III decubitus ulcers: 5 PEE vs. 5 sham	@ 12 weeks: 60% PEE; 0% sham	—
Tung et al.[612] (1995)	PEE	Case report	Stage IV decubitus ulcers: 4 PEE	All healed	—
Stiller et al.[613] (1992)	PEMF	Double-blind RCT	Venous ulcers: 18 PEMF vs. 13 sham	Not available	Significant difference in percentage of wound surface healed: PEMF lesions decreased mean of 47.1% vs. 48.7% increase in sham
Todd et al.[614] (1991)	PEMF	Double-blind RCT	Venous ulcers: 10 PEMF vs. 9 sham	Not available	No significant difference in healing rates of groups; 22.0% reduction for PEMF, 9.1% reduction for control
Itoh et al.[615] (1991)	PEE	Case series	Stage II decubitus ulcers: 9 PEE; Stage III decubitus ulcers: 13 PEE	Stage II: 100% @ 6 wks; Stage III: 100% @ 22 wks	—
Ieran et al.[616] (1990)	PEMF	Double-blind RCT	Venous ulcers: 18 PEMF vs. 19 sham	@ 90 days: 66.6% PEMF; 31.5% sham	Significantly more patients healed after 90 days with PEMF than sham; Significantly more patients healed 1 year posttherapy with PEMF (88.8%) than sham (42.1%); PEMF lesions healed in average of 71 days vs. 76 days for sham
Jeran* et al.[617] (1987)	PEMF	Double-blind RCT	Venous ulcers: 11 PEMF vs. 11 sham	PEMF: 90.9% in mean of 71 days; sham: 45.5% in mean of 78 days	—

* Preliminary study of Ieran et al. 1990

Excluded: Goldin et al. 1981[618]: study of effect on donor sites for medium-thickness split-skin grafting
Wilson 1972[619]: study of soft-tissue (non-wound) healing

Table 5.5. Outcomes Reported by Investigators in Spinal Cord Stimulation Studies of Wound Healing

Study	Electrical Stimulation	Study Type	Number of Patients or Ulcers	% Patients Healed	Other Reported Outcomes
Jivegard et al.[620] (1987)	SCS	Case series	Half of 25 arteriosclerotic + 7 diabetic patients: 16 SCS	47% of arteriosclerotic patients with lesions*; 1 diabetic patient*	—
Graber et al.[621] (1987)	SCS	Case series	Limb-threatening ischemia: 9 SCS	None	Wound healing described by investigators as “erratic”
Meglio et al.[622] (1981)	SCS	Case report	Trophic ulcer in patient with arteriosclerosis	Completely healed @ 9 months	—
Richardson et al.[623] (1979)	SCS	Case report	Decubitus ulcer in paraplegic	Completely healed (duration unspecified)	—
Cook et al.[624] (1976)	SCS	Case report	Foot ulcer in patient with obliterative arterial disease	Completely healed @ 8 weeks	—

* Number of patients with lesions and time required for healing unspecified

Excluded: Jivegard et al. 1995[625]: study of limb salvage rate

Table 5.6. Ongoing Studies of Electrical Stimulation for Wound Healing

Principal Investigator/ Performing Organization	Description of Ongoing Study
Rita Frantz University of Iowa Iowa City, IA	***Title:*** Pressure ulcers in older adults—healing with TENS ***Purpose:*** Determine the effectiveness of TENS on healing of pressure ulcers in older adults. Study will aim to compare the rate of healing of pressure ulcers treated with conventional therapy and compare to patients treated by conventional therapy plus TENS. Study will also compare rate of wound healing and presence of prognostic indicators. ***Description:*** 40 patients randomly assigned to receive TENS therapy (TID for 30 minutes) or sham therapy. All subjects to receive saline-soaked gauze. 8-week follow-up or until healing.
Dr. Carl Sutton Dept. Veterans Affairs Milwaukee, WI	***Title:*** Pulsed electromagnetic field energy in the treatment of pressure ulcers in spinal cord injured patients ***Purpose:*** Study the effectiveness of PEMF on healing of pressure ulcers in spinal cord injured patients. Study will compare healing rates and percentages of pressure ulcers healed. Study will also evaluate safety and cost-effectiveness of PEMF. ***Description:*** 15 to 25 patients in randomized, double-blind study. One group to receive standard moist wound care 7 days/week for 6 weeks; second group to receive active PEMF therapy for 6 weeks; third group to receive sham (placebo) therapy. 10-week follow-up period.
Mary Smerek Dept. Veterans Affairs St. Louis, MO	***Title:*** TENS as an alternative to hydrotherapy in treating pressure sores. ***Purpose:*** Determine if TENS is an effective alternative to hydrotherapy for healing grade III or IV pressure sores ***Description:*** 20 patients >60 years of age randomly assigned to TENS therapy or hydrotherapy for treatment of grade III or IV decubitus ulcers.
Dr. Carl Sutton Dept. Veterans Affairs Milwaukee, WI	***Title:*** Pulsed radio frequency diathermy in the treatment of pressure ulcers in spinal cord injured patients ***Purpose:*** Study the effectiveness of pulsed radio frequency diathermy (RFD) on the healing of pressure ulcers in spinal cord injured patients. Study will compare healing rates and percentages of pressure ulcers healed treated by active and inactive therapy. Will also evaluate safety and cost effectiveness. ***Description:*** 15 to 25 patients in randomized, double-blind study. One group to receive standard moist wound care 7 days/week for 6 weeks; second group to receive active RFD therapy for 6 weeks; third group to receive sham (placebo) therapy. 10-week follow-up period.

Adapted from search of Federal Research in Progress[626]

6.0 Quantitative Analysis and Meta-Analyses of Outcomes of Electrical Stimulation Studies

Three types of outcome reporting appear throughout published studies of therapies for wound healing:

- subjective assessments describing the healing process,
- objective expressions of the healing rate, and
- objective expressions of complete healing.

[See section 4.2.3.]

Subjective assessments by clinicians (e.g., ratings of granulation tissue formation, exudate, pain) are good *qualitative* measures of healing, but they are poor *quantitative* measures.

Objective assessments essentially measure the rate at which wounds heal and/or the number of patients (proportion) who completely heal. We have already discussed flaws associated with outcomes describing the percentage of patients totally healed. [See section 4.2.3.1.]

Unfortunately, wound healing rates in many ES and non-ES studies are reported inconsistently or idiosyncratically. [See section 4.2.3.2.] This makes it difficult to interpret healing-rate outcomes within a study and to generalize or compare such outcomes with other studies. We sought to determine a standardized measure of the wound healing rate that could be applied to all ES and non-ES studies.

6.1 Quantitative Analysis of Normalized Wound Healing Rates: Theta (?) Values

6.1.1 Definition and Description of Theta

Many wound healing studies have either assumed or implied that the rate of wound healing is linear. Some studies subtracted the difference between the initial and final size of a wound and divided by the time interval. This assumes a linear healing rate. Some studies obtained healing rates (percentages of wound healed) empirically at selected time intervals and averaged the results to yield a mean healing rate. If the relationship is indeed linear, then the rate would be constant between any 2 intervals. There is no clear evidence that the wound healing rate is linear. (In fact, Pierard and Pierard-Franchimont[627] recently concluded that chronic leg ulcers heal at uniform, nonlinear rates, following a "proportional change process".)

Visual Appearance—To determine whether healing rates appear linear or exponential, or have some other form, we examined curves of the percentages of wound size healed or remaining on the ordinate versus time-for-healing on the abscissa.

In figure 2 of Feedar et al.,[628] the relationship appears exponential rather than linear. The healing rate after 1 week was 20% ±5% SE. If the healing rate was linear, then one would expect 60% to 100% healing after 4 weeks. The actual healing was 65% ±5%.

In figure 1 of Griffin et al.,[629] individual patient healing was plotted for stage II through IV ulcers. The curves for patients with grade III ulcers could have been linear or exponential. However, the curves for grade II ulcers (1 patient exhibiting 80% healing after 5 days, but only 90% after 10 days) and grade IV ulcers (1 patient exhibiting 30% healing after 5 days, only 55% after 20 days) appear exponential.

The healing rate curves in figure 1 of Gentzkow et al.[630] may be linear or exponential. The variance is so large that either might be appropriate.

The healing rate curves in figures 1 and 2 of Gogia et al.[631] do not appear linear, but there is no measure of variance.

In figure 1 of Wood et al.,[632] the stimulation therapy curve appears exponential. Approximately 20% of lesion area decreased after 1 week. If healing was linear, we would expect complete healing after 5 weeks instead of 80% healing after 8 weeks.

Healing rate curves in figures 3 and 5 of Karba et al.[633] are exponential.

In figure 2 of Kaada & Emru,[634] all wound healing curves of individual patients followed a nonlinear, seemingly exponential path.

We examined many conventional therapy RCTs for wound healing and found similar appearances for healing rate curves. Based on our visual inspection, healing rates appear exponential rather than linear.

Exponential Model—Karba et al.[635] and Stefanovska et al.[636] have used an exponential model to describe the rate of wound healing. Using an exponential model enables one to express the healing rate as a constant independent of wound size. Karba et al. have described this constant as the **normalized healing rate** or **theta (?)**, usually expressed as a fraction value per week.

The normalized healing rate (?) is derived from the basic equation for an exponential decay:

$$S_t = S_0 \times e^{-?t}$$

where S_t is the size of a wound at a time "t" and S_0 is the initial size of the wound (at time 0; i.e., the size of the wound at the beginning of the study). Solving for theta

$$S_t/S_0 = e^{-?t}$$
$$\ln(S_t/S_0) = -?t$$
$$\ln(S_0/S_t) = ?t$$
$$? = [\ln(S_0/S_t)]/t$$

Time "t" is usually expressed in weeks. For example, if the initial size of a wound is 4 cm^2 and the size 8 weeks later is 0.25 cm^2, then ? = [ln(4 ÷ 0.25)] ÷ 8 = 0.3466/week.

In an exponential process, the rate constant ? should be the same for all time intervals. Wound sizes can be measured by surface area and/or by volume. (The latter is more representative of the healing process.) Assuming healing is exponential, the normalized healing rate can employ either surface area or volume measurements to represent wound size. However, the value of the normalized healing rate depends on whether one measures surface area or volume. For example, if the initial wound size had been 4 cm^2 with 3 mm depth (0.12 cm^3) and the measured size 8 weeks later had been 0.25 cm^2 with 2 mm depth (.0025 cm^3), then $?_{vol}$ = [ln(0.12 ÷ 0.0025)] ÷ 8 = 0.4839/week. We observe that the numerical value of the exponential-modeled normalized healing rates depend on whether one measures surface area or volume. [Throughout this report, ? will represent normalized healing rates for surface area (or in general), and $?_{vol}$ will represent normalized healing rates measured by volume.]

Validating the Exponential Model—To validate the model, we (1) determined whether ? is independent of initial wound size and (2) determined that the percentage of wound healing fits a negative exponential curve.

To determine whether ? values are independent of wound size, we calculated ? values, when possible, for the placebo (or control) groups used in controlled trials of electrical stimulation for wound healing. (We chose placebo and standard groups to be certain that there was no correlation between initial size and the value of ?.) The correlation between ? and initial wound size (surface area) for control groups from ES studies was not significant ($r = 0.0636$, $p = 0.8419$, $N = 16$ treatment groups). This implies that there is no linear relationship. We plotted ? versus initial wound size and found no other apparent relationships. [See **Figure 6.1**.] We then calculated ? values for the standard (or placebo) treatment groups taken from RCTs of conventional therapies for venous ulcers and for decubitus ulcers. [See section 7 for description of study inclusion.] The correlation between ? and initial size was not significant for control groups in venous ulcer RCTs ($r = -0.3740$, $p = 0.1696$, $N = 15$) and for control groups in decubitus ulcer RCTs ($r = 0.0969$, $p = 0.8363$, $N = 7$). This implies that there is no linear relationship. We plotted ? versus initial wound size and found no other apparent relationships. [See **Figure 6.1**.]

If a sufficient number of time points are provided, the model can be validated. The more time points available, the better the validation process. Unfortunately, few published studies provided data on wound size as a function of time. Fewer still provided individual patient data. We used summary data from two studies mentioned previously in this section (Wood et al. 1993[637] and Feedar et al.[638]) to determine whether data generally fits the negative exponential model. From Wood et al., we plotted summary statistics of percentage of initial surface area of lesions against time; we generated a negative exponential curve to test for goodness of fit. [See **Figure 6.2a**.] The data appeared to fit the negative exponential model. We repeated this procedure for summary data from Feedar et al. and observed a similar fit. [See **Figure 6.2b**.] When we used individual patient data, the model did not fit as well. We observed that the normalized exponential healing rate, ?, appears to be a better descriptor of the healing rate for groups of patients than individual patients.

One can think of ? as a "time constant." When $t = 1/?$, the area (or volume) of S_t is approximately 37% of the initial size S_0. With each successive time interval, 1/?, lesion size decreased 63%. For example, if ? = 0.1, then at the time interval of 10 weeks ($t = 1/.1 = 10$), approximately 63% of lesion size would have healed. In integral multiples of ?, at 20 weeks ($2 \times (1/?)$), 86% of the lesion size would be healed; at 30 weeks ($3 \times (1/?)$), 95% of the lesion size would be healed; at 40 weeks ($4 \times (1/?)$), 98.2% of the lesion size would be healed; and at 50 weeks ($5 \times (1/?)$), 99.3% of the lesion size would be healed. On the other hand, if

? = 0.05, then the time interval 1/? would be 20 weeks. Therefore, with a ? of 0.05, at 40 weeks, 86% of lesion size would be healed compared to 98.2% if ? = 0.1.

One difficulty in calculating the value of ? is that the exponential approaches but never reaches zero. In actual life, when a wound heals at some given time `t,' its surface area or volume is 0. By the exponential decay model, ? = $[\ln(S_0/S_t)]/t = [\ln(S_0/0)]/t = [\ln(\infty)]/t$—which has no meaning. Therefore, to calculate for ? when given the initial size and time for complete healing, one needs to choose as an endpoint a fraction that is near complete healing. We empirically chose 99% healing as the endpoint of a lesion. For example, if a 4 cm^2 lesion healed in 8 weeks, the 99% endpoint is 0.04 cm^2; ? = [ln (4 ÷ .04)] ÷ 8 = 0.5756. A disadvantage of this empirically based endpoint is that small changes in wound size can lead to large changes in ? values.

Although the normalized healing rate, ?, has these shortcomings, it is the best quantitative descriptor of wound healing available.

Calculating Thetas From Studies—We calculated the ? values for all ES studies (excluding case reports) which presented adequate data (i.e., initial wound size {required}, duration of healing, difference in wound size at ≥1 time periods). We used the following procedures:

(1) Theta values calculated from studies which reported wound size by surface area were not combined with ? values from studies reporting wound size by volume.

(2) Studies which expressed wound sizes as length and width were converted to surface areas by multiplying length times width. Studies which expressed wound sizes as length, width, and depth were converted to volumes by multiplying length time width times depth. (These can lead to systematic errors.)

(3) Some studies reported outcomes only as medians. In these cases, median values were treated as if they were mean values. It was often the only method for handling study data.

(4) In studies that reported healing at different time intervals and the time required to complete healing, only one ? value was used. This was calculated from an average ? value using all reported times except the ? value calculated at complete healing (99% of original wound size). These latter values were excluded because calculations of ? based on the time to complete healing involves an assumption,

and we sought to avoid empirically based assumptions wherever possible.

(5) For studies providing only the time for complete healing, we calculated ? by assuming that the final wound size was 1% of the original (99% healed). This enabled us to calculate ? values from studies only providing time-to-complete-healing data.

Confidence intervals (CI) are essential for determining whether the healing rate in one treatment group of a study significantly differs from those reported in other groups in the study. We determined variance (and from them, confidence intervals) using the following procedures:

(1) If a study provided the variance at a time "t" during healing but did not provide the variance at the initial time (t = 0), then we assumed that the initial variance was the same at time "t."

(2) If a study provided the variance at the initial time (t = 0), but did not provide it at later or final times, we assumed that the variance at time "t" or final times was the same as the initial time.

(3) Standard error (SE) = standard deviation (SD) ÷ $n^{0.5}$ (where n is the number of patients in a group). The 95% confidence interval (CI) = mean ±(1.96 × SE).

(4) Groups were considered statistically significantly different when their 95% confidence intervals did not overlap.

6.1.2 Theta Outcomes for Individual Electrical Stimulation Studies

DIRECT CURRENT STUDIES—Theta values for DC studies are presented in **Table 6.1**. Only 2 studies provided sufficient information for calculating ? values: Katelaris et al. (1987)[639] and Carley & Wainapel (1985).[640]

In the Katelaris et al. trial, the normalized healing rate after ES was not significantly greater than conventional therapies. In fact, LIDC with povidone therapy had a significantly *smaller* healing rate than povidone therapy alone. However, this is a nonrandomized, controlled study.

In the Carley & Wainapel trial, ? is significantly greater for LIDC therapy than saline gauze therapy. However, the study did not specify the types of lesions being treated. These ? values are clinically uninterpretable because we do not know whether they apply to diabetic, venous, decubitus, neurotrophic, or some other chronic lesion.

Based on these findings, DC stimulation has not been shown to increase the normalized healing rate of chronic lesions.

PULSED CURRENT STUDIES—Theta values for PC studies are presented in **Table 6.2**. Six studies provided sufficient information for calculating ? values. However, 1 study (Gogia et al. [1993][641]) provided no measure of variance.

Three studies had no significant difference in normalized healing rates: the double-blind RCT by Gentzkow et al. (1991)[642] comparing PDC to placebo therapy for patients with stage III/IV decubitus ulcers; the single-blind RCT by Griffin et al. (1991)[643] comparing HVPC to placebo therapy for patients with "grades II to IV" decubitus ulcers; and the double-blind RCT by Feedar et al. (1991)[644] comparing PDC to placebo therapy for patients with different types of lesions.

Two studies demonstrated a significant difference between patients who received ES and those who received sham therapy.

In the Wood et al. double-blind RCT, PDC yielded a significantly greater ? than placebo therapy for patients with stage II or stage III decubitus lesions. The only appreciable flaw of this study was that the investigators did not specify the duration of treatment sessions.

In the Kloth & Feedar single-blind RCT, HVPC had a significantly greater ? than placebo therapy for patients with stage IV decubitus ulcers. However, this study has several major flaws, which makes this outcome suspect: (1) small study size, (2) differences between patients in the 2 groups, and (3) possible confounding concomitant therapy.

Based on these findings, it appears that the type of PDC device used by Wood et al. does improve the normalized rate of wound healing compared to placebo therapy for patients with stage II or III decubitus ulcers. Studies using HVPC have either yielded no significant improvement compared to placebo therapy or highly-suspect outcomes.

ALTERNATING CURRENT AND TRANSCUTANEOUS ELECTRICAL NERVE STIMULATION STUDIES—Theta values for AC and TENS studies are presented in **Table 6.3**. Six studies provided sufficient information for calculating ? values; 4 were uncontrolled case series. (Theta values for uncontrolled trials tended to be much larger than those for controlled trials.) There were 2 controlled studies.

In the RCT by Stefanovska et al. (1993),[645] the normalized healing rate for AC therapy was greater than the value for standard therapy for patients with decubitus ulcers. However, this study has several flaws: (1) the investigators did not specify the standard therapy to which AC stimulation was being compared; (2) they did not specify any aspect of concomitant therapy; and

(3) they did not specify the stage of decubitus ulcers.

In the double-blind RCT by Lundeberg et al. (1992),[646] there was no significant difference between TENS and placebo therapy for patients with diabetic ulcers.

Based on these findings, there is no evidence that TENS therapy improves any type of chronic wound healing. There is weak evidence that AC therapy may provide some improvement in the healing rate of patients with decubitus ulcers, but it is not clear for which stage and compared to what type of therapy.

PULSED ELECTROMAGNETIC INDUCTION STIMULATION STUDIES—Theta values for pulsed electromagnetic stimulation studies are presented in **Table 6.4**. Four studies provided sufficient information for calculating ? values. One study (Itoh et al. [1991][647]) is a case series. (The ? values for this uncontrolled trial are much higher than in controlled trials.) One double-blind RCT (Todd et al [1991][648]) provided no measure of variance.

In the double-blind RCT by Salzberg et al. (1995),[649] there was a significant difference between the normalized healing rates of PEE (95% CI for ? = 1.3114 to 1.6370) and placebo therapy for patients with stage II decubitus ulcers (95% CI for ? = 0.1488 to 0.6740).

In the double-blind RCT by Stiller et al. (1992),[650] there was a small, significant difference in the normalized healing rates between PEMF and placebo therapies for patients with venous ulcers. However, the effect of PEMF appears quite small (mean ? = +0.0824, 95% CI = +0.0596 to +0.0975). This study also has 2 flaws: (1) inconsistencies in concomitant therapy and (2) inadequate monitoring of patient compliance.

Based on these findings, there is evidence that PEE therapy improves any type of chronic wound healing. There is weak evidence that PEMF therapy may provide some benefit for patients with venous ulcerations.

SPINAL CORD STIMULATION STUDIES—None of the SCS studies of wound healing was controlled. They consisted of case reports and small case series. In the absence of control groups, normalized healing rates tend to be higher and reflect confounding population characteristics. Therefore, we did not calculate theta values for the case series.

6.1.3 Summary of Normalized Healing Rates for Electrical Stimulation Studies

The statistical significance of normalized healing rate (? values) for controlled trials of ES for wound healing are presented in **Table 6.5**.

Based on these outcomes, we conclude that there is **evidence** of the following:

- There is evidence that PDC improves the healing rate of stage II or III decubitus ulcers compared to sham (placebo) therapy. There is weak evidence that HVDC improves the healing rate of stage IV decubitus ulcers compared to sham therapy, but these are suspect due to small study size.

- There is evidence that PEE stimulation improves the healing rate of stage II decubitus ulcers.

Based on these outcomes, we conclude that there is **weak evidence** of the following:

- There is weak evidence that AC stimulation improves the healing of decubitus ulcers compared to "standard" therapy, but these results are suspect because the standard therapy was not specified.

- There is weak evidence that PEMI stimulation improves the healing rate of chronic venous ulcers compared to sham therapy, but these results are suspect because of possible inconsistencies in concomitant therapy.

Based on these outcomes, we conclude that there is **no evidence** of the following:

- There is no evidence that DC stimulation improves the healing rate of chronic venous, decubitus, or diabetic ulcerations.

- There is no evidence that PC stimulation improves the healing rate of chronic venous or diabetic ulcerations.

- There is no evidence that AC (including transcutaneous electrical nerve stimulation) improves the healing rate of chronic decubitus or diabetic ulcerations.

- There is no evidence that PEMI stimulation improves the healing rate of chronic decubitus or diabetic ulcerations.

- There is no evidence that any other form of ES improves the healing rate of chronic lesions.

Although some ES studies have shown an improved healing rate (effect) compared to placebo therapy, this does not demonstrate whether it is as effective

or more effective than established wound healing therapies—that is, whether it is clinically useful. [See section 8.]

6.2 Meta-Analyses of Outcomes of Electrical Stimulation for Wound Healing

6.2.1 Overview of Meta-Analytic Methods

We performed 2 meta-analyses to determine

- whether ES increases the normalized wound healing rate (?), and
- whether ES increases the proportion of wounds that completely heal.

These 2 outcome variables are potentially correlated and could be evaluated in a single analysis. We have not done so for 2 reasons: (1) pooling different outcomes is appropriate only when outcome measures are highly correlated, and when these correlations are high, there is only a modest gain the efficiency of the analysis (as noted by Hedges and Olkin[651]); and (2) presenting results separately is more informative than are results from a single analysis.

Both of our meta-analyses are designed to answer 2 questions:

- Does ES promote wound healing?
- If ES does promote wound healing, then is there a particular patient or treatment subgroup for whom ES is most effective?

We used the **Hedges' *d*** statistic in our meta-analyses. Hedges' *d* is a measure of the effect size of treatment. It is the difference between the experimental and control groups expressed in units of standard deviation and corrected for errors in treatment effect estimations that arise in studies with few patients. [See Appendix II, section 11.1.1.1 for formulae to calculate Hedges' *d*.] We calculated a *d* for each study in the meta-analysis. Values of $d > 0$ imply that ES therapy promotes wound healing; values of $d < 0$ imply that ES therapy hinders wound healing. A $d = 0$ implies that ES therapy has no effect. Because the differences between treatment and control groups (effect sizes) are in standard deviation units, $d = +0.5$ implies that wound healing in the average patient in the treatment group is >69% of control group patients; $d = -0.5$ implies that wound healing in the average patient in the treatment group is <31% of control group patients.

The value of *d* by itself does not indicate whether the results from a study are statistically significant. That requires constructing 95% confidence intervals (95% CI or CI) intervals around each study's *d*. These intervals, calculated from the pooled variances of treatment and control groups, provide a range of values in which there is only a 5% probability that the *d* for any particular study could fall

outside of them by chance. As a result, if the 95% CI for a particular study does not contain 0, then there is a statistically significant difference between the outcomes of treatment and control groups. In other words, a treatment effect that promotes healing (d >0) is statistically significant if its lower confidence limit (CL_{lower}) is greater than zero; a treatment effect that hinders healing (d <0) is statistically significant if its upper confidence limit (CL_{upper}) is less than 0.

Once d values are calculated for individual studies, one must combine them to determine an overall estimate of the effects of treatment (i.e., a d based on all relevant studies). This is accomplished by weighting each study's d value by the inverse of the study's variance, averaging the weighted d values, then constructing 95% CI around the overall d (d_o) value. These confidence intervals around d_o determine whether the overall treatment effect is statistically significant.

Another important statistic in this meta-analysis is the Q statistic, which tests the homogeneity of studies—that is, whether all studies in the meta-analysis share a common effect size.[652] [See Appendix II, section 11.1.1.2 for formulae to calculate the Q statistic.] If the value of Q is statistically significant, then the studies in the meta-analysis are not homogeneous; some studies may not be measuring the same statistical parameter.[653] This implies that one may be observing the effect of something other than treatment. For example, the observed effect may depend on the type of ulcer, patient age, ulcer size, etc. A statistically significant Q means that it may not be appropriate to conduct the meta-analysis or that the source of the heterogeneity needs to be explained.[654,655]

Proper selection of studies is crucial for conducting an appropriate meta-analysis. One of the most common methods of study selection is choosing studies with the best experimental design. Although this may be theoretically sound, in practice, different analysts have different opinions about which studies are “best.” These different opinions reflect potential subjectivity in assessing study quality, and can possibly undermine the analysis. Therefore, in our meta-analysis, we included studies with different experimental quality and then sought to determine whether these differences could have affected outcomes. Our position is justifiable because although some design flaws create the potential for bias, they do not automatically create bias. In such cases, if there is actual bias, it may be determined empirically.

Our analysis also included different types of statistical models. There is controversy in the medical community whether it is better to use a ***fixed****-effects* or a ***random****-effects* statistical model. [Fleiss and Gross,[656] in paraphrasing an argument by Bailey,[657] have suggested that when the question concerns whether a treatment has produced an effect *in the studies* ***at hand***, then the fixed-effects model is the most appropriate one. They continue, however, by noting that when the question involves whether a treatment *will* have an effect, in other words, if one wishes to generalize to a universe of similar studies and/or to consider the

possibility of future studies being conducted or discovered, then the random-effects model is preferred. On the other hand, Dements[658] argues against random-effects models, doubting whether there genuinely is a universe of studies to which one can generalize.] Because of this controversy, we elected to perform both fixed- and random-effects analyses.

6.2.2 Meta-Analysis of Normalized Wound Healing Rates

We used all 9 controlled studies obtained from our literature searches [see section 4] in our meta-analysis of normalized wound healing rates (?). These studies and relevant data are shown in **Table 6.6**.

Because there are insufficient published data from controlled trials for statistical comparisons of devices from different manufacturers, and because we wanted to determine whether different types of devices differentially affected wound healing, we were forced to group devices into broader categories than we used in previous sections of this report. These device categories have limitations but are necessary to construct statistical models to answer our questions and explain observed outcome variations.

6.2.2.1 Overall Study Analysis

FIXED-EFFECTS MODEL—We calculated the fixed-effects *d* and confidence limits for each study and the overall *d* (d_o) and its confidence limits. The *d*'s are listed in **Table 6.7** and presented graphically in an effects size plot in **Figure 6.3**.

ES has an overall statistically significant positive effect on normalized wound healing rates (d_o = +1.13, CI = +0.91 to +1.35). However, the *Q* statistic is highly significant (p <.0001), indicating that these studies are not homogeneous. [See section 6.2.1 and Appendix II, section 11.1.1.2 for explanation.]

Because these studies are heterogeneous, we first sought to determine whether the apparently positive effects of ES were due to statistical outliers. (An outlier is defined in terms of the *Q* statistic, which accounts for both deviation of a study's *d* value from d_o **and** a study's variance.) Whether a study is an outlier is determined by assessing the effect on the *Q* statistic when that study is removed from the meta-analysis. Removing the greatest outlier from the meta-analysis has the greatest effect on *Q*, removal of the second greatest outlier has the second greatest effect on *Q*, etc. For example, suppose the *Q* statistic has a p value of .0001. If we remove study A and the p value of *Q* becomes nonsignificant (e.g., p = 0.23), then study A is the only outlier. If, on the other hand, removing study A leaves us with a *Q* statistic that is still significant (e.g., p =.009), then we would still need to remove 1 or more additional studies to make the *Q* statistic

nonsignificant (i.e., p ≥.05) and the group homogeneous. If removing study A did not affect the *Q* statistic (e.g., p = .0001), then it would be inappropriate to remove study A from the analysis.

In our outlier analysis, we discarded 3 outlying ES studies: (1) Katelaris et al.,[659] (2) Gentzkow et al.,[660] and (3) Salzberg et al.[661]—leaving us with an apparently homogeneous group of studies. The resulting overall *d* (d_o) was +1.32 (CI = +1.07 to +1.57). Because the CL_{lower} is greater than zero, ES still has a statistically significant, positive effect on the normalized rate of wound healing (?). These results also suggest that the statistically significant effects of ES obtained in all 9 studies (including outliers) are not attributable to a few aberrant trials.

RANDOM-EFFECTS MODEL—For illustrative purposes, we analyzed all 9 studies using a random-effects statistical model. Random-effects models do not correct study heterogeneity problems, but they provide a more conservative statistical test and suggest how generalizable results are from a data set.

We obtained a d_o of +1.11 (CI = +0.56 to +1.65). These results indicate that ES has a statistically significant positive effect on the normalized rate of wound healing.

6.2.2.2 Analysis of Study Heterogeneity

The analysis above established that ES has a statistically significant positive effect on the rate of normalized wound healing but as shown by the statistically significant *Q* statistic, the studies are not homogeneous. We wanted to determine the source of this heterogeneity. We investigated 2 main sources: (1) study design and (2) patient or wound characteristics and treatment.

6.2.2.2.1 Influence of Study Design

We wanted to determine whether the statistically significant effects of ES on ? was due to study design (e.g., randomization, blinding).

FIXED-EFFECTS MODEL—We searched for a relationship between study design and *d* using a fixed-effects model. (A fixed-effects model is an appropriate first step because it is less conservative than a random-effects model. If the fixed-effects model demonstrates no statistically significant effects, then the random-effects model must also be nonsignificant.)

Failure to randomize or to blind groups is widely believed to create a potential for bias. In our analysis of study design variations, we looked for potential biases of outcomes caused by (1) not randomizing patients to groups and (2) not blinding physicians to which groups patients belonged.

First, we analyzed studies by blinding. The *d* statistic for the 5 studies without blinding was +1.04 (CI = +0.76 to +1.32); the *d* statistic for the 4 studies with blinding was +1.27 (CI = +0.92 to +1.61). These confidence intervals overlap, suggesting that study design by blinding does not affect the measurement or reporting of healing rates. The *Q* test for differences between these two classes of studies was not significant (p = .322). The *Q* statistics for heterogeneity within these two groups were both significant (p = .0003 for nonblind studies, p = .0007 for blind studies), indicating that categorizing studies by blinding does not account for the heterogeneity we observed in the original (overall) meta-analysis.

Second, we analyzed studies by randomization. The 2 nonrandomized studies had a *d* value of +1.18 (CI = +0.82 to +1.54); the 7 randomized studies had a *d* of +1.10 (CI = +0.82 to +1.35). These confidence intervals overlap, indicating that categorizing study design by randomization does not affect outcomes. The *Q* statistic for between-group differences was not significant (p = .74); the *Q* statistics for within-group differences were significant (p = .0007 for nonrandomized studies, p = .001 for randomized studies), indicating that categorizing studies by randomization does not account for the heterogeneity we observed in the original meta-analysis.

Third, we compared results from studies that were (a) not randomized, (b) randomized but not blinded, and (c) randomized and blinded. The *Q* statistic for this between-groups comparison was not significant (p = .29) and the within-group *Q* statistics for the controlled, nonrandomized and randomized, nonblinded studies were significant (p = .00007 for both groups). This indicates that grouping studies in this manner does not account for the heterogeneity we observed in the original analysis.

In conclusion, we found no statistical evidence suggesting that variations in study design influenced the results of our meta-analysis or accounted for the heterogeneity detected by the *Q* statistic.

6.2.2.2.2 Influence of Patient Characteristics, Wound Characteristics, or Treatment

We wanted to determine whether the statistically significant effects of ES on ? were due to patient characteristics (e.g., age), wound characteristics (e.g., initial lesion size), and/or treatment (e.g., DC versus AC).

FIXED-EFFECTS MODEL—This type of analysis requires the use of a multivariate technique that is a meta-analytic version of multiple regression. In such calculations, one attempts to "predict" *d* from variables that represent relevant patient or treatment characteristics. In a meta-analysis, when *d* is appropriately predicted by a regression model, the model is said to be

"correctly specified." In other words, a correctly specified model explains enough of the variation in *d* values so that the amount of unexplained variation is not statistically significant. For multivariate meta-analyses, one uses the Q_E statistic to assess whether the between-studies variation (heterogeneity) has been adequately accounted for.

In our analysis, we initially considered type of device, type of wound, initial wound size, patient age, and follow-up duration. [See **Table 6.6**.] However, we only used variables whose relationship with *d* were statistically significant and were reported in all studies used in the analysis. (Analyzing variables which were not reported by all studies could not be done using currently available software because it deletes studies with missing data. This would have created data sets different from the one consisting of all studies. In such a situation, if some studies are deleted, one could be explaining only the heterogeneity of the smaller data set but not of the full set consisting of all studies.) We constructed our models using variables whose relationship with *d* was statistically significant according to pilot univariate tests. For categorical variables, we performed univariate tests as described above for study design variations. For continuous variables such as age, we searched for linear relationships with d_o using Rosenthal's method of focused contrasts.[662] [See Appendix II, section 11.1.1.3 for formulae to calculate Rosenthal's method of focused contrasts.]

Because there were a relatively large number of devices and relatively small number of studies, we were forced to analyze device types differently than other variables. We created a variable called "device" (*dv*) that consisted of the 4 device types shown in **Table 6.6** (direct current {DC}, pulsed current {PDC}, alternating current {AC}, and pulsed electromagnetic induction {PEMI}). The device variable (*dv*) was a composite in which each of the 4 device types was denoted by a "dummy" code. If the relationship between *d* and the *dv* was not statistically significant, we concluded that the type of device did not affect outcome. If, on the other hand, *dv* and outcome were significantly associated, we decomposed this variable into different combinations of device types to discern whether there were more specific relationships between device types and outcomes. (This strategy of decomposing the device variable was necessary because although we could predict *a priori* that different device types might have different effects, it was not possible to make specific predictions about which device(s) might be superior.) For example, suppose the effect from devices A, B, and C are not different from each other. In such a situation, it is possible that if devices A and B are treated as a single device class (A/B), then A/B could be superior to device C. Searching for such relationships can lead to a very large number of possible relationships between device types and outcomes. If these were combined with other relevant patient or wound variables (e.g., age, lesion size), this could easily lead to "overfitting" of the regression model.[r]

[r] "Overfitting" often occurs when one puts variables into a model simply to explain variance without regard to a hypothesis. This can lead to correctly specified models that make little theoretical sense.

All models we used to explain heterogeneity in the meta-analysis of all 9 studies were unsuccessful; they all yielded statistically significant values of Q_E. Therefore, we conducted an analysis excluding one study, Salzberg et al.[663]; this study was the second-most extreme outlier in terms of the *Q* statistic and the most extreme outlier in terms of outcomes (effect size *d*)[s]. Excluding this trial made the analysis more conservative. Overall findings of the remaining 8 studies were similar to the full set (including Salzberg et al.) A fixed-effects meta-analysis on the remaining 8 studies yielded d_o of +1.07 (CI = +0.85 to +1.29), a statistically significant positive effect of ES on the normalized wound healing rate (?). These 8 studies are also heterogeneous (*Q* statistic p value <.0001). A random-effects meta-analysis of this subset of studies also yielded statistically significant results (d_o = +0.92, CI = +0.42 to +1.42).

We constructed our model with criteria previously described using these 8 studies. We found a fixed-effects model in which the composite device variable (*dv*) was statistically significant. We decomposed *dv* and obtained a correctly specified model which showed (a) a statistically significant positive correlation between ulcer type[t] and *d*, (b) a statistically significant negative correlation between initial ulcer size[u] and *d*, and (c) a statistically significant negative correlation between the combined group of direct current and pulsed direct current devices (DC/PC)[v] and *d*. The equation appears as follows:

d = wound type + initial wound size + DC/PC

These results suggest that wounds responding most favorably to ES therapy are initially small, decubitus, and are not treated by DC or PC devices.

RANDOM EFFECTS MODEL—We found slightly different results using a random effects analysis. The association between *d* and initial wound size (*B* = -0.06, CI = -0.11 to -0.10) and type of device (*B* = -1.25, CI = -1.88 to -0.62) remained statistically significant, but wound type (*B* = +0.60, CI = -0.02 to +1.22) was not.

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[s] We chose to exclude this trial instead of the most extreme outlier, Katelaris et al., because the reporting was less complete in the Salzberg et al. trial. Therefore, the Katelaris et al. study would have been discarded by our computer program in many cases and, hence, have led to an analysis of 7 trials instead of 8.

[t] Venous ulcers were assigned a "dummy" code, so a positive correlation indicates greater effects in patients with decubitus ulcers. The unstandardized regression coefficient (*B*) for wound type was +0.55 (CI = +0.01 to +1.10).

[u] Unstandardized regression coefficient (*B*) = -0.06, CI = -0.10 to -0.02.

[v] Unstandardized regression coefficient (*B*) = -1.20, CI = -1.74 to -0.66.

6.2.3 Meta-Analysis of Complete Wound Healing

We used all 9 controlled studies obtained from our literature search in our meta-analysis of complete wound healing. These studies and relevant data are shown in **Table 6.8**. Details of this table are similar to those described for **Table 6.6**. Our strategy for the meta-analysis of complete healing was similar to that described for the normalized healing rate.

6.2.3.1 Overall Study Analysis

FIXED-EFFECTS MODEL—We calculated the fixed-effects *d* statistic and confidence limits for each study and the overall *d* statistic (d_o) and its confidence limits. The *d* statistics are listed in **Table 6.9** and presented graphically in an effects size plot in **Figure 6.4**.

ES has an overall statistically significant positive effect on complete wound healing (d_o = +0.85, CI = +0.59 to +1.12). However, the *Q* statistic is highly significant (p <.0001), indicating that these studies are not homogeneous.

Because these studies are heterogeneous, we first sought to determine whether the apparently positive effects of ES were due to statistical outliers.
(See section 6.2-2.1.)

In our outlier analysis, we discarded 2 outlying ES studies to yield a nonsignificant *Q* statistic (p = .31): Kloth & Feedar[664] and Wood et al.,[665] leaving us with an apparently homogeneous group . The resulting overall *d* (d_o) was +0.57 (CI = +0.26 to +0.87). Because the CL_{lower} is greater than zero, ES still demonstrates a statistically significant, positive effect on complete wound healing. These results also suggest that the statistically significant effects obtained in all 9 studies (including outliers) are not attributable to a few aberrant trials.

RANDOM EFFECTS MODEL—For illustrative purposes, we analyzed the 8 studies using a random effects statistical model. We obtained a d_o of +0.95 (CI = +0.39 to +1.52). These results indicate that ES has a statistically significant positive effect on complete wound healing.

6.2.3.2 Analysis of Study Heterogeneity

We established that ES has a statistically significant positive effect on complete wound healing but that these studies are not homogeneous. We wanted to determine the source of this heterogeneity. We investigated 2 main sources (1) study design and (2) patient or wound characteristics and treatment.

6.2.3.2.1 Influence of Study Design

FIXED-EFFECTS MODEL—We searched for a relationship between study design and *d* using a fixed-effects model.

First, we analyzed studies by blinding. The *d* values from studies in which clinicians were not blind (*d* = +0.62, CI = +0.21 to +1.03) were not significantly different than the *d* values from studies employing blinding (*d* = +1.01, CI = +0.67 to +1.35). Similarly, the *Q* statistic p value for the between-groups comparison was 0.15. As in the meta-analysis on normalized wound healing rates, the within-group *Q* statistic for nonblind studies was statistically significant (p = .0003), indicating that categorizing studies in this manner does not adequately account for heterogeneity.

Second, we evaluated differences among studies that were (a) controlled but not randomized, (b) randomized but not blinded, and (c) randomized and blinded. The *Q* statistic for the between-group comparison was not significant (p = .08). Similarly, the *d* value for the 1 controlled, nonrandomized study was 0.00 (CI = -0.83 to +0.83); the *d* value for the 3 randomized, unblinded studies was +0.82 (CI = +0.35 to +1.30); the *d* value for the 5 randomized, blinded studies was +1.01 (CI = +0.67 to +1.35). The within-group *Q* for the randomized, unblinded studies was statistically significant (p =.0003), indicating that grouping studies in this manner does not adequately account for the heterogeneity of the studies.[w]

Third, we analyzed studies by randomization.[x] The 1 nonrandomized study had a *d* value of 0.00 (CI = -0.83 to +0.83); the 8 randomized studies had a *d* value of +0.95 (CI = +0.59 to +1.12). The *Q* statistic for the within-group heterogeneity of the randomized studies was statistically significant (p = .0007), indicating that this categorization of studies does not explain the heterogeneity among all 9 studies.

Although these analyses of the influence of report quality are flawed, they are suggestive. It is generally thought that failure to blind physicians or failure to randomly assign patients to different groups creates the potential for investigators to bias their results. This putative bias could lead to investigators finding larger effects by ES in unblinded or nonrandomized studies. These studies show the converse—larger effects in blinded and/or randomized trials. Because these data run counter to prevailing hypotheses, it seems likely that randomization and blinding quality are not altering results in the expected direction.

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[w] An additional caveat to this analysis is that there was only 1 controlled, nonrandomized study. This artificially sets the variance within this group to 0 and artificially reduces the p value of the between-groups comparison.

[x] Same caveat as previous footnote.

6.2.3.2.2 Influence of Patient Characteristics, Wound Characteristics, or Treatment

We wanted to determine whether the statistically significant effects of ES on complete healing were due to patient characteristics (e.g., age), wound characteristics (e.g., initial lesion size), and/or treatment (e.g., DC versus AC).

FIXED-EFFECTS MODEL—We used the same type of multivariate technique as the meta-analysis for normalized healing rates. [See section 6.2.2.2.2.]

As with the previous analysis, all models we used to explain the heterogeneity in the meta-analysis that included the 9 studies were unsuccessful; they all yielded statistically significant values of Q_E. Therefore, we conducted an analysis excluding one study, Kloth & Feedar,[666] because it was the most extreme outlier in the complete wound healing data set, both in terms of the Q statistic and in terms of the deviation of its d from d_o. A fixed-effects meta-analysis on the remaining 8 studies yielded d_o of +0.78 (CI = +0.52 to +1.05), a statistically significant positive effect of ES on complete wound healing. These 8 studies were also heterogeneous (Q statistic p = .048). A random-effects meta-analysis of this subset also yielded statistically significant results (d_o = +0.73, CI = +0.33 to +1.13).

Fixed-effects univariate analyses of relevant variables (e.g., wound type, device type) suggested that the only variable that could explain the heterogeneity of d values was wound type. Studies of patients with decubitus ulcers had a d_o of +1.22 (CI = +0.82 to +1.62); studies of patients with venous ulcers had a d_o of +0.45 (CI = +0.09 to +0.80.) The Q statistic for the between-group differences was statistically significant, and the Q statistic for within-group differences was not significant for decubitus ulcers (p = 0.56) or for venous ulcers (p = 0.53).

We conducted multiple regression analyses to confirm these results and to determine whether any other variable could modify the effects of ES on complete wound healing. We used the same strategy as for the meta-analysis of normalized healing rates. A fixed-effects regression analysis showed that the effects of type of wound were statistically significant (the unstandardized regression coefficient B = +0.77, CI = +0.24 to +1.30). The Q_E statistic showed that the model was correctly specified (p = 0.41). No other variable showed a statistically significant relationship with d when entered into the model.

RANDOM-EFFECTS MODEL—The random-effects variance was zero. Therefore, the random-effects model is identical to the fixed-effects model.

6.2.4 Publication Bias

Publication bias[y] occurs when the meta-analysis tends to contain studies that show statistically significant results but does not contain studies that tend to show non significant results. Publication bias presents major problems for a meta-analysis because the analysis itself becomes predicated on a biased sample of studies.

Funnel plots are an important means for detecting publication bias. In theory, results of smaller studies will be more variable than those from larger studies. If there is no publication bias, a scatter plot (funnel plot) of the *d* value for each study (plotted on the x-axis) versus the number of patients in that study (plotted on the y-axis) should be shaped like a funnel with the spout pointing up. Points nearest the x-axis (*d* values) should be spread apart and those farthest from this axis should be close together. On the other hand, if there is publication bias, small or negative effects of smaller studies will be absent from the plot. The resulting plot will not look like a funnel.

Funnel plots for the analyses of ? and complete wound healing are shown in **Figure 6.5** and **Figure 6.6**. Neither funnel plot shows the expected pattern of publication bias. These plots also show that the trials excluded from the multiple regression analyses (Salzberg et al. from normalized healing rates, Kloth & Feedar from complete healing) were among the smallest trials we analyzed.[z]

There are several reasons why these plots do not conclusively rule out bias. First, each plot is based on only 9 studies. The addition of only 2 or 3 studies with "aberrant" results could easily change the perception of possible publication bias. Second, the plots depict results obtained from both patients with decubitus ulcers and from patients with venous ulcers. It is not clear that data from different ulcer types can be unambiguously contained within the same funnel plot, especially when evaluating complete wound healing. Third, funnel plots can be difficult to interpret. For example, if studies reporting positive results have an 80% chance of being published and studies obtaining nonsignificant results have a 10% chance of being published, then interpreting a funnel plot becomes more difficult because it partly depends on one's ability to discern differences in the density and distribution of points, and not merely detecting the absence of points in the lower left hand corner of the plot.

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[y] For the purposes of this report, publication bias will be defined in a broad sense, and includes the bias that occurs when studies finding statistically significant results are accepted for publication and studies failing to find such results are not, and the failure of investigators to submit non-significant results for publication. This latter form of bias has also been called reporting bias.

[z] As noted above, the results of small trials tend to be highly variable, so omitting such trials from the meta-analyses may not appreciably hinder interpretation of results.

Another way of accounting for publication bias is determining the number of studies with an average effect size of 0 that would be needed to overturn the results of the meta-analysis. Rosenthal's method[667] involves converting each study's effect size into a *z* score and then computing the number of studies needed to bring this score below a specified level of significance—in this case, $p = 0.05$ level. [See Appendix II, section 11.3.] If only a few such studies are required, then even a small amount of publication bias would alter the conclusions of the meta-analysis. If, however, a large number of studies are needed to overturn the results, then the conclusions of the analysis are robust. Using Rosenthal's method, 95 studies with nonsignificant results are required to overturn the significance of the meta-analysis of normalized healing rates (for all 9 studies), 51 when the Salzberg et al. trial is excluded. Sixty-seven studies are required to overturn the meta-analysis of complete wound healing (for all 9 studies), 31 when the Kloth & Feedar trial is excluded. It seems unlikely that this number of unpublished RCTs exists.

Another method by Orwin[668] is based on determining how many studies would be required to drop d_o to a negligible level. [See Appendix II, section 11.3 for determining negligible levels of d_o.] According to the Orwin method, 20 studies would be required to overturn the results of the meta-analysis on ? (for all 9 studies), 16 when the Salzberg et al. trial is excluded. Thirty-three studies would be required to overturn the meta-analysis of complete wound healing (for all 9 studies), 31 when the Kloth & Feedar trial is excluded. It seems unlikely that this number of unpublished trials exists.

These methods are open to criticism. These criticisms are discussed in Appendix II, section 11.3.

Although these methods of assessing publication bias are experimental, they provide no evidence that publication affected the results of our meta-analysis.

6.2.5 Conclusions of Meta-Analyses of Electrical Stimulation for Wound Healing

Our meta-analyses are not conclusive, having been hampered by a number of limitations in the literature. First, we could only meta-analyze the data by excluding 1 or 2 outliers from each analysis. Second, many of the studies are relatively small. Although this does not appreciably affect values of *d*, it does affect the *Q* statistic. The heterogeneity statistic works reasonably well when the treatment and control groups each contain ≥10 patients.[669] However, 2 studies in our analyses of ? and 3 studies in our analyses of complete wound healing

contained less than 20 patients.[aa] The *Q* statistic is less reliable under such circumstances. Third, it is not clear whether our random-effects models contained enough studies to accurately estimate the true random-effects variance. For example, a random-effects meta-analysis on wound healing rates conducted prior to 1995 would not have "anticipated" the Salzberg trial, which was a statistical outlier that prevented combining all trials into the analysis. This failure to "anticipate" is probably due to the relatively small number of studies in our meta-analyses. Fourth, our conclusions are limited by weaknesses in the literature. We were unable to account for ulcer stage in both meta-analyses. Only 1 study in each meta-analysis specified using a homogeneous-staged group. The remainder used an unspecified mixture of ulcer stages or completely failed to specify ulcer stage at all. This means that our meta-analytic conclusions may not be generalizable beyond stage II decubitus ulcerations. Another weakness in the literature is that some studies either failed to specify the control treatment or primarily used saline-soaked gauze as the control treatment. (These treatments were employed in 5 of 8 studies included in the multiple regressions of complete wound healing and 4 of 8 multiple regressions of normalized healing rates.) Therefore, it is not possible for us to meta-analytically determine whether ES is superior to treatments that do not rely primarily on untreated or saline-soaked gauze.

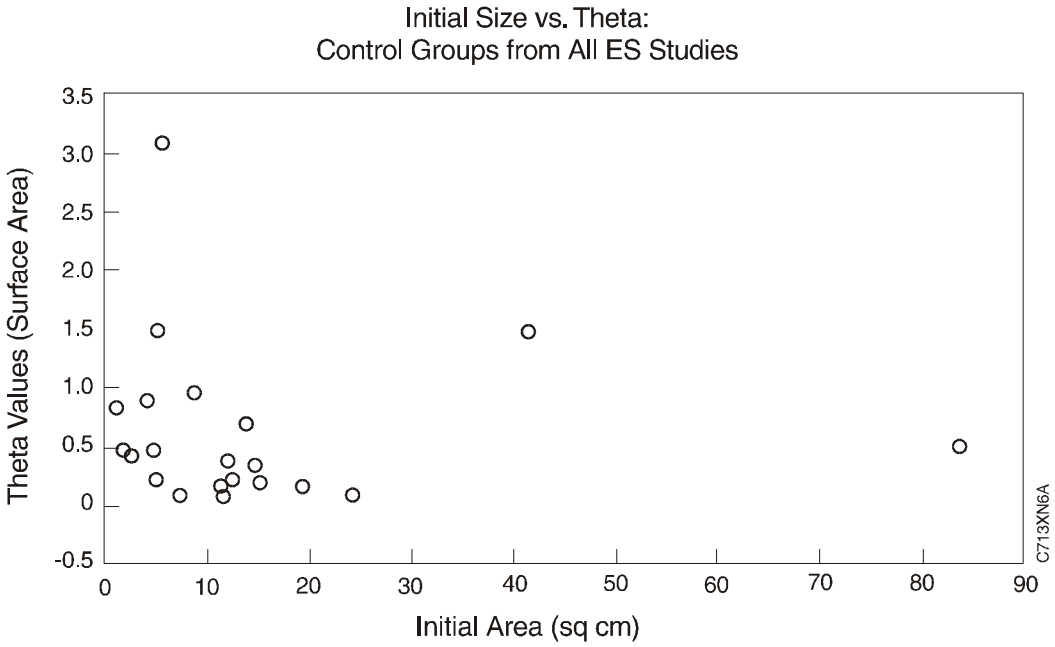
In spite of these weaknesses, our meta-analyses suggest that ES increases the normalized healing rate and the complete healing of chronic ulcers. However, the relationship between these outcomes and ES is not always direct. The effects of ES on wound healing rates appear to decrease in patients with larger wounds and is affected by the type of stimulator. There is also weaker evidence suggesting that decubitus ulcers have greater healing rates than venous ulcers. Finally, ES appears more likely to enhance complete healing of decubitus ulcers.

[aa] There were 2 studies with less than 20 patients in the analysis of all 9 studies of healing rates and the analysis wherein the Salzberg et al. trial was excluded, 4 such studies in our analysis of complete healing based on all 9 trials, and 3 such studies in our analysis of complete healing from which the Kloth and Feedar trial was excluded. The Kloth and Feedar trial was 1 of these small trials.

6.3 Figures and Tables

Figure 6.1. Plots of Initial Wound Size versus Normalized Healing Rates (?)

A



B

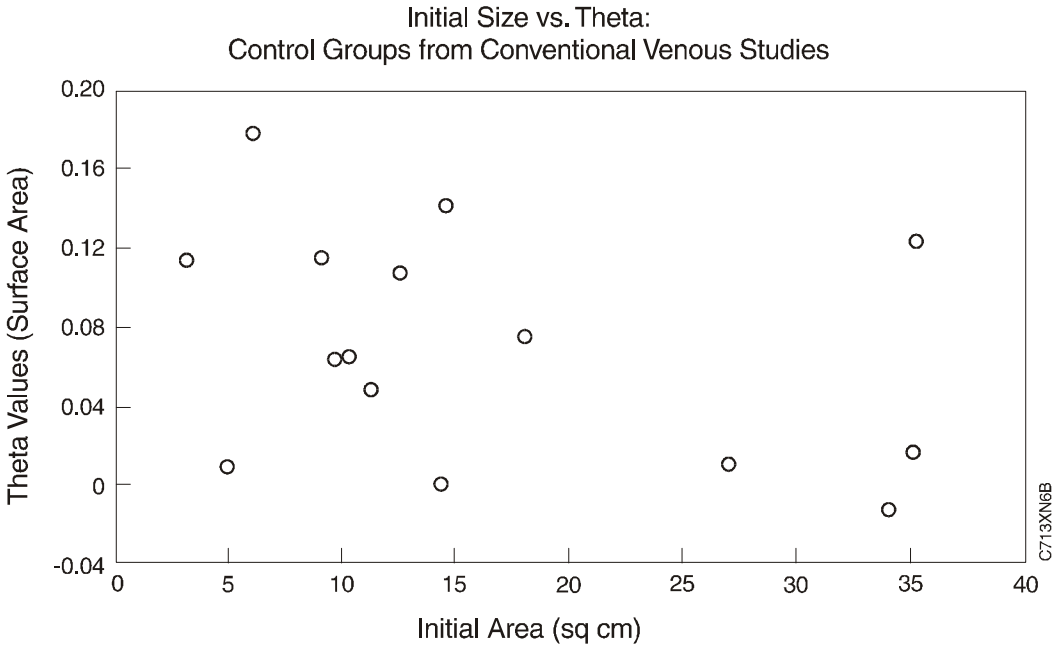
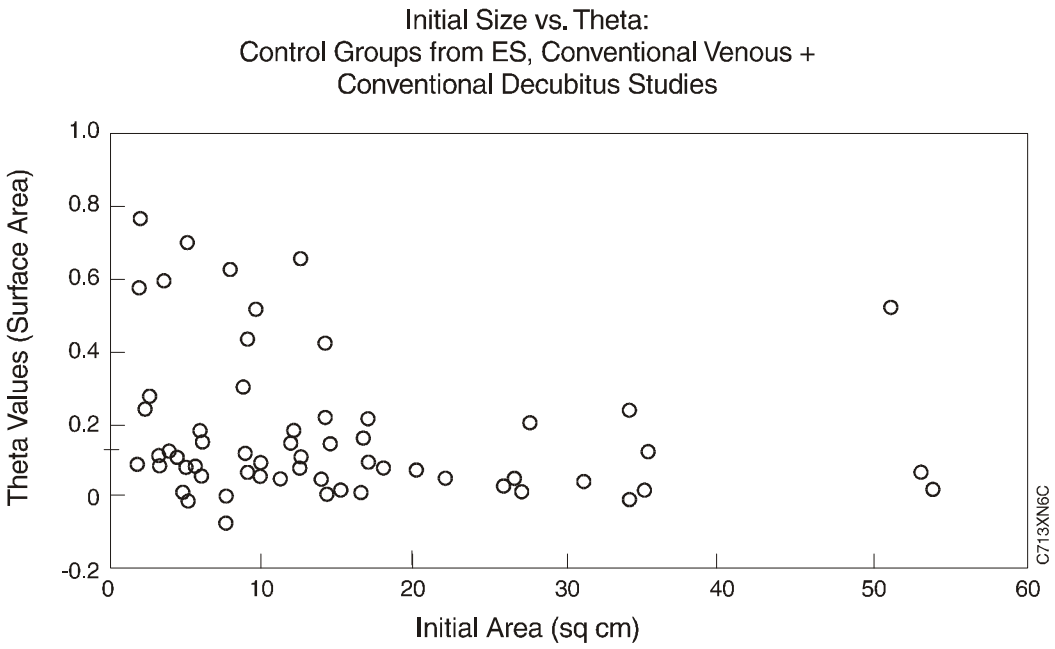


Figure 6.1. Plots of Initial Wound Size vs. Normalized Healing Rates (?) (continued)

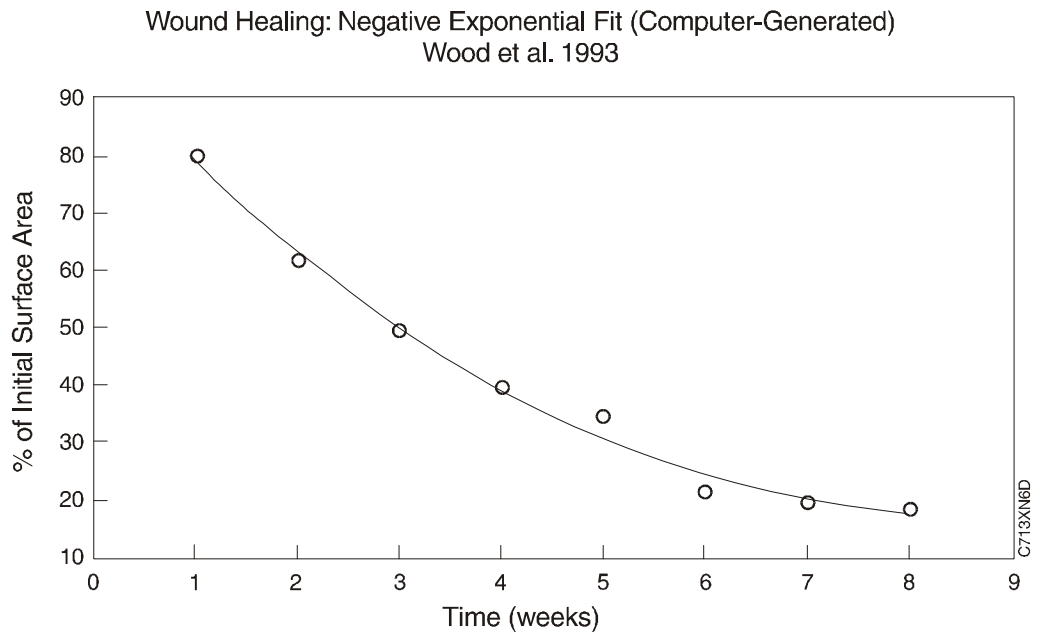
C



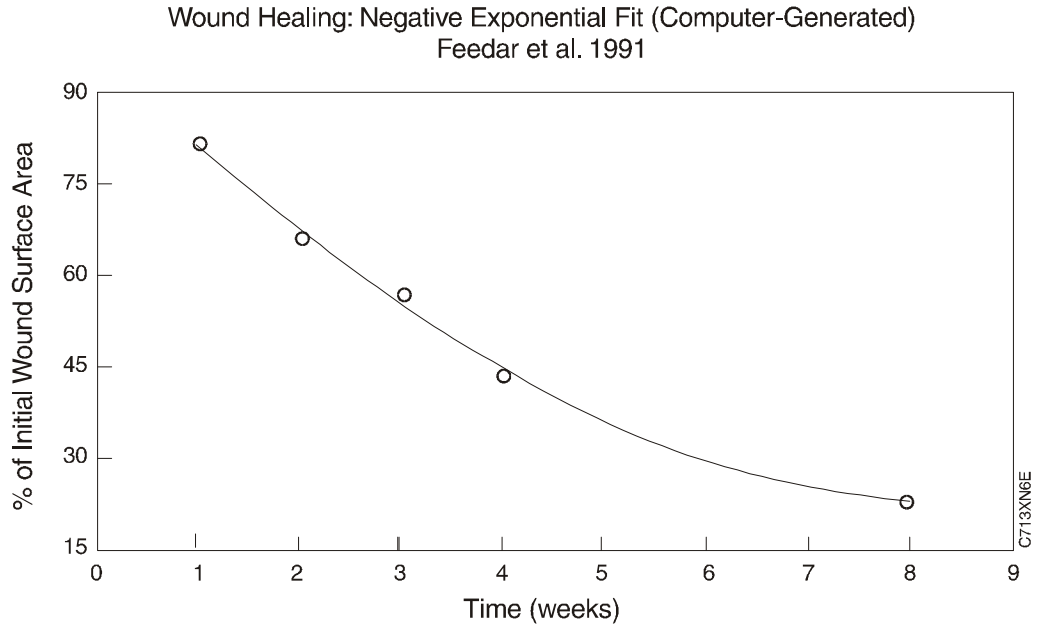
Plots of normalized healing rates (?) versus initial wound size of control groups for (A) all controlled ES studies, (B) conventional therapies for venous ulcers, and (C) all controlled ES studies and conventional therapies for venous and decubitus ulcers.

Figure 6.2. Computer-Generated Negative Exponential Model Plots of Wound Healing

A



B



Computer-generated fit for exponential decay model using data from (A) Wood et al.[670] and (B) Feedar et al.[671]

Table 6.1. Normalized Healing Rates for Direct Current Stimulation Studies of Wound Healing

Study	Stimulation	Study Type	Lesions	Treatment Group	Number Patients or Lesions	Initial Wound Size	Mean Normalized Healing Rate (?)	95% CI around Mean ?	Statistical Significance
Katelaris et al.[672] (1987)	LIDC	Comparative Controlled	Venous	LIDC + povidone Povidone LIDC + saline Saline (Gauze)	4 11 5 4	12.0 cm^2 12.4 cm^2 13.7 cm^2 5.1 cm^2	0.3779[a] 0.6552 0.7023 0.6993	.3243 to .4315 .5594 to .7510 .5516 to .8530 .5354 to .8632	Significant NS
Carley & Wainapel[673] (1985)	LIDC	RCT	—	LIDC Saline Gauze	15 15	4.74 cm^3 (vol) 3.92 cm^3 (vol)	0.4720[b] ($?_{vol}$) 0.1227 ($?_{vol}$)	.4620 to .4820 .1163 to .1291	Significant
Akers & Gabrielson[674] (1984)	DC	Comparative Controlled	Decubitus	DC DC + Whirlpool Whirlpool	— — —	— — —	— — —	— — —	—
*Gault & Gatens[675] (1976)	LIDC	Case series	Mixed	LIDC	100	—	—	—	—
		"Embedded" RCT*	Mixed	LIDC Conventional	6 6	— —	— —	— —	—
Wolcott et al.[676] (1969)	LIDC	Case series	Mixed	LIDC	75	—	—	—	—
		"Embedded" RCT*	Mixed	LIDC Conventional	8 8	— —	— —	— —	—

Case reports excluded

* Contralateral lesions on same patient

a Theta calculations for study based on complete healing time

b Theta calculations for study based on wound sizes at different time intervals

NS = nonsignificant;

— = not specified or not applicable

Table 6.2. Normalized Healing Rates for Pulsed Current Stimulation Studies of Wound Healing

Study	Stimulation	Study Type	Lesions	Treatment Group	Number Patients or Lesions	Initial Wound Size	Mean Normalized Healing Rate (?)	95% CI around Mean ?	Statistical Significance
Wood et al.[677] (1993)	PDC	Double-blind RCT	Decubitus (stage II/III)	PDC Sham (placebo)	43 31	2.61 cm^2 1.91 cm^2	0.4199[b] 0.0859	.3571 to .4827 -.0008 to +.0859	Significant
Gogia et al.[678] (1993)	HVPC	RCT	Mixed	HVPC Whirlpool	6 6	11.5 cm^2 10.0 cm^2	0.0762[a] 0.0892	No variance provided in study	—
Gentzkow et al.[679] (1991)	PDC	Double-blind RCT	Decubitus (stage III/IV)	PDC Sham (placebo)	21 19	19.2 cm^2 12.5 cm^2	0.1582[b] 0.0771	.0297 to .2867 .0634 to .0908	NS
Griffin et al.[680] (1991)	HVPC	Single-blind RCT	Decubitus (grades II-IV)	HVPC Sham (placebo)	8 8	2.34 cm^2 2.72 cm^2	0.4783[a] 0.2750	.3390 to .9568 .1924 to .5060	NS
Feedar* et al.[681] (1991)	PDC	Double-blind RCT	Mixed	PDC Sham (placebo)	26 24	14.7 cm^2 16.9 cm^2	0.3375[a] 0.2111	.1964 to .4785 .0792 to .2111	NS
Unger et al.[682] (1991) [Abstract]	HVPC	Double-blind RCT	Decubitus	HVPC Sham (placebo)	9 8	— —	— —	— —	—
Unger[683] (1991) [Abstract]	HVPC	Case series	—	HVPC	223	—	—	—	—
Kloth & Feedar[684] (1988)	HVPC	Single-blind RCT	Decubitus (stage IV)	HVPC Sham (placebo)	9 7	4.08 cm^2 5.20 cm^2	0.8835[b] -0.0143	.4201 to 1.3469 -.0893 to +.0607	Significant
Feedar & Kloth[685] (1985) [Abstract]	HVPC	Single-blind RCT	Decubitus (stage IV)	HVPC Sham (placebo)	5 3	— —	— —	— —	—

Case reports excluded

* Mulder et al. (1991)[686] included

[a] Theta calculations for study based on complete healing time (or single point)

[b] Theta calculations for study based on wound sizes at different time intervals

NS = nonsignificant;

— = not specified or not available

Table 6.3. Normalized Healing Rates for Alternating Current and TENS Stimulation Studies of Wound Healing

Study	Stimulation	Study Type	Lesions	Treatment Group	Number Patients or Lesions	Initial Wound Size	Mean Normalized Healing Rate (?)	95% CI around Mean ?	Statistical Significance
Stefanovska et al.[687] (1993)	AC	RCT	Decubitus	AC DC Standard	82 18 50	12.0 cm^2 12.4 cm^2 16.6 cm^2	0.3801[c] 0.2177 0.1547	.3461 to .4141 .1545 to .2809 .1223 to .1871	Significant* NS*
Lundeberg et al.[688] (1992)	TENS	Double-blind RCT	Diabetic	TENS Sham (placebo)	32 32	24.2 cm^2 22.0 cm^2	0.0846[b] 0.0473	.0640 to .1007 .0283 to .0663	NS
Karba et al.[689] (1991)	AC	Case series	Decubitus	AC	14	1.03 cm^2	0.8300[c]	0.1862 to 1.4768	—
			Vascular	AC	32	1.77 cm^2	0.4700[a]	.2936 to .6464	—
Frantz[690] (1990) [Pilot study]**	TENS	Case series	Decubitus	TENS	4	11.3 cm^2	0.1603[a]	-.4801 to +.8009	—
Kaada & Emru[691] (1988)	TENS	Case series	Leperomatous	TENS	32	5.2 cm^3	0.8350[b] $?_{vol}$	0.6696 to 1.0003	—
Alon et al.[692] (1986) [Abstract]	TENS	Case series	Diabetic	TENS	15	—	—	—	—
Barron et al.[693] (1985)	TENS	Case series	Decubitus	TENS	6	5.09 cm^2	1.4827[a]	0.7468 to 2.2185	—

Case studies excluded

* Compared to standard therapy; ** Insufficient data in preliminary RCT for analysis

[a] Theta calculations for study based on complete healing time (or single point)

[b] Theta calculations for study based on wound sizes at different time intervals

[c] Theta values specified by investigators

NS = non-significant;

— = not specified or not applicable

Table 6.4. Normalized Healing Rates for Pulsed Electromagnetic Induction Stimulation Studies of Wound Healing

Study	Stimulation	Study Type	Lesions	Treatment Group	Number Patients or Lesions	Initial Wound Size	Mean Normalized Healing Rate (?)	95% CI around Mean ?	Statistical Significance
Salzberg et al.[694] (1995)	PEE	Double-blind RCT	Decubitus (stage II)	PEE Sham (placebo)	10 10	15 cm^2 (median) 33 cm^2 (median)	1.4740[a] 0.5209	1.3114 to 1.6370 0.1488 to 0.6740	Significant
			Decubitus (stage III)	PEE Sham (placebo)	5 5	— —	— —	— —	—
Stiller et al.[695] (1992)	PEMF	Double-blind RCT	Venous	PEMF Sham (placebo)	18 13	7.25 cm^2 7.66 cm^2	+0.0824[a] -0.0754	.0596 to .0975 -.0984 to +.0082	Significant
Todd et al.[696] (1991)	PEMF	Double-blind RCT	Venous	PEMF Sham (placebo)	10 9	83.5 cm^2 53.8 cm^2	0.4753[a] 0.0148	No variance measures specified	—
Itoh et al.[697] (1991)	PEE	Case series	Decubitus (stage II)	PEE	9	5.56 cm^2	3.1002	1.7377 to 4.4627	—
			Decubitus (stage III)	PEE	13	8.78 cm^2	0.9614[a]	0.2683 to 1.6546	—
Ieran et al.[698] (1990)	PEMF	Double-blind RCT	Venous	PEMF Sham (placebo)	18 19	— —	— —	— —	—
Jeran* et al.[699]	PEMF	Double-blind RCT	Venous	PEMF Sham (placebo)	11 11	— —	— —	— —	—

Case studies excluded

* Preliminary early study of Ieran et al. (1990)

[a] Theta calculations for study based on complete healing time (or single point)

— = not specified or not available

Table 6.5. Summary of Normalized Healing Rates in Controlled Trials of Electrical Stimulation for Chronic Wound Healing

Type of Lesion	Direct Current (DC)		Pulsed Current (PC)		Alternating Current (AC)/TENS		Pulsed Electromagnetic Induction (PEMI)	
	Study	? Significance	Study	? Significance	Study	?Significance	Study	? Significance
Venous Ulcers	Katelaris[700*] (1987)	NS**	—	—	—	Significant	Stiller[701] (1992) Todd[702] (1991) Ieran[703] (1990) Jeran[704] (1987)	Significant — — —
Decubitus Ulcers	Akers[705*] (1984) Stefanovska[706] (1993)	— NS	Wood[707] (1993) Gentzkow[708] (1991) Griffin[709] (1991) Unger[710#] (1991) Kloth[711] (1988) Feedar[712#] (1985)	Significant NS NS — Significant —	Stefanovska[713] (1993)	—	Salzberg[714] (1995)	Significant
Diabetic Ulcers	—	—	—	—	Lundeberg[715] (1992)	No	—	—
Groups of Mixed Lesions or Unspecified Lesions	Carley[716] (1985) Gault[717***] (1976) Wolcott[718***] (1969)	Significant — —	Gogia[719] (1993) Feedar[720] (1991)	— NS	—	—	—	—

* Nonrandomized comparative controlled study

** In one comparison, ? for LIDC + povidone < ? for povidone alone

*** Randomized therapy ("embedded" RCT) on same patient

Abstract

NS = nonsignificant;

— = not specified or not available

Table 6.6. Studies and Relevant Data for Meta-Analysis of Normalized Wound Healing Rates

Study	Year	Randomization[a]	Blinding[b]	Device Type	Wound Type	Initial Wound Size (cm^2)[c,d]	Patient Age[d]	Study Length (weeks)[e]
Katelaris et al.[721] [f]	1987	No	No	DC	Venous	12.00	72.6	104.0
Kloth & Feedar[722]	1988	Yes	No	PC	Decubitus	4.57	68.1	7.4
Gentzkow et al.[723]	1991	Yes	Yes	PC	Decubitus	16.01	62.7	4.0
Griffin et al.[724]	1991	Yes	No	PC	Decubitus	2.55	28.8	2.9
Lundberg et al.[725]	1992	No	Yes	AC	Venous	23.16	66.7	12.0
Stiller et al.[726]	1992	Yes	Yes	PEMI	Venous	7.42	63.5	8.0
Stefanovska et al.[727]	1993	No	No	AC[g]	Decubitus	13.74	36.9	2.1
Wood et al.[728]	1993	Yes	Yes	PC	Decubitus	2.32	75.3	8.0
Salzberg et al.[729] [i]	1995	Yes	Yes	PEMI	Decubitus	24.00	54.0	12.0

AC = alternating current; DC = direct current; PDC = pulsed direct current; PEM = pulsed electromagnetic

a "Random" refers to whether patients were randomly assigned to treatment and control groups.

b "Blinding" refers to whether physicians were blinded.

c Initial wound size refers to the size of the wound at the beginning of the study.

d Initial wound sizes and patient ages were typically reported separately for experimental and control groups. When this occurred, an average, weighted by the number of patients in each group, was computed.

e Study length includes the follow-up. It does not necessarily refer to the length of time treatment was given.

f This study contained 4 groups, providone-iodine, providone-iodine with ES, normal saline, and normal saline with ES. For the purposes of analysis, outcomes from the 2 groups without ES were combined, and outcomes from the 2 groups with ES were combined.

g This study included 82 patients treated with AC devices and 18 patients given treatment with DC devices and who showed a lower normalized rate of healing. These latter data were not used in the meta-analysis because these results may not be independent and may, therefore, create errors in tests of statistical significance. In excluding this set of results we follow Rosenthal's recommendation "to have each study contribute only a single effect size estimate and a single significance level to the overall analysis."[730]

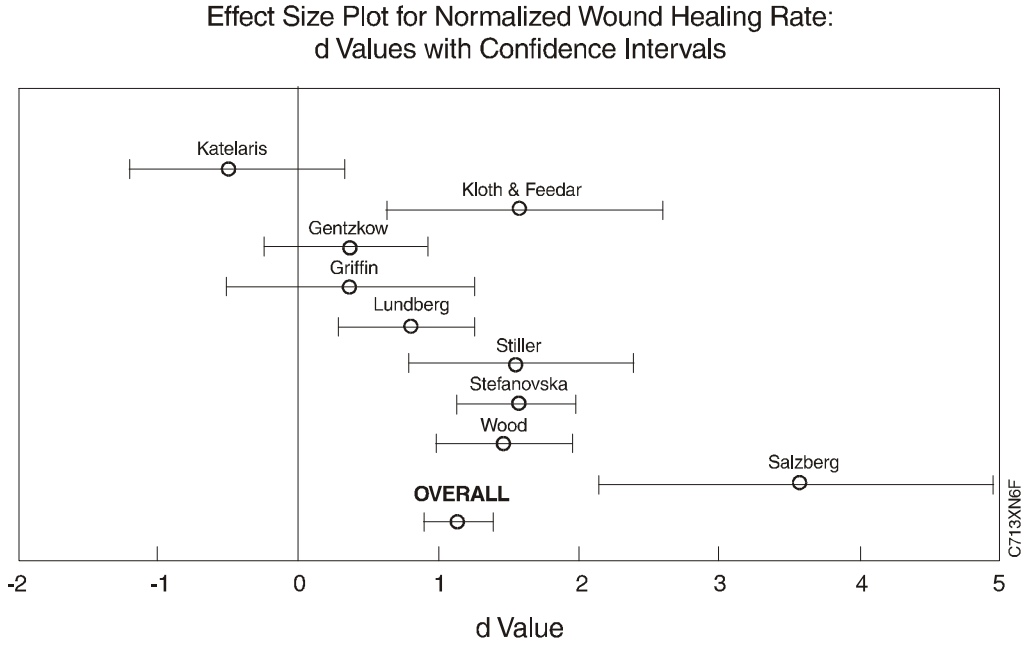
i This study reported data on patients with stage II and III ulcers. Patient characteristics shown to be relevant to outcomes by pilot analyses were only reported for patients with stage II ulcers. Therefore, even though patients with stage III ulcers may be of more clinical interest than those with stage II ulcers (this is because stage III ulcers are presumably more difficult to heal than stage II ulcers), stage III data from this study were not used in the meta-analysis. An additional reason for excluding 1 set of data from the analysis is provided in the previous note.

Table 6.7. Meta-Analysis (Fixed Effects) of Normalized Wound Healing Rates: *d* Statistic with Confidence Limits

Study	d	CL_{lower}	CL_{upper}
Katelaris et al.	-0.51	-1.25	0.33
Kloth and Feedar	1.57	0.44	2.70
Gentzkow et al.	0.36	-0.26	0.99
Griffin et al.	0.36	-0.60	1.32
Lundberg et al.	0.80	0.23	1.37
Stiller et al.	1.55	0.74	2.36
Stefanovska et al.	1.56	1.17	1.96
Wood et al.	1.46	0.95	1.98
Salzberg et al.	3.57	2.16	4.99
OVERALL	1.13	0.91	1.35

CL_{lower} = lower 95% confidence limit
CL_{upper} = upper 95% confidence limit

Figure 6.3. Effect Size Plot (*d* values) for Normalized Wound Healing Rates



Effect sizes (expressed in terms of Hedges' *d*) with confidence intervals for ? in all 9 studies and overall *d* (d_o). Studies with $CL_{lower} > 0$ exhibit a positive effect on normalized wound healing rate. (6 studies exhibit a positive effect; 3 studies exhibit no effect.) There is a positive overall effect.

Table 6.8. Studies and Relevant Data for Meta-Analysis of Complete Wound Healing

Study	Year	Randomization[a]	Blinding[b]	Device Type	Wound Type	Initial Wound Size (cm^2)[c,d]	Patient Age[d]	Study Length (wks)[d,e]
Katelaris et al.[731] [f]	111987	No	No	DC	Venous	12.00	72.6	104.0
Kloth and Feedar[732] [g]	1988	Yes	No	PC	Decubitus	4.57	68.1	7.4
Ieran et al.[733] [h]	1990	Yes	Yes	PEMI	Venous	Not available	65.5	12.8
Griffin et al.[734]	1991	Yes	No	PC	Decubitus	2.55	32.5	2.9
Todd et al.[735] [i]	1991	Yes	Yes	PEMI	Venous	52.27	74.4	6.0
Unger et al.[736]	1991	Yes	Yes	PC	Decubitus	Not available	Not available	Not available
Lundberg et al.[737] [j]	1992	Yes	No	AC	Venous	23.16	Not available	Not available
Wood et al.[738]	1993	Yes	Yes	PC	Decubitus	2.32	75.3	8
Salzberg et al.[739] [k]	1995	Yes	Yes	PEMI	Decubitus	Not available	Not available	Not available

AC = alternating current; DC = direct current; PDC = pulsed direct current; PEM = pulsed electromagnetic device

a "Random" refers to whether patients were randomly assigned to treatment and control groups.

b "Blinding" refers to whether physicians were blinded.

c Initial wound size refers to the size of the wound at the beginning of the study.

d Initial wound sizes patient ages, and, occasionally study length were reported separately for experimental and control groups. When this occurred, an average weighted by the number of patients in each group was computed.

e Study length includes follow-up. It does not necessarily refer to the length or time treatment was given.

f This study contained 4 groups: providone-iodine, providone-iodine with ES, normal saline, and normal saline with ES. For the purposes of analysis, outcomes from the 2 groups without ES were combined, and outcomes from the 2 groups with ES were combined.

g In this study, 0 of 7 controls, and 9 of 9 treated subjects healed. This led to incalculable variances. To allow for computation of a variance, we arbitrarily assumed that 0.5 wounds in the control group healed.

h Authors presented results gathered after 90 days and 1 year of follow-up. In this analysis, only the results gathered at 90 days were used because this is more similar to the follow-up time of other studies. We also excluded the 1 year data from the meta-analysis because the results from both sets are not likely to be independent. Nonindependence of results can create errors in tests of statistical significance. In excluding 1 set of results we follow Rosenthal's recommendation "to have each study contribute only a single effect size estimate and a single significance level to the overall analysis".[740]

i That no healing occurred was inferred from the data. This inference is reasonable because the authors did not explicitly state that any wounds healed, because the maximum percentage of the area of healing is low (17.5%), and because the authors not that they failed to "show a statistically significant improvement in the ulcers treated with active coils." Because this created a study for which variance was incalculable, we arbitrarily assumed that 0.5 patients in the experimental group healed.

j Thirty-two patients in each of the treatment and control groups began the study, but 5 control and 8 experimental subjects did not complete it. Authors state that there was no statistically significant difference between groups in failure to complete the study. Patient characteristics in this table are based on the patients who entered the study because article does not separately provide information on only those patients who completed the study.

Table 6.8. Studies & Relevant Data for Meta-Analysis of Complete Wound Healing (continued)

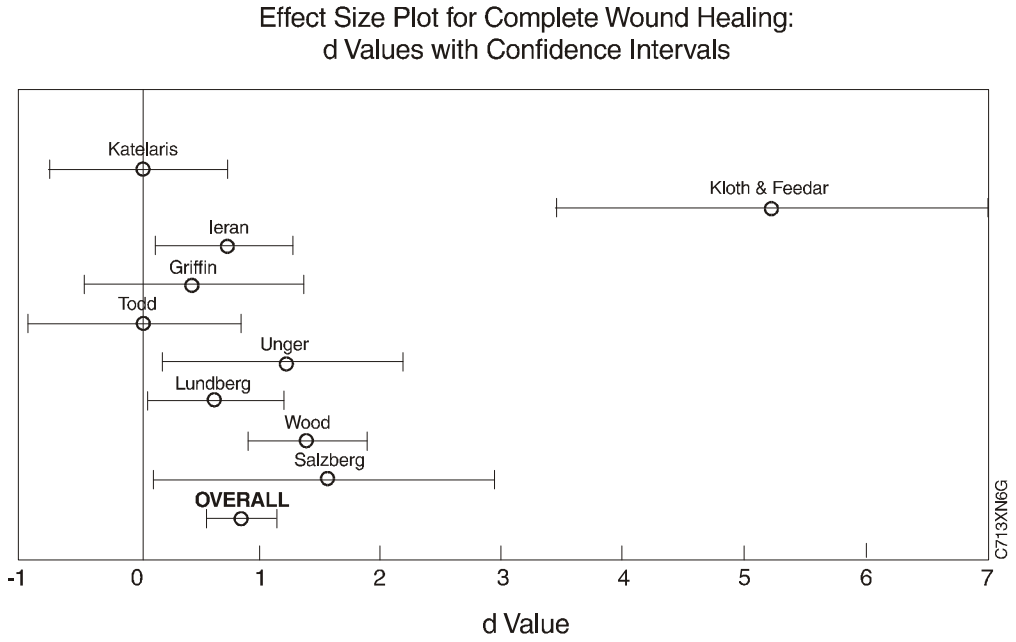
[k] This study reported data on patients with stage II and III ulcers. Because stage III ulcers may be of more clinical interest than those with stage II ulcers (because stage III ulcers are presumably more difficult to heal than stage II ulcers), and because patient characteristics shown to be relevant to outcomes by pilot analyses were reported for patients with stage III ulcers, data from patients with stage II ulcers were excluded from this analysis. This contrasts with the data used in the meta-analysis of wound healing rates. An additional reason for excluding 1 set of data is that the data from both types of ulcers may be nonindependent. Nonindependence of results can create errors in tests of statistical significance. In excluding one set of results we follow Rosenthal's recommendation "to have each study contribute only a single effect size estimate and a single significance level to the overall analysis."[741]

Table 6.9. Meta-Analysis (Fixed Effects) of Complete Wound Healing: *d* Statistic with Confidence Limits

Study	*d*	CL_{lower}	CL_{upper}
Katelaris et al.	0.00	-0.83	0.83
Kloth and Feedar	5.21	3.15	7.26
Ieran et al.	0.73	0.07	1.40
Griffin et al.	0.43	-0.57	1.43
Todd et al.	0.00	-0.90	0.90
Unger et al.	1.21	0.18	2.25
Lundberg et al.	0.62	0.06	1.18
Wood et al.	1.38	0.87	1.89
Salzberg et al.	1.56	0.15	2.98
OVERALL	0.85	0.59	1.12

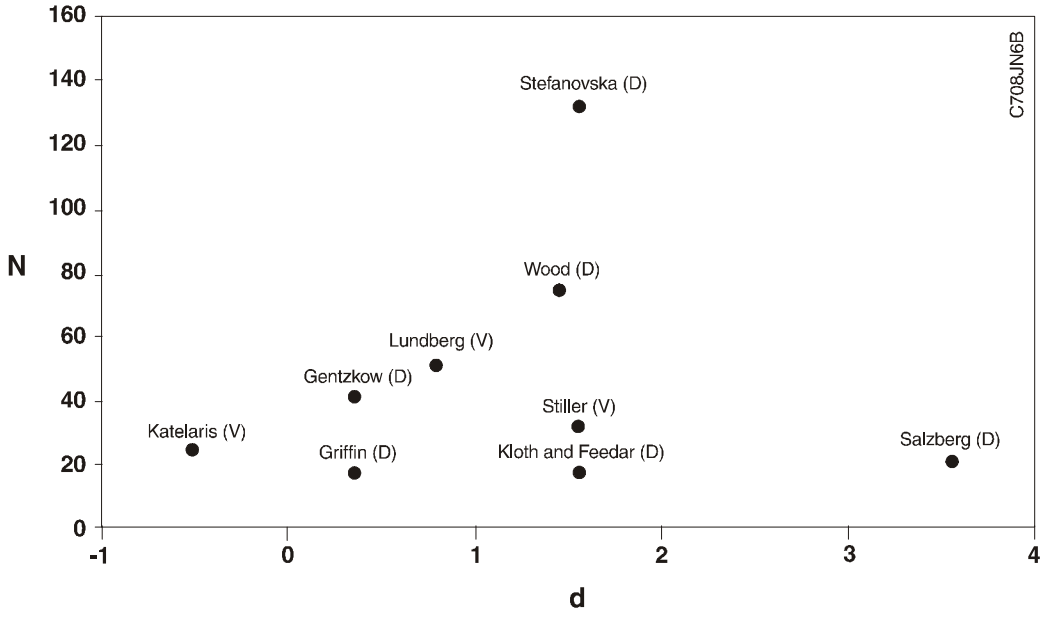
CL_{lower} = lower 95% confidence limit.
CL_{upper} = upper 95% confidence limit.

Figure 6.4. Effect Size Plot (*d* Values) for Complete Wound Healing



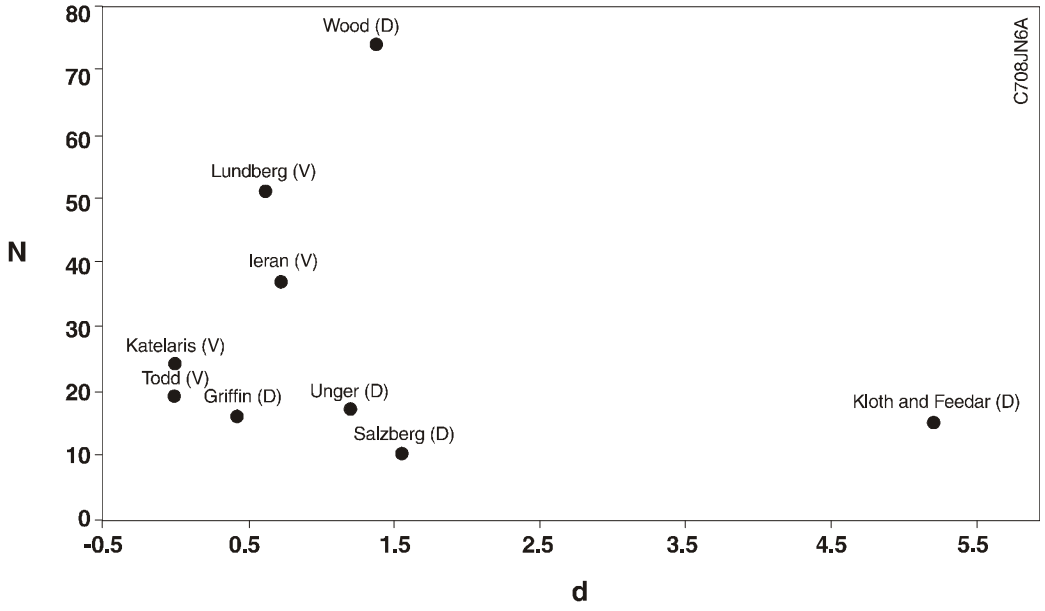
Effect sizes (expressed in terms of Hedges' *d*) with confidence intervals for complete healing in all 9 studies and overall *d* (d_o). Studies with $CL_{lower} > 0$ exhibit a positive effect on complete healing. (6 studies exhibit a positive effect; 3 studies exhibit no effect.) There is a positive overall effect.

Figure 6.5. Funnel Plot for Detecting Publication Bias in Normalized Healing Rates



Plot depicts effect size (d) on the x-axis and number of patients (N) in each study on the y-axis. Study authors names are shown above each point, and denoted in parentheses next to these names is whether the study was on venous (V) or decubitus (D) ulcers.

Figure 6.6. Funnel Plot for Detecting Publication Bias in Complete Healing



Plot depicts effect size (d) on the x-axis and number of patients (N) in each study on the y-axis. Study authors names are shown above each point, and denoted in parentheses next to these names is whether the study was on venous (V) or decubitus (D) ulcers.

7.0 Quality of Study Comparison: Electrical Stimulation versus Conventional and Alternative Therapies for Wound Healing

The RCTs of ES therapy for wound healing have many design and reporting weaknesses. [See sections 4 and 5.] We wanted to determine whether these flaws are unique to ES studies or are common shortcomings throughout published studies of wound healing.

In the fourth part of our analysis, we compare the quality of ES studies to that reported in non-ES therapies for venous and for decubitus ulcers. [We excluded RCTs of diabetic ulcerations because only one ES study (Lundeberg et al. {1992}) evaluated them.]

7.1 Quality Comparison for Venous Ulcers

7.1.1 Comparison with Conventional Therapies

We used the search strategy specified in section 4.1 to identify RCTs of venous ulcers treated by different conventional therapies (e.g., dressings, topical agents). We excluded studies

- that did not appear to be randomized controlled,
- that did not define the type of ulceration,
- in which <80% of the patients (in any treatment group) had venous ulcers,
- that were published before 1970,
- that did not directly address the healing of wounds (e.g., studies of bacterial counts in lesions),
- that did not specify the number of patients in each treatment group, or
- in which most (specified) wounds were <30 days duration.

Our definition of *conventional* RCT was any therapeutic study of venous ulcers that evaluated debridement, cleaning agents, topical agents, dressings, bandages, antibiotics (systemic or local), compression therapies, systemic medications, or nutritional supplements.[bb]

Our search identified 40 conventional RCTs for the treatment of venous ulcers that met our exclusion criteria. [See **Table 7.1**.]

We compared the quality of these 40 conventional RCTs to the ES RCTs (Stiller et al.[742] 1992, Todd et al.[743] 1991, and Ieran et al.[744] 1990). [The study by Jeran et al.[745] 1987 was not analyzed because it was a preliminary version of the study by Ieran et al.] We evaluated study homogeneity; study size; whether the study specified the randomization technique; blinding of groups; patient age; gender; location of lesions; duration of lesions; stage of lesions; specifications of lesion size; the use of pre-therapy vascular perfusion, inclusion criteria; possible confounding by patient selection (e.g., infection, peripheral arterial disease;

[bb] The term "conventional" is not meant to imply that the (experimental group) therapy or therapies in the RCT are accepted treatment regimens.

diabetes; rheumatoid arthritis; steroid usage; nutritional status); specification of concomitant therapy; and possible confounding by inconsistencies in concomitant therapy (e.g., debridement, use of topical and/or cleansing agents, dressings, and oral or systemic antibiotics). [See **Table 7.2**.] These are the same study characteristics that we used to evaluate the quality of ES studies.

The study quality of the 40 conventional RCTs for venous ulcers appears similar to the individual RCTs for ES, with the following exceptions:

(1) Stiller et al. 1992: PEMF therapy

- Possibly confounded by concomitant therapy: debridement (reported in none of conventional RCTs), dressings (12.5% of conventionals), and antibiotic therapy (7.5% of conventionals)

(2) Todd et al. 1991: PEMF therapy

- Smaller study size than most conventionals (smaller than 25th percentile of 40 RCTs)

- Did not specify inclusion or exclusion of patients with peripheral arterial disease (reported in 62.5% of conventional RCTs) or diabetes (40% of conventionals)

(3) Ieran et al. 1990: PEMF therapy

- Possibly confounded by inclusion of diabetic patients (reported in 7.5% of conventional RCTs)

- Possibly confounded by antibiotic therapy (7.5% of conventionals)

In general, the design and reporting shortcomings presented in the RCT studies of ES for venous ulcers are common throughout published studies of conventional therapies for venous ulcers. However, because the Stiller et al. study showed several different types of potential confounding by concomitant therapy and because this type of confounding appeared only infrequently in conventional RCTs, the Stiller et al. study appears inferior in quality to conventional RCTs for venous ulcers.

7.1.2 Comparison with Alternative Therapies

We used the databases specified in section 4.1 to identify RCTs of venous ulcers treated by alternative therapies, which we defined as (1) hyperbaric oxygen (HBO), (2) growth factors, (3) ultrasound, (4) lasers, and (5) ultraviolet light. (Our definition of "alternative" was based on the definition of "active therapy" described in section 2.3.)

Our search strategies for identifying alternative therapies used the following keywords:

- *Debridement; bandages, dressings; hydrotherapy; whirlpool; hyperbaric oxygenation; drug therapy; antibiotics; electrocoagulation; dermatologic agents; ultrasonic therapy; lasers; growth substances; pressure surfaces; ultraviolet light; physical therapy devices.*

Our exclusion criteria was the same used for conventional therapies in section 7.1.1.

We identified 10 alternative therapy RCTs for the treatment of venous ulcers that met our exclusion criteria. [See **Table 7.3**.] These included 4 growth factor studies (2 human growth factor {hGF}, 1 human epidermal growth factor {hEGF}, and 1 placental growth factor {PGF}); 4 ultrasound (US) studies; and 2 laser studies (1 gallium-arsenide {GaAs} and 1 helium-neon {HeNe}).

We compared the quality of these 10 alternative RCTs to the same ES studies listed in section 7.1.1 (Stiller et al.[746] 1992, Todd et al.[747] 1991, and Ieran et al.[748] 1990) and evaluated the same study features. [See **Table 7.4**.]

We observed the following differences between study quality of the 10 alternative RCTs for venous ulcers and individual RCTs for ES:

(1) Stiller et al. 1992: PEMF therapy

- Reported lesion duration by group with variance (compared to 80% of alternatives which did not report lesion durations)
- Did not specify inclusion or exclusion or patients with rheumatoid arthritis (60% of alternatives)
- Does not appear to be confounded by infections of lesions (compared to 20% of alternatives)
- Possibly confounded by concomitant therapy: debridement (reported in none of conventional RCTs), dressings (12.5% of conventionals), and antibiotic therapy (7.5% of conventionals)

(2) Todd et al. 1991: PEMF therapy

- Smaller study size than most alternatives (smaller than 25th percentile of 10 RCTs)
- Did not describe randomization process (reported in 50% of alternative RCTs)
- Did not specify inclusion or exclusion or patients with peripheral arterial disease (reported in 90% of alternatives), diabetes (80% of alternatives) or rheumatoid arthritis (60% of alternatives)
- Does not appear to be confounded by infections of lesions (compared to 20% of alternatives)

(3) Ieran et al. 1990: PEMF therapy

- Did not specify inclusion or exclusion or patients with rheumatoid arthritis (60% of alternatives)
- Does not appear to be confounded by infections of lesions (compared to 20% of alternatives)
- Possibly confounded by inclusion of diabetic patients (reported in 7.5% of conventional RCTs)
- Possibly confounded by antibiotic therapy (7.5% of conventionals)

In general, the design and reporting shortcomings presented in the RCTs of ES for venous ulcers are common throughout published studies of alternative therapies for venous ulcers. However, 2 of the 3 ES studies may have been confounded by inconsistencies in concomitant therapy whereas none of the 10 alternative studies was confounded. Therefore, ES study quality may be slightly inferior to that in other alternative-therapy studies of venous lesions.

7.2 Quality Comparison for Decubitus Ulcers

7.2.1 Comparison with Conventional Therapies

We used the search strategy specified in section 4.1 to identify RCTs of decubitus ulcers (pressure sores) treated by different conventional therapies (e.g., dressings, topical agents). Using similar criteria to section 7.1.1, we excluded studies

- that did not appear to be randomized controlled,
- that did not define the type of ulceration,
- in which <80% of the patients (in any treatment group) had decubitus ulcers,
- that were published before 1970,
- that did not directly address the healing of wounds (e.g., studies of bacterial counts in lesions),
- that did not specify the number of patients in each treatment group, or
- in which most (specified) wounds were <30 days duration.

Our definition of *conventional* RCT was any therapeutic study of decubitus ulcers that evaluated debridement, cleaning agents, topical agents, dressings, bandages, antibiotics (systemic or local), pressure relief, systemic medications, or nutritional supplements.[cc]

We identified 16 conventional RCTs for the treatment of decubitus ulcers which also met our exclusion criteria. [See **Table 7.5**.]

We compared the quality of these 16 conventional RCTs to the following ES RCTs for decubitus ulcers (Wood et al.[749] 1993, Stefanovska et al.[750] 1993, Gentzkow et al.[751] 1991, Griffin et al.[752] 1991, Kloth & Feedar[753] 1988, and Salzberg et al.[754] 1995). [We did not include abstracts by Unger et al.[755] and Feedar et al.[756] because it would be inappropriate to compare the quality of an abstract with journal articles.] We evaluated these studies for the same quality criteria specified in section 7.1. [See **Table 7.6**.]

[cc] The term "conventional" does not imply that the (experimental group) therapy or therapies in the RCT are accepted treatment regimens for decubitus ulcers.

We observed the following differences between study quality of the 16 conventional RCTs for decubitus ulcers and individual RCTs for ES:

(1) Wood et al. 1993: PDC therapy

- Used double blinding (compared to only 6.3% of conventional RCTs)
- Reported patient age and duration of lesions by subject (compared to 0% for conventionals)
- Did not specify inclusion or exclusion of patients with infected lesions (43.8% of conventionals), peripheral arterial disease (37.5% of conventionals), diabetes (56.3% of conventionals), or patient nutritional status (56.3% of conventionals)
- Outcomes not confounded by patients with diabetes (25% of conventionals)
- Outcomes not confounded by concomitant therapy including debridement (18.8% of conventionals), topical and/or cleansing agents (31.3% of conventionals), and dressings (25% of conventionals)

(2) Stefanovska et al. 1993: AC therapy

- Larger study size than most conventional studies (greater than 75th percentile)
- Reported duration of lesions by group with variance (compared to 18.8% of conventionals)
- Did not specify stage of lesions (compared to 81.3% of conventionals)
- Did not specify inclusion or exclusion of patients with infected lesions (43.8% of conventionals), diabetes (56.3% of conventionals), or patient nutritional status (56.3% of conventionals)
- Did not specify use of debridement agents (18.8% of conventionals), topical or cleansing agents (56.3% of conventionals), dressings (87.5% of conventionals), or use of pressure-relieving devices (43.8% of conventionals).

(3) Gentzkow et al. 1991: PDC therapy

- Used double blinding (compared to only 6.3% of conventional RCTs)
- Did not specify inclusion or exclusion of patients with infected lesions (43.8% of conventionals), peripheral arterial disease (37.5% of conventionals), diabetes (56.3% of conventionals), or patient nutritional status (56.3% of conventionals)
- Outcomes not confounded by patients with diabetes (25% of conventionals)
- Outcomes not confounded by dressings (25% of conventionals)

(4) Griffin et al. 1991: HVPC therapy

- Smaller study size than most conventionals (smaller than 25th percentile of 16 RCTs)
- Did not specify inclusion or exclusion of patients with infected lesions (43.8% of conventionals), peripheral arterial disease (37.5% of conventionals), diabetes (56.3% of conventionals), or patient nutritional status (56.3% of conventionals)
- Outcomes not confounded by patients with diabetes (25% of conventionals)
- Outcomes not confounded by concomitant therapy including debridement (18.8% of conventionals), topical and/or cleansing agents (31.3% of conventionals), and dressings (25% of conventionals)

(5) Kloth & Feedar 1988: HVPC therapy

- Smaller study size than most conventionals (smaller than 25th percentile of 16 RCTs)
- Reported patient age by subject (compared to 0% for conventionals)
- Did not specify location of lesions (75% of conventionals)
- Did not specify inclusion or exclusion of patients with infected lesions (43.8% of conventionals) or patient nutritional status (56.3% of conventionals)

- Outcomes possibly confounded by inclusion of patients with peripheral arterial disease

- Outcomes not confounded by topical and/or cleansing agents (31.3% of conventionals) and dressings (25% of conventionals)

(6) Salzberg et al. 1995: PEE therapy

- Smaller study size than most conventionals (smaller than 25th percentile of 16 RCTs)

- Used double blinding (compared to only 6.3% of conventional RCTs)

- Did not specify location of lesions (75% of conventionals)

- Did not specify inclusion or exclusion of patients with peripheral arterial disease (37.5% of conventionals) or diabetes (56.3% of conventionals)

- Outcomes not confounded by patients with diabetes (25% of conventionals)

- Outcomes not confounded by concomitant therapy including debridement (18.8% of conventionals), topical and/or cleansing agents (31.3% of conventionals), and dressings (25% of conventionals)

In general, the design and reporting shortcomings presented in the RCT studies of ES for decubitus ulcers are common throughout published studies of conventional therapies for decubitus ulcers. However, because ES studies were usually blinded and were usually not confounded by the inclusion of diabetic patients or concomitant therapy, particularly topical/cleansing agents and dressings, it appears that their quality may be slightly superior to RCTs of conventional therapies for decubitus ulcers—with the possible exception of the study by Stefanovska et al.

7.2.2 Comparison with Alternative Therapies

We searched the databases specified in section 4.1 to identify RCTs of decubitus ulcers treated by alternative therapies, which we defined as (1) HBO, (2) growth factors, (3) ultrasound, (4) lasers, and (5) ultraviolet light.

We identified 7 alternative therapy RCTs for the treatment of decubitus ulcers that met our exclusion criteria. [See **Table 7.7**.] These included 3 growth factor studies (2 platelet-derived growth factor-BB {PDGF-BB} and 1 recombinant basic

fibroblast growth factor {bFGF}; 3 ultrasound (US) therapy studies; and 1 ultraviolet (UV) study.

We compared the quality of these 7 alternative RCTs to the same ES studies listed in section 7.2.1 (Wood et al.[757] 1993, Stefanovska et al.[758] 1993, Gentzkow et al.[759] 1991, Griffin et al.[760] 1991, Kloth & Feedar[761] 1988, and Salzberg et al.[762] 1995) and evaluated the same study features. [See **Table 7.8**.]

We observed the following differences between study quality of the 7 alternative RCTs for decubitus ulcers and individual RCTs for ES:

(1) Wood et al. 1993: PDC therapy

- Larger study size than most alternative studies (greater than 75th percentile of 7 RCTs)
- Did not specify inclusion or exclusion of patients with infected lesions (28.6% of alternatives), peripheral arterial disease (42.9% of alternatives), diabetes (57.1% of alternatives), or patient nutritional status (42.9% of alternatives)
- Specified duration of lesions (compared to 71.4% not specified by alternatives)
- Outcomes not confounded by concomitant therapy of pressure-relieving devices (28.6% of alternatives)

(2) Stefanovska et al. 1993: AC therapy

- Larger study size than most alternative studies (greater than 75th percentile of 7 alternative RCTs)
- Not blind (compared to 71.4% of alternatives double-blind and 14.3% single-blind)
- Reported duration of lesions by group with variance (compared to none of alternatives)
- Did not specify stage of lesions (compared to 57.1% of alternatives)
- Did not specify inclusion or exclusion of patients with infected lesions (28.6% of alternatives), with diabetes (57.1% of alternatives), who used steroids (57.1% of alternatives), or patient nutritional status (42.9% of alternatives)

- Did not specify use of debridement agents (57.1% of alternatives), topical or cleansing agents (85.7% of alternatives), dressings (71.4% of alternatives), or pressure-relieving devices (57.1% of alternatives)

(3) Gentzkow et al. 1991: PDC therapy

- Did not specify inclusion or exclusion of patients with infected lesions (28.6% of alternatives), peripheral arterial disease (42.9% of alternatives), diabetes (57.1% of alternatives), or patient nutritional status (42.9% of alternatives

- Specified duration of lesions (compared to 71.4% not specified by alternatives)

- Outcomes possibly confounded by concomitant therapy using debridement and topical or cleansing agents

- Outcomes not confounded by concomitant therapy of pressure-relieving devices (28.6% of alternatives)

(4) Griffin et al. 1991: HVPC therapy

- Did not specify inclusion or exclusion of patients with infected lesions (28.6% of alternatives), peripheral arterial disease (42.9% of alternatives), diabetes (57.1% of alternatives), or patient nutritional status (42.9% of alternatives)

- Specified duration of lesions (compared to 71.4% not specified by alternatives)

- Outcomes not confounded by concomitant therapy of pressure-relieving devices (28.6% of alternatives)

(5) Kloth & Feedar 1988: HVPC therapy

- Smaller study size than most alternative studies (smaller than 25th percentile of 7 RCTs)

- Did not specify location of lesions (57.1% of alternatives)

- Did not specify inclusion or exclusion of patients with infected lesions (28.6% of alternatives) or patient nutritional status (42.9% of alternatives)

- Outcomes possibly confounded by patient heterogeneity: inclusion of patients with peripheral arterial/venous disease or diabetes

- Outcomes possibly confounded by concomitant therapy of debridement

- Outcomes not confounded by concomitant therapy of pressure-relieving devices (28.6% of alternatives)

(6) Salzberg et al. 1995: PEE therapy

- Did not specify location of lesions (57.1% of alternatives),

- Did not specify inclusion or exclusion of patients with peripheral arterial disease (42.9% of alternatives) or diabetes (57.1% of alternatives)

- Outcomes not confounded by concomitant therapy of pressure-relieving devices (28.6% of alternatives)

In general, the design and reporting shortcomings presented in the RCT studies of ES for decubitus ulcers are common throughout published studies of alternative therapies for decubitus ulcers. Two of the 6 ES studies were possibly confounded by patient heterogeneity (peripheral arterial/venous disease and diabetes) and/or concomitant therapy (inconsistencies in debridement and use of topical/cleansing agents). Two of the 7 alternative studies were possibly confounded by inconsistencies in concomitant therapy (use of pressure-relieving devices). Therefore, the quality of ES randomized controlled studies of decubitus ulcers appears to be similar to the quality of alternative therapy RCTs.

7.3 Tables

Table 7.1. Randomized Controlled Studies of Conventional Therapies for Venous Ulcers Used in Qualitative Comparative Analysis

Venous Ulcer Study	Year	Number of Patients/Ulcers	Description
Bowszyc et al.[763]	1995	82	RCT: Hydrocolloid dressing vs. polyurethane foam dressing
Ohlsson* et al.[764]	1994	28	RCT: Hydrocolloid dressing vs. saline gauze dressing
Werner-Schlenzka* & Kuhlmann[765]	1994	128	Double-blind RCT: Topical iloprost vs. placebo
Greguric et al.[766]	1994	110	RCT: Hydrocolloid dressing vs. magnesium sulfate paste dressing
Smith*[767]	1994	28	RCT: Hydrocolloid dressing vs. alginate dressing
Arnold et al.[768]	1994	30	RCT: Hydrocolloid + zinc paste dressing vs. standard + zinc paste dressing
McCullough et al.[769]	1994	22	RCT: Pneumatic compression + Unna boot vs. Unna boot alone
Layton* et al.[770]	1994	20	Double-blind RCT: Aspirin + compression vs. placebo + compression
Huovinen* et al.[771]	1994	31	Double-blind RCT: Ciprofloxacin (antibiotic) vs. trimethoprim vs. placebo
Nikolova*[772]	1994	42	Single-blind RCT: Flunarizine (Ca-channel blocker) vs. placebo
Teepe* et al.[773]	1993	43	RCT: Hydrocolloid dressing vs. cryopreserved cultured allograft
Cordts* et al.[774]	1992	30	RCT: Hydrocolloid dressing vs. Unna boot dressing
Barbarino*[775]	1992	12	Double-blind RCT: Pentoxifylline (intravenous) vs. placebo
Davis et al.[776]	1992	12	RCT: Semi-permeable polyurethane + Unna boot dressing vs. Unna boot alone
Bishop* et al.[777]	1992	86	Double-blind RCT: 1% silver sulfadiazine cream vs. 0.4% tripeptide copper complex vs. placebo
Brandrup* et al.[778]	1990	31	RCT: Hydrocolloid dressing vs. zinc oxide paste dressing
Colgan et al.[779]	1990	80	Double-blind RCT: Oxpentifylline vs. placebo
Rubin et al.[780]	1990	36	Single-blind RCT: Polyurethane foam dressing vs. Unna boot dressing
Queral et al.[781]	1990	25	RCT: Sclerotherapy + Unna boot vs. Unna boot alone
Smith* et al.[782]	1990	45	RCT: Intermittent pneumatic pressure + compression stockings vs. compression stockings alone

Table 7.1. Randomized Controlled Studies of Conventional-Type Therapies for Venous Ulcers Used in Qualitative Comparative Analysis (continued)

Venous Ulcer Study	Year	Number of Patients/Ulcers	Description
Valtonen et al.[783]	1989	26	RCT: Ciprofloxacin antibiotic + standard therapy vs. standard therapy alone
Roelens[784]	1989	23	Double-blind RCT: Ketanserin ointment vs. placebo
Rudofsky[785]	1989	42	Double-blind RCT: Intravenous prostaglandin E_1 vs. placebo
Holloway* et al.[786]	1989	75	RCT: Cadexomer iodine vs. standard dressing
Hillstrom*[787]	1988	74	RCT: Cadexomer iodine vs. standard dressing in infected ulcers
Kikta et al.[788]	1988	69	RCT: Hydrocolloid dressing vs. Unna boot dressing
Handfield-Jones et al.[789]	1988	10	RCT: Hydrocolloid dressing vs. paraffin wax dressing
Blair et al.[790]	1988	40	RCT: 4-layer bandage vs. adhesive plaster dressing
Laudanska* & Gustavson[791]	1988	60	RCT: Cadexomer iodine vs. standard dressing
Poskitt et al.[792]	1987	103	RCT: Pinch skin grafts vs. porcine dermis
Backhouse* et al.[793]	1987	56	RCT: Hydrocolloid dressing vs. nonocclusive (nonadherent) dressing
Eriksson[794]	1986	34	RCT: Hydrocolloid dressing vs. double-layer bandage
Alinovi* et al.[795]	1986	47	RCT: Systemic antibiotics + standard therapy vs. standard therapy alone
Harvey* et al.[796]	1985	21	Double-blind RCT: 3 amino acids (l-cysteine, glycine, dl-threonine) vs. placebo
Biland et al.[797]	1985	197	Double-blind RCT: (a) Intravenous solcoseryl + solcoseryl ointment vs. (b) intravenous solcoseryl + placebo ointment vs. (c) placebo IV + solcoseryl ointment vs. (d) placebo IV + placebo ointment
Ormiston* et al.[798]	1985	60	RCT: Cadexomer iodine vs. standard dressing
Mann* et al.[799]	1981	26	Double-blind RCT: Oral rutoside vs. placebo
Phillips et al.[800]	1977	42	Double-blind RCT: Oral zinc vs. placebo
Hallbook* & Lanner[801]	1972	26	Double-blind RCT: Oral zinc vs. placebo
Greaves & Ive[802]	1972	36	Double-blind RCT: Oral zinc vs. placebo

* Theta value(s) calculated

Table 7.2. Comparison of Quality of Conventional RCTs and Electrical Stimulation RCTs for the Treatment of Venous Ulcers

Study or Studies Specified...	Number (Percentage) of 40 RCTs of Conventional Therapies for Venous Ulcers Specifying...	Electrical Stimulation Studies for Venous Ulcers		
		Stiller[803] (1992): PEMF	Todd[804] (1991): PEMF	Ieran[805] (1990): PEMF
Study Homogeneity	Yes = 32 (80%)	Yes	Yes	Yes
N (Patients or Lesions)	49 ±5.8 (SE); Q_1 = 26, median = 38, Q_3 = 64.5	31	19	37
Randomization technique	Yes = 6 (15%)	Yes	No	Yes
Blinding	Single = 13 (32.5%) Double = 15 (37.5%) Not blinded = 12 (30%)	Double-blind	Double-blind	Double-blind
Patient Age	By subject = 0 By group (no variance) = 13 (32.5%) By group + variance = 16 (40%) Not specified = 11 (27.5%)	By group alone	By group alone	By group alone
Gender	Yes = 24 (60%)	Yes	Yes	Yes
Location of Lesions	Yes = 39 (97.5%)	Yes	Yes	Yes
Duration of Lesions	By subject = 0 By group (no variance) = 10 (25%) By group + variance = 14 (35%) Not specified = 16 (40%)	By group + variance	By group alone	By group alone

Table 7.2. Comparison of Quality of Conventional-Type RCTs and Electrical Stimulation RCTs for the Treatment of Venous Ulcers (continued)

Study or Studies Specified...	Number (Percentage) of 40 RCTs of Conventional Therapies for Venous Ulcers Specifying...	Electrical Stimulation Studies for Venous Ulcers		
		Stiller[803] (1992): PEMF	Todd[804] (1991): PEMF	Ieran[805] (1990): PEMF
Stage of Lesions	Yes = 7 (17.5%)	No	No	No
Size of Lesions	By surface area = 33 (82.5%) By volume = 0 Not specified = 7 (17.5%)	Surface area	Surface area	Surface area
Initial Size of Lesions	By subject = 3 (7.5%) By group (no variance) = 14 (35%) By group + variance = 15 (37.5%) Not specified = 8 (20%)	By group + variance	By group alone	By group alone
Pre-tx Vascular Perfusion Performed	Yes = 23 (57.5%)	Yes	Yes	Yes
Inclusion criteria considered:				
Infection	Yes = 10 (25%)	No	Yes	No
PAD/PVD	Yes = 25 (62.5%)	Yes	No	Yes
Diabetes	Yes = 16 (40%)	Yes	No	Yes
Rheumatoid Arthritis	Yes = 7 (17.5%)	No	No	No
Steroids	Yes = 9 (22.5%)	No	No	No
Nutrition	Yes = 0	Yes	No	No
Possibly confounded by:				
Infection	Yes = 3 (7.5%)	No	No	No
PAD/PVD	Yes = 4 (10%)	No	No	No
Diabetes	Yes = 3 (7.5%)	No	No	Yes
Rheumatoid Arthritis	Yes = 0	No	No	No
Steroids	Yes = 0	No	No	No
Nutrition	Yes = 0	No	No	No

Table 7.2. Comparison of Quality of Conventional-Type RCTs and Electrical Stimulation RCTs for the Treatment of Venous Ulcers (continued)

Study or Studies Specified...	Number (Percentage) of 40 RCTs of Conventional Therapies for Venous Ulcers Specifying...	Electrical Stimulation Studies for Venous Ulcers		
		Stiller[803] (1992): PEMF	Todd[804] (1991): PEMF	Ieran[805] (1990): PEMF
Specified use of:				
Debridement	Yes = 8 (20%)	Yes	No	No
Topical/Cleansing Agents	Yes = 25 (62.5%)	Yes	Yes	No
Dressings	Yes = 36 (90%)	Yes	Yes	No
Antibiotics	Yes = 5 (12.5%)	Yes	Yes	Yes
Possibly confounded by:				
Debridement	Yes = 0	Yes	No	No
Topical/Cleansing Agents	Yes = 2 (5%)	No	No	No
Dressings	Yes = 5 (12.5%)	Yes	No	No
Antibiotics	Yes = 3 (7.5%)	Yes	No	Uncertain

Q_1 = 1st quartile (25th percentile)
Q_3 = 3rd quartile (75th percentile)

Table 7.3. Randomized Controlled Studies of Alternative Therapies for Venous Ulcers Used in Qualitative Comparative Analysis

Venous Ulcer Study	Year	Type of Therapy	Number of Patients/Ulcers	Description
Rasmussen et al.[806]	1994	(Human) growth hormone	92	Double-blind RCT: intravenous injections of low-dose hGH vs. intermediate-dose hGH vs. high-dose hGH vs. placebo
Falanga* et al.[807]	1992	(Human) epidermal growth factor	35	Double-blind RCT: topical hEGF vs. placebo
Rasmussen et al.[808]	1991	(Human) growth hormone	29	Double-blind RCT: intravenous injections of hGH vs. placebo
Burgos et al.[809]	1989	Placental growth factor	18	Double-blind RCT: topical PGF vs. placebo
Eriksson et al.[810]	1991	Ultrasound	38	Single-blind RCT: ultrasound + standard therapy vs. sham (placebo) + standard therapy
Lundeberg* et al.[811]	1990	Pulsed ultrasound	44	Single-blind RCT: ultrasound + standard therapy vs. sham (placebo) + standard therapy
Callam* et al.[812]	1987	Ultrasound	108	RCT: ultrasound + standard therapy vs. standard therapy alone
Dyson et al.[813]	1976	Ultrasound	18	Single-blind RCT: ultrasound vs. sham (placebo) therapy
Malm et al.[814]	1991	Gallium-Arsenide laser	42	Double-blind RCT: GaAs laser + standard therapy vs. sham (placebo) + standard therapy
Lundeberg & Malm[815]	1991	Helium-Neon laser	46	Single-blind RCT: HeNe laser + standard therapy vs. sham (placebo) + standard therapy

* Theta value(s) calculated

Table 7.4. Comparison of Quality of Alternative RCTs and Electrical Stimulation RCTs for the Treatment of Venous Ulcers

Study or Studies Specified...	Number (Percentage) of 10 RCTs of Alternative Therapies for Venous Ulcers Specifying...	Electrical Stimulation Studies for Venous Ulcers		
		Stiller[816] (1992): PEMF	Todd[817] (1991): PEMF	Ieran[818] (1990): PEMF
Study Homogeneity	Yes = 7 (70%)	Yes	Yes	Yes
N (Patients or Lesions)	48.0 ±9.3 (SE); Q_1 = 18, median = 43, Q_3 = 45.5	31	19	37
Randomization technique	Yes = 5 (50%)	Yes	No	Yes
Blinding	Single = 4 (40%) Double = 5 (50%) Not blinded = 1 (10%)	Double-blind	Double-blind	Double-blind
Patient Age	By subject = 0 By group (no variance) = 2 (20%) By group + variance = 6 (60%) Not specified = 2 (20%)	By group alone	By group alone	By group alone
Gender	Yes = 8 (80%)	Yes	Yes	Yes
Location of Lesions	Yes = 10 (100%)	Yes	Yes	Yes
Duration of Lesions	By subject = 0 By group (no variance) = 20 (20%) By group + variance = 0 Not specified = 80 (80%)	By group + variance	By group alone	By group alone

Table 7.4. Comparison of Quality of Alternative-Type RCTs and Electrical Stimulation RCTs for the Treatment of Venous Ulcers (continued)

Study or Studies Specified...	Number (Percentage) of 10 RCTs of Alternative Therapies for Venous Ulcers Specifying...	Electrical Stimulation Studies for Venous Ulcers		
		Stiller[816] (1992): PEMF	Todd[817] (1991): PEMF	Ieran[818] (1990): PEMF
Stage of Lesions	Yes = 3 (30%)	No	No	No
Size of Lesions	By surface area = 9 (90%) By volume = 0 Not specified = 1 (10%)	Surface area	Surface area	Surface area
Initial Size of Lesions	By subject = 0 By group (no variance) = 3 (30%) By group + variance = 4 (40%) Not specified = 3 (30%)	By group + variance	By group alone	By group alone
Pre-tx Vascular Perfusion Performed	Yes = 4 (40%)	Yes	Yes	Yes
Inclusion criteria considered:				
Infection	Yes = 2 (20%)	No	Yes	No
PAD/PVD	Yes = 9 (90%)	Yes	No	Yes
Diabetes	Yes = 8 (80%)	Yes	No	Yes
Rheumatoid Arthritis	Yes = 6 (60%)	No	No	No
Steroids	Yes = 2 (20%)	No	No	No
Nutrition	Yes = 0	Yes	No	No
Possibly confounded by:				
Infection	Yes = 2 (20%)	No	No	No
PAD/PVD	Yes = 0	No	No	No
Diabetes	Yes = 0	No	No	Yes
Rheumatoid Arthritis	Yes = 0	No	No	No
Steroids	Yes = 0	No	No	No
Nutrition	Yes = 0	No	No	No

Table 7.4. Comparison of Quality of Alternative-Type RCTs and Electrical Stimulation RCTs for the Treatment of Venous Ulcers (continued)

Study or Studies Specified...	Number (Percentage) of 10 RCTs of Alternative Therapies for Venous Ulcers Specifying...	Electrical Stimulation Studies for Venous Ulcers		
		Stiller[816] (1992): PEMF	Todd[817] (1991): PEMF	Ieran[818] (1990): PEMF
Specified use of:				
Debridement	Yes = 3 (30%)	Yes	No	No
Topical/Cleansing Agents	Yes = 8 (80%)	Yes	Yes	No
Dressings	Yes = 9 (90%)	Yes	Yes	No
Antibiotics	Yes = 0	Yes	Yes	Yes
Possibly confounded by:				
Debridement	Yes = 0	Yes	No	No
Topical/Cleansing Agents	Yes = 0	No	No	No
Dressings	Yes = 0	Yes	No	No
Antibiotics	Yes = 0	Yes	No	Uncertain

Q_1 = 1st quartile (25th percentile)
Q_3 = 3rd quartile (75th percentile)

Table 7.5. Randomized Controlled Studies of Conventional Therapies for Decubitus Ulcers Used in Qualitative Comparative Analysis

Decubitus Ulcer Study	Year	Number of Patients/Ulcers	Description
Day et al.[819]	1995	96	RCT: Triangular vs. oval shaped hydrocolloidal dressing in stage II/III sacral pressure ulcers
Honde et al.[820]	1994	168	RCT: Copolymer dressing vs. hydrocolloid dressing in grade II-IV pressure ulcers
Colwell et al.[821]	1993	70	RCT: Hydrocolloid dressing vs. moist gauze dressing in stage II/III pressure ulcers
Kraft et al.[822]	1993	17	RCT: Polyurethane foam dressing vs. saline-soaked gauze dressing in stage II/III pressure ulcers
Xakellis & Chrischilles[823]	1992	39	RCT: Hydrocolloid dressing vs. saline-soaked wet-to-dry dressing in grade II/III pressure ulcers
LaVasseur* & Helme[824]	1991	21	Double-blind RCT: Topical F14001 cream vs. placebo in grade I/II pressure ulcers
Darkovich* et al.[825]	1990	90	RCT: Hydrogel dressing vs. hydrocolloid dressing in stage I/II pressure sores
Alm* et al.[826]	1989	56	Single-blind RCT: Hydrocolloid dressing vs. saline-soaked gauze dressing
Neill* et al.[827]	1989	87	RCT: Hydrocolloid dressing vs. saline-soaked gauze dressing in grade II/III pressure sores
Gorse & Messner[828]	1987	128	RCT: Hydrocolloid dressing vs. Dakin's solution in wet-to-dry dressings in grades II-IV pressure sores
Allman et al.[829]	1987	65	RCT: Air-fluidized beds vs. air-mattress beds with standard therapy
Oleske* et al.[830]	1986	15	RCT: Polyurethane dressing vs. saline-soaked gauze dressing in grade I/II pressure ulcers
Sebern*[831]	1986	77	RCT: Transparent moist vapor permeable dressing vs. gauze dressing in grade II/III pressure ulcers
Agren & Stromberg[832]	1985	25	Single-blind RCT: Varidase (streptokinase-streptodornase) enzymatic debridement vs. zinc oxide in necrotic pressure ulcers
Moberg* et al.[833]	1983	34	Single-blind RCT: Cadexomer iodine vs. standard therapy used in each participating institution in study
Taylor et al.[834]	1974	20	Single-blind RCT: Oral ascorbic acid vs. placebo

* Theta value(s) calculated

Table 7.6. Comparison of Quality of Conventional RCTs and Electrical Stimulation RCTs for the Treatment of Decubitus Ulcers

Study or Studies Specified...	Number (Percentage) of 16 RCTs of Conventional Therapies for Decubitus Ulcers Specifying...	Electrical Stimulation Studies for Decubitus Ulcers					
		Wood[835] (1993): PDC	Stefanovska[836] (1993): AC	Gentzkow[837] (1991): PDC	Griffin[838] (1991): HVPC	Kloth[839] (1988): HVPC	Salzberg[840] (1995): PEE
Study Homogeneity	Yes = 10 (62.5%)	Yes	Yes	Yes	Yes	Yes	Yes
N (Patients or Lesions)	64.5 ±10.6 (SE); Q_1 = 31, median = 60.5, Q_3 = 85.5	74	150	40	17	16	20
Randomization technique	Yes = 5 (31.3%)	No	No	No	No	Yes	No
Blinding	Single = 4 (25%) Double = 1 (6.3%) Not blinded = 11 (68.7%)	Double-blind	Not blinded	Double-blind	Single-blind	Single-blind	Double-blind
Patient Age	By subject = 0 By group alone = 3 (18.8%) By group + variance = 8 (50%) Not specified = 5 (31.2%)	By subject	By group + variance	By group + variance	By group only	By subject	By group only
Gender	Yes = 10 (62.5%)	Yes	Yes	Yes	No	Yes	No
Location of Lesions	Yes = 12 (75%)	Yes	Yes	Yes	Yes	No	No
Duration of Lesions	By subject = 0 By group alone = 3 (18.8%) By group + variance = 3 (18.8%) Not specified = 10 (62.4%)	By subject	By group + variance	By group only	By group only	By group only	No

Table 7.6. Comparison of Quality of Conventional-Type RCTs and Electrical Stimulation RCTs for the Treatment of Decubitus Ulcers (continued)

Study or Studies Specified...	Number (Percentage) of 16 RCTs of Conventional Therapies for Decubitus Ulcers Specifying...	Electrical Stimulation Studies for Decubitus Ulcers					
		Wood[835] (1993): PDC	Stefanovska[836] (1993): AC	Gentzkow[837] (1991): PDC	Griffin[838] (1991): HVPC	Kloth[839] (1988): HVPC	Salzberg[840] (1995): PEE
Stage of Lesions	Yes = 13 (81.3%)	Yes	No	Yes	Yes	Yes	Yes
Size of Lesions	By surface area = 14 (87.5%) By volume = 0 Not specified = 2 (12.5%)	Surface area + volume	Surface area	Surface area	Surface area	Surface area	Surface area
Initial Size of Lesions	By subject = 2 (12.5%) By group alone = 8 (50%) By group + variance = 4 (25%) Not specified = 2 (12.5%)	By subject	By group + variance	By group + variance	By group only	By subject	By subject
Pre-tx Vascular Perfusion Performed	Yes = 0	No	No	No	No	No	No
Inclusion criteria considered:							
Infection	Yes = 7 (43.8%)	No	No	No	No	No	Yes
PAD/PVD	Yes = 6 (37.5%)	No	Yes	No	No	Yes	No
Diabetes	Yes = 9 (56.3%)	No	No	No	No	Yes	No
Rheumatoid Arthritis	Yes = 0	No	No	No	No	No	No
Steroids	Yes = 0	Yes	No	Yes	No	No	No
Nutrition	Yes = 9 (56.3%)	No	No	No	No	No	Yes
Possible confounding by:							
Infection	Yes = 0	No	No	No	No	No	No
PAD/PVD	Yes = 0	No	No	No	No	Yes	No
Diabetes	Yes = 4 (25%)	No	No	No	No	Yes	No
Rheumatoid Arthritis	Yes = 0	No	No	No	No	No	No
Steroids	Yes = 0	No	No	No	No	No	No
Nutrition	Yes = 0	No	No	No	No	No	No

Table 7.6. Comparison of Quality of Conventional-Type RCTs and Electrical Stimulation RCTs for the Treatment of Decubitus Ulcers (continued)

Study or Studies Specified...	Number (Percentage) of 16 RCTs of Conventional Therapies for Decubitus Ulcers Specifying...	Electrical Stimulation Studies for Decubitus Ulcers					
		Wood[835] (1993): PDC	Stefanovska[836] (1993): AC	Gentzkow[837] (1991): PDC	Griffin[838] (1991): HVPC	Kloth[839] (1988): HVPC	Salzberg[840] (1995): PEE
Specified use of:							
Debridement	Yes = 3 (18.8%)	No	No	Yes	Yes	Yes	No
Topical/Cleansing Agents	Yes = 9 (56.3%)	No	No	Yes	Yes	Yes	No
Dressings	Yes = 14 (87.5%)	Yes	No	No	Yes	Yes	Yes
Pressure-relieving Devices	Yes = 7 (43.8%)	No	No	No	Yes	No	No
Antibiotics	Yes = 0	No	No	No	No	No	No
Possible confounding by:							
Debridement	Yes = 3 (18.8%)	No	No	Yes	No	Yes	No
Topical/Cleansing Agents	Yes = 5 (31.3%)	No	No	Yes	No	No	No
Dressings	Yes = 4 (25%)	No	No	No	No	No	No
Pressure-relieving Devices	Yes = 0	No	No	No	No	No	No
Antibiotics	Yes = 0	No	No	No	No	No	No

Excluded electrical stimulation RCTs reported as abstracts

Table 7.7. Randomized Controlled Studies of Alternative Therapies for Decubitus Ulcers Used in Qualitative Comparative Analysis

Decubitus Ulcer Study	Year	Type of Therapy	Number of Patients/Ulcers	Description
Mustoe* et al.[841]	1994	Platelet-derived growth factor-BB	31	Double-blind RCT: Topical low-dose PDGF-BB vs. topical high-dose PDGF-BB vs. placebo for stage III/IV pressure ulcers
Robson* et al.[842]	1992	Platelet-derived growth factor-BB	20	Double-blind RCT: Topical low-dose PDGF-BB vs. topical intermediate-dose PDGF-BB vs. topical high-dose PDGF-BB vs. placebo for grades III/IV pressure ulcers
Robson et al.[843]	1992	Recombinant basic fibroblast growth factor	49	Single-blind RCT: Topical bFGF vs. placebo for grade III/IV pressure sores
ter Riet et al.[844]	1995	Ultrasound	88	Double-blind RCT: US therapy vs. sham (placebo) for stage II or worse pressure ulcers
Nussbaum* et al.[845]	1994	Pulsed ultrasound, ultraviolet-C, and laser	17	RCT: US + UV-C therapy vs. laser therapy vs. standard care therapy for pressure ulcers
McDiarmid et al.[846]	1985	Ultrasound	40	Double-blind RCT: US therapy vs. sham (placebo) for pressure sores
Wills* et al.[847]	1983	Ultraviolet	16	Double-blind RCT: UV therapy vs. sham (placebo) for superficial pressure sores

* Theta value(s) calculated

Table 7.8. Comparison of Quality of Alternative RCTs and Electrical Stimulation RCTs for the Treatment of Decubitus Ulcers

Study or Studies Specified...	Number (Percentage) of 7 RCTs of Alternative Therapies for Decubitus Ulcers Specifying...	Electrical Stimulation Studies for Decubitus Ulcers					
		Wood[848] (1993): PDC	Stefanovska[849] (1993): AC	Gentzkow[850] (1991): PDC	Griffin[851] (1991): HVPC	Kloth[852] (1988): HVPC	Salzberg[853] (1995): PEE
Study Homogeneity	Yes = 6 (85.7%)	Yes	Yes	Yes	Yes	Yes	Yes
N (Patients or Lesions)	37.3 ±9.7 (SE); Q_1 = 17, median = 31, Q_3 = 49	74	150	40	17	16	20
Randomization technique	Yes = 0	No	No	No	No	Yes	No
Blinding	Single = 1 (14.3%) Double = 5 (71.4%) Not blinded = 1 (14.3%)	Double-blind	Not blind	Double-blind	Single-blind	Single-blind	Double-blind
Patient Age	By subject = 0 By group alone = 2 (28.6%) By group + variance = 3 (42.9%) Not specified = 2 (28.5%)	By subject	By group + variance	By group + variance	By group only	By subject	By group only
Gender	Yes = 4 (57.1%)	Yes	Yes	Yes	No	Yes	No
Location of Lesions	Yes = 4 (57.1%)	Yes	Yes	Yes	Yes	No	No
Duration of Lesions	By subject = 0 By group alone = 2 (28.6%) By group + variance = 0 Not specified = 5 (71.4%)	By subject	By group + variance	By group only	By group only	By group only	No
Stage of Lesions	Yes = 4 (57.1%)	Yes	No	Yes	Yes	Yes	Yes

Table 7.8. Comparison of Quality of Alternative-Type RCTs and Electrical Stimulation RCTs for the Treatment of Decubitus Ulcers (continued)

Study or Studies Specified...	Number (Percentage) of 7 RCTs of Alternative Therapies for Decubitus Ulcers Specifying...	Electrical Stimulation Studies for Decubitus Ulcers					
Size of Lesions	By surface area = 2 (28.6%) By volume = 3 (42.9%) Not specified = 2 (28.5%)	Surface area + volume	Surface area	Surface area	Surface area	Surface area	Surface area
Initial Size of Lesions	By subject = 2 (28.6%) By group alone = 1 (14.3%) By group + variance = 2 (28.6%) Not specified = 2 (28.5%)	By subject	By group + variance	By group + variance	By group only	By subject	By subject
Pre-tx Vascular Perfusion Performed	Yes = 0	No	No	No	No	No	No
Inclusion criteria considered:							
Infection	Yes = 2 (28.6%)	No	No	No	No	No	Yes
PAD/PVD	Yes = 3 (42.9%)	No	Yes	No	No	Yes	No
Diabetes	Yes = 4 (57.1%)	No	No	No	No	Yes	No
Rheumatoid Arthritis	Yes = 0	No	No	No	No	No	No
Steroids	Yes = 4 (57.1%)	Yes	No	Yes	No	No	No
Nutrition	Yes = 3 (42.9%)	No	No	No	No	No	Yes
Possible confounding by:							
Infection	Yes = 0	No	No	No	No	No	No
PAD/PVD	Yes = 0	No	No	No	No	Yes	No
Diabetes	Yes = 0	No	No	No	No	Yes	No
Rheumatoid Arthritis	Yes = 0	No	No	No	No	No	No
Steroids	Yes = 0	No	No	No	No	No	No
Nutrition	Yes = 0	No	No	No	No	No	No
Specified use of:							
Debridement	Yes = 4 (57.1%)	No	No	Yes	Yes	Yes	No
Topical/Cleansing Agents	Yes = 6 (85.7%)	No	No	Yes	Yes	Yes	No
Dressings	Yes = 5 (71.4%)	Yes	No	No	Yes	Yes	Yes
Pressure-relieving Devices	Yes = 4 (57.1%)	No	No	No	Yes	No	No
Antibiotics	Yes = 0	No	No	No	No	No	No

Table 7.8. Comparison of Quality of Alternative-Type RCTs and Electrical Stimulation RCTs for the Treatment of Decubitus Ulcers (continued)

Study or Studies Specified...	Number (Percentage) of 7 RCTs of Alternative Therapies for Decubitus Ulcers Specifying...	Electrical Stimulation Studies for Decubitus Ulcers					
Possible confounding by:							
Debridement	Yes = 0	No	No	Yes	No	Yes	No
Topical/Cleansing Agents	Yes = 0	No	No	Yes	No	No	No
Dressings	Yes = 0	No	No	No	No	No	No
Pressure-relieving Devices	Yes = 2 (28.6%)	No	No	No	No	No	No
Antibiotics	Yes = 0	No	No	No	No	No	No

Excluded electrical stimulation RCTs reported as abstracts

8.0 Comparison of Normalized Healing Rates: Electrical Stimulation versus Conventional and Alternative Therapies for Wound Healing

In section 6.1, we calculated the normalized healing rates (? values) for ES RCTs. There was a significant difference in the normalized healing rates between some types of ES ($?_{tx}$) and control ($?_{con}$) groups. In section 6.2.2, we determined that the effect sizes (Hedges' *d*) for ? for some studies were significant.

However, these studies only demonstrate that patients treated by ES may heal faster than those undergoing no therapy at all. These outcomes, by themselves, are not clinically useful because they do not compare ES to wound healing therapies patients are likely to receive. The best way to determine whether ES therapy is effective is to conduct RCTs that compare ES therapy to common therapies for chronic wound healing. In the absence of such RCTs, we can only compare ES outcomes with outcomes from RCTs of other therapies.

A good outcome for comparing ES with non-ES therapies is the normalized healing rate (?). This value allows us to assess whether one therapy appears to accelerate wound healing compared to another. Currently, it is the only way to determine whether healing rates of patients treated by ES are less, roughly equivalent to, or greater than other therapies. For example, from the Wood et al. RCT, we know that the mean ? is +0.4199 (95% CI = +0.3571 to +0.4827). If we were treating a 10 cm^2 lesion, we would expect it to heal (99%) in approximately 10.9 weeks ($t = [\ln (10\ cm^2/.1\ cm^2)] \div ? = 10.9$). Without the context of ? values from other therapies, one wonders if this is a poor or excellent healing time. If another therapy, such as hydrocolloidal dressing, typically has ? values between +0.1 and +0.2, then the identical lesion would require 23 to 46 weeks to heal. If, on the other hand, it typically has values between +0.6 and +0.7, then the same lesion would require 6.6 to 7.7 weeks.

Unfortunately, we cannot directly compare normalized healing rates from different studies because of heterogeneity, numerous variables, confounding factors—and too few studies. These weaknesses and the poor quality of published studies of wound healing circumvent any analysis that would account for different patient and wound characteristics. We can only conduct crude comparisons to assess whether ? values from ES studies appear greater than, smaller than, or similar to those for other therapies.

Therefore, we compared ES RCTs to non-ES RCTs that used (a) patients with similar types of lesions (i.e., venous, decubitus) and (b) control groups with similar healing rates. We performed the latter by comparing ? values for ES control groups with ? values for non-ES control groups. If the 95% confidence intervals for the control groups of ES and non-ES studies overlapped, then we compared the experimental groups of the studies. [Sacks et al.[854] noted that bigger effect sizes are found in historically controlled trials than in RCTs because

the control groups in these types of designs are different—not because of differences between treatment groups. By matching control-group ? values from different RCTs, we eliminate this problem.] This provides a crude comparison of ES therapy and non-ES therapy for venous and for decubitus ulcers.

8.1 Comparison of Normalized Healing Rates for Venous Ulcers

8.1.1 Comparison with Conventional Therapies

Twenty-one of the 40 conventional RCTs (in section 7.1.1) for the treatment of venous ulcers provided sufficient data to calculate normalized healing rates. Theta values for these studies are presented in **Table 8.1**.

Stiller et al.[855] (1992), using PEMF therapy, was the only ES RCT study of venous ulcers that provided sufficient data for calculating ? values. It also demonstrated a positive significant difference from its control group. [See **Table 6.5**.] Seven of the 21 conventional RCTs (8 treatment arms) had control groups with 95% CI ? values that overlapped the Stiller trial ($?_{con}$ = -0.0984 to +0.0082). A study-by-study comparison is presented in **Table 8.2.**

In our crude comparison, which did not consider possible patient and wound differences, normalized healing rates of PEMF therapy appeared greater than 1 conventional therapy (12.5% of conventional treatment groups), less than 2 (25%), and showed no discernible difference from 5 others (62.5%). PEMF healing rates appeared greater than trimethoprim therapy but were substantially less than rates for hydrocolloidal dressing and for pentoxifylline therapy.

Based on these findings, it appears that PEMF produces a normalized healing rate appearing roughly similar to most conventional RCTs.[dd] (From the Stiller et al. 95% CI ? value interval, we would expect a 10 cm^2 lesion to be 99% healed in 47.2 to 77.3 weeks.) However, this is substantially less than found in hydrocolloid dressing, a common therapy. (From the Cordts et al.[856] 95% CI ? value interval, we would expect a 10 cm^2 lesion to be 99% healed in 23.0 to 29.1 weeks.)

8.1.2 Comparison with Alternative Therapies

Three of the 10 alternative RCTs (in section 7.1.2) for the treatment of venous ulcers provided sufficient data to calculate normalized healing rates. Theta values for these studies are presented in **Table 8.3**. Only 2 studies had control groups with 95% CI ? values that overlapped the Stiller trial ($?_{con}$ = -0.0984 to +0.0082). A study by study comparison is presented in **Table 8.4.**

In our crude comparison, which did not consider possible patient and wound heterogeneity, normalized healing rates of PEMF therapy appeared less than

[dd] For which ? values can be calculated.

1 study of ultrasound therapy; there was no discernible difference from another US therapy. From the Callam et al.[857] study, which had a 95% CI ? value interval, we would expect a 10 cm^2 lesion to be 99% healed in 17.3 to 41.3 weeks.

Based on these findings, the clinical value of PEMF therapy for accelerating the healing of venous ulcerations is minimal.

8.2 Comparison of Normalized Healing Rates for Decubitus Ulcers

8.2.1 Comparison with Conventional Therapies

Seven of the 16 conventional RCTs (in section 7.2.1) for the treatment of decubitus ulcers provided sufficient data to calculate normalized healing rates. Theta values for these studies are presented in **Table 8.5**.

Eight RCTs evaluated the effect of ES on decubitus ulcers. Two provided insufficient data for calculating ? (Unger et al.[858] and Feedar & Kloth[859]) and 3 studies (3 treatment arms) showed no significant difference between ES and control groups (Gentzkow et al.,[860] Griffin et al.,[861] and Stefanovska et al.[862] {DC therapy alone}). We analyzed the 4 ES studies that demonstrated significant differences between $?_{tx}$ and $?_{con}$:

- Salzberg et al.[863] (1995): PEE therapy
- Wood et al.[864] (1993): PDC therapy
- Stefanovska et al.[865] (1993): AC therapy
- Kloth & Feedar[866] (1988): HVPC therapy

We compared conventional RCTs that had control groups with normalized healing rates that overlapped the 95% CI ? values of the ES studies:

- Salzberg et al. (95% CI $?_{con}$ = +0.1488 to +0.6740),
- Wood et al. (95% CI $?_{con}$ = -0.0008 to +0.0859),
- Stefanovska et al. (95% CI $?_{con}$ = +0.1223 to +0.1871), and
- Kloth & Feedar (95% CI $?_{con}$ = -0.0893 to +0.0607).

[See **Table 8.6**.]

In our crude comparison, which did not consider possible patient and wound differences (including lesion stage), PEE therapy (Salzberg et al.) normalized healing rates for stage II decubitus ulcers appeared greater than those in 1 conventional therapy (cadexomer iodine) but showed no discernible difference from 3 others (including hydrocolloid and polyurethane dressings for grade I/II lesions). PDC therapy (Wood et al.) ? values for stage II/III ulcers appeared greater than those in 2 conventional therapies (hydrocolloid for grade III ulcerations and cadexomer iodine) but showed no discernible difference from 2 others (hydrocolloid for grade II and polyurethane dressing for grade I/II).

AC therapy (Stefanovska et al.) ? values (for unstaged lesions) appeared greater than cadexomer iodine (for unstaged lesions), but there was no detectable difference when compared with polyurethane dressings (for grade I/II lesions). HVPC therapy (Kloth & Feedar) ? values for stage IV lesions yielded similar comparative outcomes to PDC (Wood et al.).

The following are based on these crude comparisons:

- PEE therapy for stage II decubitus ulcers yields normalized healing rates that are indistinguishable from established therapies.
- PDC therapy for stage II or III decubitus ulcers yield normalized healing rates that are indistinguishable from established therapies.
- There is insufficient data to compare HVPC therapy for stage IV decubitus ulcers to conventional therapies.
- There is insufficient information to compare AC therapy to conventional therapies for decubitus ulcers.

However, even this crude comparison may not be valid because most of the conventional RCTs used grade I through III ulcers or stage I or II lesions, whereas all patients in HVPC were stage IV.

8.2.2 Comparison with Alternative Therapies

Four of the 7 alternative RCTs (in section 7.2.2) for the treatment of decubitus ulcers provided sufficient data to calculate the exponential decay normalized healing rates. Theta values for these studies are presented in **Table 8.7**. We compared them with the 4 ES studies showing significant effect sizes. [See **Table 8.8**.]

In our crude comparison, which did not consider possible patient and wound differences (including lesion stage), PEE therapy (Salzberg et al.) normalized healing rates for stage II decubitus ulcers appeared greater than those for laser therapy but showed no discernible difference from 3 others (including US and UV, and bFGF in different grade lesions). PDC therapy (Wood et al.) ? values for stage II/III lesions appeared greater than those for stage III or IV decubitus ulcers treated by high-dose PDGF-BB but were not discernible from low-dose PDGF-BB. There were no alternative RCTs for decubitus ulcers with $?_{control}$ values suitable for comparison with AC therapy (Stefanovska et al.). HVPC therapy (Kloth & Feedar) ? values for stage IV decubitus ulcers appeared greater than those for stage III/IV lesions treated by high-dose PDGF-BB but were not discernible from low-dose PDGF-BB.

The following are based on these crude comparisons:

- PEE therapy for stage II decubitus ulcers yields normalized healing rates that are indistinguishable from established and alternative therapies.

- PDC therapy for stage II or III decubitus ulcers yield normalized healing rates that are indistinguishable from established or alternative therapies.

- There is insufficient data to compare HVPC therapy for stage IV decubitus ulcers to conventional therapies. Normalized rates for HVPC may, however, be indistinguishable from PDGF-BB therapy.

- There is insufficient information to compare AC therapy with non-ES therapies for decubitus ulcers.

8.3 Tables

Table 8.1. Normalized Healing Rates for RCTs of Conventional Therapies for Venous Ulcers

Study	Year	Number of Patients/Ulcers	Normalized Healing Rates for Experimental Group ($?_{tx}$)		Normalized Healing Rates for Control Group ($?_{con}$)	
			Mean $?_{tx}$ Value	95% Confidence Interval	Mean $?_{con}$ Value	95% Confidence Interval
Ohlsson et al.[867]	1994	28	.1193	Not available	.0347	Not available
Werner-Schlenzka & Kuhlmann[868]	1994	128	.0364	Not available	.0155	Not available
Smith[869]	1994	28	.1407	Not available	.0715	Not available
Layton et al.[870]	1994	20	.0079	Not available	0	Not available
Huovinen et al.[871]	1994	31	.0630[a]	.0536 to .0765	.0099	.0061 to .0137
			.0376[b]	.0277 to .0588	.0099	.0061 to .0137
Nikolova[872]	1994	42	.0786	.0415 to .2568	.0095	.0066 to .0129
Teepe et al.[873]	1993	43	.1487	.1317 to .1657	.1155	.1071 to .1254
Cordts et al.[874]	1992	30	.1790	.1582 to .1998	.0634	-.0396 to +.1664
Barbarino[875]	1992	12	.4230	.2371 to .6090	.1419	-.0632 to +.3470
Bishop et al.[876]	1992	86	.0517[c]	.0198 to .0836	.0637	.0466 to .0733
			.1450[d]	.1225 to .1566	.0637	.0466 to .0733
Brandrup et al.[877]	1990	31	.0874	.0571 to .1177	.0901	.0492 to .1310
Smith et al.[878]	1990	45	.2343	.1366 to .3319	.0753	.0120 to .1387
Holloway et al.[879]	1989	75	.0701	.0575 to .0827	.0482	.0353 to .0611

Table 8.1. Normalized Healing Rates for RCTs of Conventional-Type Therapies for Venous Ulcers (continued)

Study	Year	Number of Patients/Ulcers	Normalized Healing Rates for Experimental Group ($?_{tx}$)		Normalized Healing Rates for Control Group ($?_{con}$)	
			Mean $?_{tx}$ Value	95% Confidence Interval	Mean $?_{con}$ Value	95% Confidence Interval
Hillstrom[880]	1988	74	.0805	-.0038 to +.1648	-.0128	-.0143 to -.0113
Laudanska & Gustavson[881]	1988	60	.2007	.1980 to .2088	.1233	.1033 to .1433
Backhouse et al.[882]	1987	56	.1063	.0783 to .1343	.1140	.0813 to .1467
Alinovi et al.[883]	1986	47	.2163	.1842 to .2484	.1073	.0724 to .1422
Harvey et al.[884]	1985	21	.0724	Not available	.0010	Not available
Ormiston et al.[885]	1985	60	.1785	.1258 to .2312	.0649	.0532 to .0766
Mann et al.[886]	1981	26	.0876	-.0423 to +.2172	.0538	-.0922 to .1998
Hallbook & Lanner[887]	1972	26	.1418	Not available	.1393	Not available

[a] Treatment group received oral ciprofloxacin.
[b] Treatment group received oral trimethoprim.
[c] Treatment group received topical copper mixture.
[d] Treatment group received topical silvadene.

Table 8.2. Comparison of Individual Electrical Stimulation RCTs with Normalized Healing Rate Control Group-Matched ($?_{con}$) Conventional RCTs for Venous Ulcers

Electrical Stimulation RCT		Control-matched Conventional Venous RCT*		Crude Comparison of Normalized Healing Rates** by $?_{tx}$ 95% Confidence Interval Values
Study	**Treatment: $?_{tx}$ 95% CI**	**Study**	**Treatment: $?_{tx}$ 95% CI**	
Stiller et al.[888]: PEMF	.0596 to .0975	Layton et al.[889]: oral aspirin	.0079 (mean)	No difference
		Huovinen et al.[890]: ciprofloxacin	.0536 to .0765	No difference
		: trimethoprim	.0277 to .0588	PEMF therapy > trimethoprim
		Nikolova[891]: flunarizine	.0415 to .2568	No difference
		Hillstrom[892]: cadexomer iodine	-.0038 to +.1648	No difference
		Cordts et al.[893]: hydrocolloid	.1582 to .1998	PEMF therapy < hydrocolloid
		Barbarino[894]: pentoxifylline	.2371 to .6090	PEMF therapy < pentoxifylline
		Mann et al.[895]: oral rutoside	-.0423 to +.2172	No difference

* $?_{con}$ 95% CI of ES study overlaps $?_{con}$ 95% CI of non-ES study

** Note: This comparison does not consider patient and wound differences and therefore is not a statistical comparison.

Excluded: Todd et al.[896]: Comparison not possible because no variance available.

Ieran et al.[897]: Comparison not possible because cannot calculate theta values.

Table 8.3. Normalized Healing Rates for RCTs of Alternative Therapies for Venous Ulcers

Study	Year	Type of Therapy	Number of Patients/Ulcers	Normalized Healing Rates for Experimental Group ($?_{tx}$)		Normalized Healing Rates for Control Group ($?_{con}$)	
				Mean $?_{tx}$ Value	95% Confidence Interval	Mean $?_{con}$ Value	95% Confidence Interval
Falanga et al.[898]	1992	(Human) Epidermal Growth Factor	35	.0654	Not available	.0139	Not available
Lundeberg et al.[899]	1990	Pulsed Ultrasound	44	.0805	-.0401 to +.1260	-.0679	-.1666 to .3072
Callam et al.[900]	1987	Ultrasound	108	.1888	.1114 to .2662	.0971	-.0164 to .2106

Table 8.4. Comparison of Individual Electrical Stimulation RCTs with Normalized Healing Rate Control Group-Matched ($?_{con}$) Alternative RCTs for Venous Ulcers

Electrical Stimulation RCT		Control-matched Alternative Venous RCT*		Crude Comparison of Normalized Healing Rates** by $?_{tx}$ 95% Confidence Interval Values:
Study	**Treatment: ? 95% CI**	**Study**	**Treatment: ? 95% CI**	
Stiller et al.[901]: PEMF	.0596 to .0975	Lundeberg et al.[902]: ultrasound Callam et al.[903]: ultrasound	-.0401 to +.1260 .1114 to .2662	No difference PEMF therapy < ultrasound

*$?_{con}$ 95% CI of ES study overlaps $?_{con}$ 95% CI of non-ES study

** Note: This comparison does not consider patient and wound differences and therefore is not a statistical comparison.

Excluded: Todd et al.[904]: Comparison not possible because no variance available.

Ieran et al.[905]: Comparison not possible because cannot calculate theta values.

Table 8.5. Normalized Healing Rates for RCTs of Conventional Therapies for Decubitus Ulcers

Study	Year	Number of Patients/Ulcers	Normalized Healing Rates for Experimental Group ($?_{tx}$)		Normalized Healing Rates for Control Group ($?_{con}$)	
			Mean $?_{tx}$ Value	95% Confidence Interval	Mean $?_{con}$ Value	95% Confidence Interval
LaVasseur & Helme[906]	1991	21 (grade I/II)	.5157	.1488 to .8827	.4350	.1962 to .6739
Darkovich et al.[907]	1990	90 (grade I/II)	.1336	Not available	.0600	Not available
Alm et al.[908]	1989	56*	.7675	Not available	.2388	Not available
Neill et al.[909]	1989	87	.3010 (grade II)	.1162 to .4862	.0817	.0521 to .1113
			.0004 (grade III)	.0003 to .0005	.0446	.0289 to .0603
Oleske et al.[910]	1986	15 (grade I/II)	.5965	0.0194 to 1.1738	.6274	-0.3552 to 1.6064
Sebern[911]	1986	77	.5756 (stage II)	Not available	.0817	Not available
			.0501 (stage III)	Not available	.1026	Not available
Moberg et al.[912]	1983	34*	.1513	.1045 to .1927	.0897	.0242 to .1558

* Stage or grade of ulcerations not specified

Table 8.6. Comparison of Individual Electrical Stimulation RCTs with Normalized Healing Rate Control Group-Matched ($?_{con}$) RCTs for Decubitus Ulcers

Electrical Stimulation RCT		Control-matched Conventional Decubitus RCT*		Crude Comparison of Normalized Healing Rates** by $?_{tx}$ 95% Confidence Interval Values:
Study	**Treatment: $?_{tx}$ 95% CI**	**Study**	**Treatment: $?_{tx}$ 95% CI**	
Salzberg et al.[913]: PEE stage II	.3114 to 1.6370	LaVasseur et al.[914]: F14001 cream (grade I/II) Alm et al.[915]: hydrocolloid (unstaged) Oleske et al.[916]: polyurethane dress (grade I/II) Moberg et al.[917]: cadexomer iodine (unstaged)	.1488 to .8827 .7675 (mean) 0.0194 to 1.1738 .1045 to .1927	No difference No difference No difference PEE > cadexomer iodine
Wood et al.[918]: PDC stage II/III	.3571 to .4827	Darkovich et al.[919]: hydrogel (stage I/II) Neill et al.[920]: hydrocolloid (grade II) : hydrocolloid (grade III) Oleske et al.[921]: polyurethane dress (grade I/II) Sebern[922]: MVP dressing (stage II) Moberg et al.[923]: cadexomer iodine (unstaged)	.1336 (mean) .1162 to .4862 .0003 to .0005 0.0194 to 1.1738 .5756 (mean) .1045 to .1927	? No difference PDC therapy > hydrocolloid No difference ? PDC > cadexomer iodine
Stefanovska et al.[924]: AC unspecified stage	.3461 to .4141	Oleske et al.[925]: polyurethane dress (grade I/II) Moberg et al.[926]: cadexomer iodine (unstaged)	0.0194 to 1.1738 .1045 to .1927	No difference AC > cadexomer iodine
Kloth & Feedar[927]: HVPC stage IV	.4201 to 1.3469	Darkovich et al.[928]: hydrogel (stage I/II) Neill et al.[929]: hydrocolloid (grade II) : hydrocolloid (grade III) Oleske et al.[930]: polyurethane dress (grade I/II) Moberg et al.[931]: cadexomer iodine (unstaged)	.1336 (mean) .1162 to .4862 .0003 to .0005 0.0194 to 1.1738 .1045 to .1927	? No difference HVPC therapy > hydrocolloid No difference HVPC > cadexomer iodine

* $?_{con}$ 95% CI of ES study overlaps $?_{con}$ 95% CI of non-ES study

** Note: This comparison does not consider patient and wound differences and therefore is not a statistical comparison.

Excluded: Unger et al.,[932]
Feedar & Kloth[933]: Comparison not possible because cannot calculate theta values.
Stefanovska et al. (DC therapy), Gentzkow et al.,[934]
Griffin et al.,[935]
Salzberg et al.[936]: No significant difference between ES & control group within study

MVP = moisture vapor permeable

Table 8.7. Normalized Healing Rates for RCTs of Alternative Therapies for Decubitus Ulcers

Study	Year	Type of Therapy	Number of Patients/Ulcers	Normalized Healing Rates for Experimental Group ($?_{tx}$)		Normalized Healing Rates for Control Group ($?_{con}$)	
				Mean $?_{tx}$ Value	95% Confidence Interval	Mean $?_{con}$ Value	95% Confidence Interval
Mustoe et al.[937]	1994	Platelet-derived growth factor-BB	31	.2906* (stages III/IV)	.1436 to .4376	.0550	.0320 to .0780
				.1927** (stages III/IV)	.0900 to .2954	.0550	.0320 to .0780
Nussbaum et al.[938]	1994	Pulsed ultrasound, ultraviolet-C, and laser	17	.5565# (unstaged)	.5000 to .6130	.2937	.2285 to .3589
				.2284## (unstaged)	.1532 to .3036	.2937	.2285 to .3589
Robson et al.[939]	1992	Recombinant basic fibroblast growth factor	49	.6636 (grades III/IV)	.6291 to .6981	.3677	.3287 to .4067
Wills et al.[940]	1983	Ultraviolet	16	.8101 (superficial)	.5398 to 1.0803	.5651	.4772 to .6530

* Low-dose regimen; ** High-dose regimen

Ultrasound + ultraviolet-C therapy;

Laser therapy

Table 8.8. Comparison of Individual Electrical Stimulation RCTs with Normalized Healing Rate Control Group-Matched ($?_{con}$) Alternative RCTs for Decubitus Ulcers

Electrical Stimulation RCT		Control-matched Conventional Decubitus RCT*		Crude Comparison of Normalized Healing Rates** by $?_{tx}$ 95% Confidence Interval Values:
Study	**Treatment: $?_{tx}$ 95% CI**	**Study**	**Treatment: $?_{tx}$ 95% CI**	
Salzberg et al.[941]: PEE stage II	.3144 to 1.6370	Nussbaum et al.[942]: US/UV-C (unstaged) Laser (unstaged) Robson et al.[943]: bFGF (grades III/IV) Wills et al.[944]: UV (superficial)	.5000 to .6130 .1532 to .3036 .6291 to .6981 .5398 to 1.0803	No difference PEE therapy > laser No difference No difference
Wood et al.[945]: PDC stage II/III	.3571 to .4827	Mustoe et al.[946]: PDGF-BB+ (stages III/IV) PDGF-BB++ (stages III/IV)	.1436 to .4376 .0900 to .2954	No difference PDC therapy > high-dose PDGF-BB
Stefanovska et al.[947]: AC unspecified stage	.3461 to .4141	No studies for comparison	—	—
Kloth & Feedar[948]: HVPC stage IV	.4201 to 1.3469	Mustoe et al.[949]: PDGF-BB+ (stages III/IV) PDGF-BB++ (stages III/IV)	.1436 to .4376 .0900 to .2954	No difference HVPC therapy > high-dose PDGF-BB

+ Low-dose regimen; ++ High-dose regimen

* $?_{con}$ 95% CI of ES study overlaps $?_{con}$ 95% CI of non-ES study

** Note: This comparison does not consider patient and wound differences and therefore is not a statistical comparison.

Excluded: Unger et al.[950]
Feedar & Kloth[951]: Comparison not possible because cannot calculate theta values.
Stefanovska et al. (DC therapy), Gentzkow et al.,[952]
Griffin et al.,[953]
Salzberg et al.[954]: No significant difference between ES and control group within study

9.0 General Summary

9.1 Basic Description of Electrical Stimulators

Because human skin may act like a battery that can drive electrical currents into a wound, electrical stimulation (ES) has been studied as a possible therapy for accelerating wound healing. Preclinical studies have shown that externally applied ES can increase ATP (adenosine triphosphate) concentrations in tissues, increase DNA synthesis, promote healing of soft tissue or ulcers, cause epithelial and fibroblasts to migrate into wound sites, accelerate the recovery of damage neural tissue, reduce edema, and the inhibit the growth of some pathogens.

ES has been used or studied for many different therapeutic applications. It has been used for stimulating the healing of fractures in the lower leg, spine, and wrist and for relieving chronic intractable pain in the spine. Studies have also tested the effectiveness of ES to heal jaw fractures, reduce pain and swelling in soft tissue injuries, alleviate spinal cord lesions, eliminate intermittent claudication, improve healing from assorted hand injuries, reduce cerebral edema in cases of head trauma, reduce swelling in grades I and II ankle sprains, and accelerate healing after foot, dental, or oral surgery.

We identified several types of ES for wound healing:

- direct current (DC),
- pulsed current (PC),
- alternating current (AC),
- pulsed electromagnetic induction (PEMI), and
- spinal cord stimulation (SCS).

Direct Current (DC)—Most published studies of DC stimulation for the treatment of wound healing used low-intensity direct current (LIDC). Clinicians applied 20 to 100 microamps (μA) of current at low voltage (< 8 volts). The cathode was usually wrapped in saturated (saline) gauze and placed directly over the wound site; the anode was placed on the skin surface near the wound. Patients underwent 2-hour sessions 2 or 3 times daily. After several days or if the wound apparently stopped healing, clinicians reversed (switched) the polarity of the electrode by placing the anode directly over the wound and the cathode at a nearby site. They reversed polarity one or more times (depending on the regimen) to stimulate healing if the wound had not improved or reached a "growth plateau."

Pulsed Current (PC)—We classified published studies of PC stimulation for the treatment of wound healing into 2 subcategories: (a) PDC and (b) HVPC. PDC studies generally used 30 to 40 mA (generated by a 6 to 12 V battery) at 128 pulses per second (Hz), although 1 study (Wood et al.[955]) used 300 to 600 µA at only 0.8 Hz. HVPC studies generally used 100 to 250 V at 80 to 100 pulses per second (Hz).

Alternating Current (AC) and TENS—We classified published studies of AC stimulation for the treatment of wound healing into 2 subcategories: (a) TENS devices and (b) biphasic pulsed. Studies of TENS generally used small, portable devices capable of generating square-wave pulses at 80 to 90 Hz with 0.1 to 0.2 ms pulse widths. Biphasic AC studies used 15 to 25 mA with 0.25 ms pulses at 40 Hz frequency.

Pulsed Electromagnetic Induction (PEMI)—We classified published studies of pulsed electromagnetic stimulation for the treatment of wound healing into 2 subcategories: (a) those using PEMF devices containing electromagnetic coils capable of generating a magnetic field and (b) those using PEE devices capable of generating a high peak wattage.[ee] Both types of devices are nonthermal and are applied externally on top of dressings. Neither uses electrodes wrapped in wet gauze. PEMF studies generally used a low-level magnetic field that induced a low-level nonthermal electrical field. PEE studies used Diapulse devices exclusively, which employed a pulsed, nonthermal high-frequency, high peak power electromagnetic energy delivered at 27.12 MHz, with a pulse repetition rate of 80 to 600 pulses/second, 65 µs pulse width, peak pulse power of 273 to 975 W, and 0.5% to 4.0% duty cycle. As with PEMF devices, the device is applied externally over existing dressings.

Spinal Cord Stimulation (SCS)—Spinal cord stimulators are primarily designed to reduce intractable pain in patients with failed back syndrome and other chronically painful disorders. These devices significantly differ from the types of electrical stimulators previously mentioned for wound healing because spinal cord stimulators (a) are invasive and (b) are not primarily intended to increase the rate of wound healing.

SAFETY OF ELECTRICAL STIMULATORS FOR WOUND HEALING—General contraindications include use in the presence of metallic implants, in the presence of neoplasms, in the presence of osteomyelitis, or on patients with demand-type cardiac pacemakers. We searched the ECRI Health Devices Alerts database and found no reported patient injuries associated with ES devices for wound healing as of December 14, 1995.

[ee] Also known as "pulsed radio frequency energy."

9.2 Analyses of Electrical Stimulation Studies

9.2.1 Quality of Electrical Stimulation Studies

We searched 17 databases and identified 41 studies of ES for the treatment of chronic wounds. They included:

- 6 studies using direct current stimulation (2 randomized controlled trials {RCTs}, 1 comparative, 2 case series {with embedded RCTs}, and 1 case report);
- 14 studies using pulsed current stimulation (9 RCTs, 2 case series, and 3 case reports);
- 9 studies using AC or TENS stimulation (2 RCTs, 6 case series {1 with a very preliminary RCT}, and 1 case report);
- 7 studies using pulsed electromagnetic induction devices (5 RCTs, 1 case series, and 1 case report); and
- 5 studies using implanted spinal cord stimulation (2 case series, 3 case reports) + 1 background article (on SCS for amputations).

These studies formed the basis of our qualitative and quantitative analyses.

Our only selection criteria was that these studies did not explicitly state that they primarily included patients with lesions <30 day duration.[ff] Our definition of chronic wounds was a duration of ≥30 days.

Outcomes of wound healing studies may be biased (compromised) by several types of confounding factors: (1) lack of homogeneity of study groups, (2) failure to account for systemic or local medical conditions that can interrupt or alter wound healing, (3) inconsistencies in regimen of primary wound therapy, and (4) inconsistencies in concomitant wound therapy.

In addition, study outcomes were often expressed with flawed measurements. For example, many wound healing studies report the number (and/or percentage) of patients healed at given time intervals. One might assume that this is a straightforward, simple measurement of a therapy to promote healing. Unfortunately, the number (percentage) of patients healed is a flawed outcome measure because it depends on study follow-up duration and initial wound size.

[ff] Throughout our analysis, we used the terms “lesion,” “wound,” and “ulcer” interchangeably.

Most wound healing studies express healing as a rate, usually the percentage of ulcer healed per week. Unfortunately, nearly all wound healing studies expressed healing rates by surface area, which may substantially differ from volumetric healing rates that more accurately represent true healing. Whenever possible, we used an exponential decay model, also known as the normalized healing rate (?), to express healing rates for wound healing.

We evaluated the quality of each electrical stimulation study for wound healing[gg] by

- study design (e.g., type of study, randomization, blinding, size);
- differences between study groups (e.g., patient age, patient gender, wound type, duration of wound, stage, anatomical location of wound, infective status of wound);
- medical conditions affecting wound healing (e.g., presence of peripheral arterial or peripheral vascular disease, rheumatoid arthritis, exogenous use of steroids, nutritional status); and
- inconsistencies in concomitant wound therapy leading to possible confounding (e.g., debridement, use of topical and/or cleansing agents, use of dressings, use of pressure devices or turning therapy if applicable, use of topical or systemic antibiotics).

For outcome measures, each trial was evaluated to determine whether it:

- specified initial wound size by surface area and/or volume, and
- specified initial wound size by subject, group (without variance), or group with variance.

Individual study critiques are presented in section 4.3. All studies had at least 1 weakness, but not all were potentially confounded by these criteria.

9.2.2 Quantitative Analysis of Electrical Stimulation Normalized Healing Rates

Many wound healing studies assumed or implied that the rate of wound healing is linear. There is little evidence that this is true.

We observed that studies appear to exhibit exponential healing rates. We used an exponential decay model reported by Karba et al.[956] and Stefanovska et al.[957]

[gg] Excluding case reports and background studies.

to describe the rate of wound healing. Using an exponential decay model enables one to express the healing rate as a constant independent of wound size. Karba et al. have described this constant as the **normalized healing rate** or **theta (?)**, usually expressed as a value per week.

The normalized healing rate (?) is derived from the basic equation for an exponential decay:

$$S_t = S_0 \times e^{-?t}$$

where S_t is the size of a wound at a time "t" and S_0 is the initial size of the wound (at time 0). Solving for theta:

$$S_t/S_0 = e^{-?t}$$
$$\ln(S_t/S_0) = -?t$$
$$\ln(S_0/S_t) = ?t$$
$$? = [\ln(S_0/S_t)]/t.$$

Time "t" is usually expressed in weeks. For example, if the initial size of a wound is 4 cm^2 and the size 8 weeks later is 0.25 cm^2, then ? = [ln(4 ÷ 0.25)] ÷ 8 = 0.3466/week. Although ? is a good measure of wound healing, it does have weaknesses.

We calculated the normalized healing rate for all ES studies that provided sufficient data.

Based on these calculations, we concluded that there is **evidence** of the following:

- For direct current devices, there is evidence that PDC improves the healing rate of stage II or III decubitus ulcers compared to sham (placebo) therapy. However, there is only weak evidence that HVPC improves the healing rate of stage IV decubitus ulcers compared to sham therapy. This evidence is weak because of small study size.

- There is evidence that PEE stimulation improves the healing rate of stage II decubitus ulcers.

Based on these calculations, we concluded that there is **weak evidence** of the following:

- There is weak evidence that AC stimulation improves the healing of decubitus ulcers compared to "standard" therapy, but these results are suspect because the standard therapy was not specified.

- There is weak evidence that PEMF stimulation improves the healing rate of chronic venous ulcers compared to sham therapy, but these results are suspect because of possible inconsistencies in concomitant therapy.

Based on these calculations, we concluded that there is **no evidence** of the following:

- There is no evidence that DC stimulation improves the healing rate of chronic venous, decubitus, or diabetic ulcerations.
- There is no evidence that PC stimulation improves the healing rate of chronic venous or diabetic ulcerations.
- There is no evidence that AC (including TENS) improves the healing rate of chronic diabetic ulcerations.
- There is no evidence that PEMI stimulation (PEMF or PEE energy) improves the healing rate of chronic decubitus or diabetic ulcerations.
- There is no evidence that any other form of ES improves the healing rate of chronic lesions.

9.2.3 Meta-Analyses of Electrical Stimulation Studies

We performed 2 meta-analyses to determine

- whether ES increases the normalized wound healing rate (?), and
- whether ES increases the proportion of wounds that completely heal.

Both of our meta-analyses are designed to answer 2 critical questions:

- Does ES promote wound healing?
- If ES does promote wound healing, then is there a particular patient or treatment subgroup for whom ES is most effective?

We used the **Hedges' *d*** statistic, which is the difference between the experimental and control groups expressed in units of standard deviation and corrected for errors in treatment effect estimations. We calculated *d* for each study in the meta-analysis. Values of $d > 0$ imply that ES therapy promotes wound healing; values of $d < 0$ imply that ES therapy hinders wound healing.

A $d = 0$ implies that ES therapy has no effect. Another important statistic we used in our meta-analysis is the Q statistic, which tests the homogeneity of studies—that is, whether all studies in the meta-analysis share a common effect size. Using all applicable controlled studies from our literature searches, we performed both fixed- and random-effects analyses.

Although there are weaknesses in our meta-analyses (e.g., excluding outliers, small study sizes, literature weaknesses), we conclude the following:

- ES increases the normalized healing rate (?) of chronic ulcers.
- ES increases the proportion of complete healing of chronic ulcers.
- However, the relationship between outcomes and ES is not always simple. For example, the effect of ES on wound healing rates appears to be small in patients with larger wounds and is affected by the type of stimulator.
- There is weak evidence suggesting that decubitus ulcers have greater healing rates than venous ulcers by ES.
- ES appears more likely to enhance complete healing of decubitus ulcers.

9.3 Comparison of Electrical Stimulation Studies with Other Therapies for Wound Healing

9.3.1 Comparison of Qualities of Studies

The RCTs of ES therapy for wound healing have many design and reporting weaknesses. We wanted to determine whether these flaws are unique to ES studies or are common shortcomings throughout published studies of wound healing.

VENOUS ULCERS: CONVENTIONAL THERAPIES—We identified 40 ***conventional***[hh] RCTs for the treatment of venous ulcers. Our definition of *conventional* RCT was any therapeutic study of venous ulcers which evaluated debridement, cleaning agents, topical agents, dressings, bandages, antibiotics (systemic or local), compression therapies, systemic medications, or nutritional supplements. We compared the quality of these conventional RCTs for wound healing to ES RCTs for healing of venous ulcers.

Based on our comparisons, we conclude the following:

- The shortcomings presented in RCTs for ES for venous ulcers are common throughout published studies of conventional therapies for venous ulcers. One ES study, however, appears inferior in quality.

VENOUS ULCERS: ALTERNATIVE THERAPIES—We identified 10 ***alternative*** RCTs for the treatment of venous ulcers. Our definition of *alternative* RCT was any therapy utilizing hyperbaric oxygen (HBO), growth factors, ultrasound (US), lasers, or ultraviolet light (UV). We compared the quality of these alternative RCTs for wound healing to ES RCTs for healing of venous ulcers.

Based on our comparisons, we conclude the following:

- The shortcomings presented in RCTs for ES for venous ulcers are common throughout published studies of alternative therapies for venous ulcers. However, 2 of the 3 ES studies may have been confounded by inconsistencies in concomitant therapy whereas none of the alternative studies was confounded. Therefore, ES study quality may be slightly inferior to those in other alternative-therapy studies of venous ulcers.

[hh] The term "conventional" is not meant to imply that the (experimental group) therapy or therapies in the RCT are accepted treatment regimens.

DECUBITUS ULCERS: CONVENTIONAL THERAPIES—We identified 16 conventional RCTs for the treatment of decubitus ulcers. We compared the quality of these conventional RCTs for wound healing to electrical stimulation RCTs for healing of decubitus ulcers.

Based on our comparisons, we conclude the following:

- The shortcomings presented in RCTs for ES for decubitus ulcers are common throughout published studies of conventional therapies for decubitus ulcers. However, because ES studies were usually blind and were usually not confounded by the inclusion of diabetic patients or concomitant therapy, particularly topical/cleansing agents and dressings, it appears that their quality may be slightly superior to RCTs of conventional therapies for decubitus ulcers—with the exception of 1 ES study.

DECUBITUS ULCERS: ALTERNATIVE THERAPIES—We identified 7 alternative RCTs for the treatment of decubitus ulcers. We compared the quality of these alternative RCTs for wound healing to ES RCTs for healing of venous ulcers.

Based on our comparisons, we conclude the following:

- The shortcomings presented in the RCTs for ES for decubitus ulcers are common throughout published studies of alternative therapies for decubitus ulcers. The quality of ES randomized controlled studies of decubitus ulcers appears to be similar to the quality of alternative therapy RCTs.

9.3.2 Comparison of Normalized Healing Rates

We calculated the ? values for ES RCTs. There was a significant difference in the normalized healing rates between some types of ES ($?_{tx}$) and control ($?_{con}$) groups. We determined that the effect sizes (Hedges' *d*) for some studies were significant.

However, these studies only demonstrate that patients treated by ES stimulation may heal faster than those undergoing no therapy at all. These outcomes, by themselves, are not clinically useful because they do not compare ES to wound healing therapies patients are likely to receive. The best way to determine whether ES therapy is effective is to conduct RCTs that compare stimulation therapy to common therapies for chronic wound healing. In the absence of such RCTs, we can only compare ES outcomes with outcomes from RCTs of other therapies.

We compared ES with non-ES therapies using the normalized healing rate (?). This value allows us to assess whether one therapy appears to accelerate wound healing compared to another. Currently, it is the only way to determine whether healing rates of patients treated by ES is less than, roughly equivalent to, or greater than other therapies. For example, if the mean ? is +0.4199 (95% CI = +0.3571 to +0.4827) and we were treating a 10 cm^2 lesion, we would expect it to heal (99%) in approximately 10.9 weeks (t = [ln (10 cm^2/.1 cm^2)] ÷ ? = 10.9). Without the context of ? values from other therapies, one wonders if this is a poor or excellent healing time. If another therapy, such as hydrocolloidal dressing, typically has ? values between +0.1 and +0.2, then the identical lesion would require 23 to 46 weeks to heal. If, on the other hand, it typically has values between +0.6 and +0.7, then the same lesion would require 6.6 to 7.7 weeks.

Unfortunately, we cannot directly compare normalized healing rates from different studies because of heterogeneity, numerous variables, confounding factors—and too few studies. These weaknesses and the poor quality of published studies of wound healing circumvent any analysis that would account for different patient and wound characteristics. We can only conduct crude comparisons to assess whether ? values from ES studies appear greater, smaller, or similar to those for other therapies.

Therefore, we compared ES RCTs to non-ES RCTs that had (a) similar types of lesions (i.e., venous, decubitus) and (b) control groups with similar healing rates. We performed the latter by comparing ? values for ES study control groups with ? values for non-ES study control groups. If the 95% confidence intervals for the control groups of ES and non-ES studies overlapped, then we compared the experimental groups of the studies. This provides a crude estimate of ES therapy compared to non-ES therapy for venous and for decubitus ulcers.

VENOUS ULCERS: CONVENTIONAL THERAPIES—Twenty-one of the 40 conventional RCTs for the treatment of venous ulcers provided sufficient data to calculate normalized healing rates. Only 1 ES study showed a significant difference between ES (using PEMF therapy) and placebo groups.

Based on our crude comparison which did not consider possible patient and wound heterogeneity,

- PEMF produces a normalized healing rate roughly similar to most conventional RCTs.

VENOUS ULCERS: ALTERNATIVE THERAPIES—Three of the 10 alternative RCTs for the treatment of venous ulcers provided sufficient data to calculate normalized healing rates. Only 1 ES study showed a significant difference between ES and placebo (using PEMF therapy) and provided sufficient data for calculating ?.

Based on our crude comparison, which did not consider possible patient and wound heterogeneity,

- the clinical value of PEMF therapy for accelerating wound healing is minimal.

DECUBITUS ULCERS: CONVENTIONAL THERAPIES—Seven of the 16 conventional RCTs for the treatment of decubitus ulcers provided sufficient data to calculate normalized healing rates. Four ES studies showed a significant difference between ES and placebo groups (1 PDC, 1 HVPC, 1 AC, and 1 PEE) and provided sufficient data for calculating ?.

The following are based on these crude comparisons, which did not consider possible patient and wound heterogeneity:

- PEE therapy for stage II decubitus ulcers yields normalized healing rates that are indistinguishable from established therapies.

- PDC therapy for stage II or III decubitus ulcers yields normalized healing rates that are indistinguishable from established therapies.

- There is insufficient data to compare HVPC therapy for stage IV decubitus ulcers to conventional therapies.

- There is insufficient information to compare AC therapy to conventional therapies for decubitus ulcers.

However, even this crude comparison may not be valid because most of the conventional RCTs used grades I through III ulcers or stage I or II lesions whereas all patients in HVPC were stage IV.

DECUBITUS ULCERS: ALTERNATIVE THERAPIES—Four of 7 alternative RCTs for the treatment of decubitus ulcers provided sufficient data to calculate normalized healing rates. Four ES studies showed a significant difference between ES and placebo groups (1 PDC, 1 HVPC, 1 AC, and 1 PEE) and provided sufficient data for calculating ?.

The following are based on findings from conventional and alternative groups:

- PEE therapy for stage II decubitus ulcers yields normalized healing rates that are indistinguishable from established and alternative therapies.

- PDC therapy for stage II or III decubitus ulcers yield normalized healing rates that are indistinguishable from established or

alternative therapies.

- There is insufficient data to compare HVPC therapy for stage IV decubitus ulcers to conventional therapies. Normalized rates for HVPC may, however, be indistinguishable from PDGF-BB therapy.

- There is insufficient information to compare AC therapy with non-ES therapies for decubitus ulcers.

10.0 Appendix I: List of Abbreviations

AC	alternating current
ADP	adenosine diphosphate
AHCPR	Agency for Health Care Policy and Research
ATP	adenosine triphosphate
B	unstandardized regression coefficient
BCOHTA	British Columbia Office of Health Technology Assessment
bFGF	(basic) fibroblast growth factor
BID	two times a day
CI	(95%) confidence interval
CL_{lower}	lower limit of confidence interval
CL_{upper}	upper limit of confidence interval
COM	chronic osteomyelitis
d	Hedges' *d* = standardized measure of effect size
d_o	overall *d*
DC	direct current
dv	device variable
EGF	epidermal growth factor
ES	electrical stimulation
FGF	fibroblast growth factor
GaAs	gallium-arsenide laser (therapy)
HBO	hyperbaric oxygen
hEGF	(human) epidermal growth factor
HeNe	helium-neon laser (therapy)
hGF	(human) growth factor
HVPC	high-voltage pulsed current
HVPG	high-voltage pulsed galvanic (direct current)
Hz	hertz (1 cycle/second)
IL-(#)	interleukin-(factor #)
LIDC	low-intensity direct current
MENS	microcurrent electrical neuromuscular stimulator]
NMES	neuromuscular electrical stimulator
NPUAP	National Pressure Ulcer Advisory Panel
ORN	osteoradionecrosis
PAF	platelet-activating factor
PC	pulsed current
PDC	pulsed direct current
PDGF(-BB)	platelet-derived growth factor(-BB)
PDWGF	(autologous) platelet-derived wound healing factors
PEE	pulsed electromagnetic energy
PEMF	pulsed electromagnetic field
PEMI	pulsed electromagnetic induction
PGF	placental growth factor
Q	*Q* statistic = measure of homogeneity

Q_E	*Q* statistic for multiple regression
Q_1	1st quartile (25th percentile)
Q_3	3rd quartile (75th percentile)
RCT	randomized controlled trial
SCS	spinal cord stimulator (stimulation)
SD	standard deviation
SE	standard error
T_cPO_2	transcutaneous oxygen level
TENS	transcutaneous electrical nerve stimulation
TGF-a	transforming growth factor-alpha
TGF-ß	transforming growth factor-beta
?	theta = normalized healing rate
$?_{con}$	normalized healing rate for control group(s)
$?_{tx}$	normalized healing rate for treatment group(s)
TID	three times a day
TNF	tumor necrosis factor
UHC	University Hospital Consortium
UMDNS	Universal Medical Device Nomenclature System
US	ultrasound (therapy)
UV	ultraviolet (therapy)
WOCN	Wound Ostomy and Continence Nurses Society
WP	whirlpool

11.0 Appendix II: Formulae Used in Meta-Analyses

11.1 Univariate Analysis

11.1.1 Formulae for Univariate Fixed Effects Models

11.1.1.1 Hedges' *d*

Meta-analyses were conducted by computing a Hedges' *d* for each study and then computing an average *d* weighted by the inverse of each study's variance. Statistical significance of this overall *d* (d_o) and of the *d*'s from individual studies is determined from the 95% confidence limits around these *d*'s. For each study, differences between experimental and control groups were initially converted into Hedges' *g*, then into Hedges' *d*.

Hedges' *g* standardizes the differences between the means of different studies by dividing each of these differences by the standard deviation. The effect of this standardization is to convert the between-group differences in each study into effect sizes that are all derived from population with a variance equal to 1, thereby eliminating dependence of the scores from their often unique units of measurement.

Unfortunately, Hedges' *g* overestimates the true effect size of small studies. This bias becomes apparent when the total number of patients in the experimental plus control groups is ≤10. Therefore, Hedges' *g* is corrected for this overestimate by converting it into Hedges' *d*.

The formula for computing each study's Hedges' *g* is:

$$g = \frac{\overline{X_e} - \overline{X_c}}{s_{pooled}} \qquad 1$$

where X_e bar is the mean of the experimental group, X_c bar is the mean of the control group, and s_{pooled} is the pooled standard deviation of the experimental and control groups. In the analysis of complete wound healing, X_e bar and X_c bar were the proportion of wounds in the experimental and control groups that healed. In the analysis of normalized wound healing rates, average values of ? were calculated from published data of experimental and control groups.

The value of S_{pooled} is given by the formula:

$$S_{pooled} = \sqrt{\frac{(n_e - 1)(S_e^2) + (n_c - 1)(S_c^2)}{n_e + n_c - 2}} \quad (2)$$

where n_e and n_c are the numbers of wounds in the experimental and control groups, respectively, and s_e^2 and s_e^2 are the variances of the experimental and control groups, respectively.

The formula used for calculating the experimental and control group variances for each study in the analyses of complete wound healing was:

$$s^2 = (p)(1-p) \quad (3)$$

where s^2 is the variance of either the experimental or control group and p is the proportion of wounds in the experimental or control group. For analysis of wound healing rates, the experimental and control group variances were taken from published variances, standard errors, standard deviations, or 95% confidence limits.

Hedges' *d* for each study is then calculated from each study's *g*, where:

$$d = (1 - \frac{3}{4N - 9})g \quad (4)$$

where N equals the sum of the number of wounds in the experimental and control groups, and where *g* is taken from the above equation.

Ninety-five percent confidence limits of each *d* are calculated from each study's variance. The variance for each study, v_i, is calculated according to the formula:

$$v_i = \frac{n_c + n_e}{n_c n_e} + \frac{d_i^2}{2(n_c n_e)} \quad (5)$$

where n_e and n_c are defined above, and d_i^2 is the squared *d* that was calculated for that study.

Because the square root of this variance equals the standard error, the 95% confidence limits for each study can be calculated from the equation:

$$C_\alpha = 1.96\sqrt{v_i} \qquad 6$$

Adding C_a to d_o gives the upper 95% confidence limit; subtracting C_a from d_o gives the lower 95% confidence limit.

Calculating the overall d (d_o) for the collection of studies involves determining an average d, where each study's contribution to d_o is weighted by the inverse of its variance. Thus, for a collection of k studies, where the d for the i^{th} study is d_i and the weight for the i^{th} study is w_i (i.e., $1/v_i$), the formula for the overall d is:

$$d_o = \frac{\sum_{i=1}^{k} w_i d_i}{\sum_{i=1}^{k} w_i} \qquad 7$$

To create 95% confidence intervals around the overall d_o, one must first calculate the conditional variance, v_c, according to the formula:

$$v_c = \frac{1}{\sum_{i=1}^{k} (1/v_i)} \qquad 8$$

(This quantity is called the conditional variance because it is conditioned upon the studies at hand, and is to be distinguished from the unconditional variance used in random effects models.)

Now, from the conditional variance, one calculates the critical level, C_a, according to the formula:

$$C_\alpha = 1.96(\sqrt{v_c}) \qquad 9$$

Adding C_a to d_o gives the upper 95% confidence limit and subtracting C_a from d_o gives the lower 95% confidence limit.

11.1.1.2 *Q* Statistic

The *Q* statistic is used to test whether the individual studies share a common population effect size. The *Q* statistic is most easily understood from the equation.

$$Q = \sum_{i=1}^{k} \frac{(d_i - d_o)^2}{v_i} \qquad \textbf{10}$$

Here, it can be seen that each study's deviation from d_o and each study's variance is taken into account in calculating the *Q* statistic.

Q is statistically significant if its value exceeds the upper-tail critical value of chi-square on k-1 degrees of freedom. If *Q* is found to be statistically significant, the studies included in the meta-analysis are not measuring the same parameter (i.e., they are heterogeneous).

The *Q* statistic can also determine whether differences between categorical subgroups are statistically significant. However, this is only possible if *Q* is statistically significant. These calculations are based on a model analogous to analysis of variance, and the overall model is described by the equation:

$$Q_T = Q_B + Q_w \qquad \textbf{11}$$

where Q_T is the *Q* statistic described above and is the "total fit" to the model of a single effect size, Q_B is the "between group fit", and Q_W is the "within class fit". If there are k studies and p categories, the degrees of freedom for Q_T equal k-1, the degrees of freedom of Q_B equal p-1, and the degrees of freedom of Q_W equal k-p.

One performs this test by first calculating Q_T (i.e. *Q*). If this value is large or statistically significant, then the studies are partitioned into groups, and one calculates Q_B and Q_W as described above for *Q*. If Q_W is not statistically significant, then the process stops because the model of a different effect size for each category is consistent with the data. In this case, the *d* for that category (calculated as described for d_o), represents the effect size for that category, and Q_B represents to which the effect sizes among classes differ. A large Q_W indicates that further, analogous partitioning is required. One performs this partitioning using the same logic. Alternatively, if one suspects that there are more than 2 categories of effects sizes, one can partition the data into these categories and use the chi-squared test to determine whether these are statistically significant differences among the categories. In this case, the d for each category and its associated 95% confidence limits are calculated as describe above for d_o and using C_a.

11.1.1.3 Rosenthal's Method of Focused Contrasts

Rosenthal's method of focused contrasts is appropriate if one is interested in whether there is a relationship between a continuous variable and *d*. Here, each *g* is converted to a *z*-score using the formula:

$$z_i = \frac{d_i}{(d_i - CL_{lower})/1.96} \quad \textbf{12}$$

where d_i is the value of *d* for the i^{th} study and CL_{lower} is the lower 95% confidence limit for that study.

These *z* scores are then inserted into the formula:

$$Z = \frac{\sum_{i=1}^{k} \lambda_i z_i}{\sqrt{\sum_{i=1}^{k} \frac{\lambda_i}{n_i - 3}}} \quad \textbf{13}$$

where n_i is the number of patients in each study and $?_i$ is a contrast weight for each study chosen from a table of orthogonal polynomials. If *Z* exceeds 1.96, the relationship between the continuous variable and *d* is statistically significant.

11.1.2 Formulae for Univariate Random Effects Models

Calculations for univariate random effects models are similar to those for fixed effects models. The major difference is in the calculation of variances. In the fixed effects model, the overall variance is simply the conditional variance. However, in the random effects model the overall variance, called the unconditional variance, is the sum of the conditional and random effects variances or:

$$v_u = \sigma_r^2 + v_c \quad \textbf{14}$$

where v_u is the unconditional variance, s_r^2 is the random effects variance, and v_c is the unconditional variance. The random effects variance is, in turn, calculated from the equation:

$$\sigma_r^2 = [Q - (k - 1)]/c \quad \textbf{15}$$

where *Q* is the value of the *Q* statistic calculated as described in equation (10), k is the number of studies, and c is a quantity calculated from the formula:

$$c = \sum_{i=1}^{k} w_i - \frac{\sum_{i=1}^{k} w_i^2}{\sum_{i=1}^{k} w_i} \qquad \textbf{16}$$

The calculations, including weighting and construction of 95% confidence limits, proceeds as outlined above for the fixed effects approach—except that each study's variance, v_i^*, is calculated according to the formula:

$$v_i^* = \sigma_r^2 + v_i \qquad \textbf{17}$$

11.2 Multivariate Analysis

11.2.1 Formulae for Multivariate Fixed Effects Models

Multiple regressions are conducted using a computer program. In constructing these models, the *d*'s are the dependent variables and the regression is weighted by the inverse of the variance of each study (i.e. $1/v_i$).

The regression output yields the Q_E statistic, which is the test for model specification. Q_E is the residual sum of squares, and one obtains its significance by using chi-square tables on k-p-1 degrees of freedom, where k =the number of studies and p =the number of predictor variables in the model.

The computer output also contains the correct unstandardized regression coefficients (*B*'s) for each of the predictor variables. However, the standard errors for these coefficients are not correct. To obtain the correct standard errors one divides them by the square root of the residual mean square of the analysis. Now, one can multiply these corrected standard errors by 1.96 and construct confidence limits as described above, divide the unstandardized regression coefficient by the corrected standard errors to convert the coefficient into a *z* score, or divide the coefficient by the corrected standard error multiplied by 1.96 to obtain a t-test.

11.2.2 Formulae for Multivariate Random Effects Models

Random effects multiple regression is similar to fixed effects regression—except for calculating variances for each study. To obtain these variances, one first conducts an ordinary, unweighted regression. Then, the residual mean square is used to calculate the random effects variance, s_r^2, according to the formula:

$$\sigma_r^2 = MS_{residual} - v \qquad 18$$

where v is given by the formula:

$$v = \frac{\sum_{i=1}^{k} v_i}{k} \qquad 19$$

Here, the v_i's are the variances calculated from the univariate fixed effects model described above, and k is the number of studies being analyzed.

The weights for each study in the multiple regression are then calculated from:

$$w_i = \frac{1}{v_i + \sigma_r^2} \qquad \textbf{20}$$

As in the fixed effects model, the unstandardized regression coefficients are correct and the standard errors for these coefficients must be corrected by dividing them by the square root of the residual mean square. Statistical tests on the regression coefficients can then be conducted as described for the fixed effects multiple regressions.

11.3 Formulae for Publication Bias

ROSENTHAL'S METHOD—The Rosenthal method for assessing publication bias first involves converting each *d* to a *z* score as described in equation (12). An overall *z* score, z_o, is then calculated from:

where k equals the number of studies in the meta-analysis and z_o is used to calculate the number of studies needed to overturn the results, k_o, according to:

$$z_o = \frac{\sum_{i=1}^{k} z_i}{\sqrt{k}} \qquad 21$$

$$k_o = \_k + (z_o/1.96)^2 \qquad 22$$

ORWIN'S METHOD—The Orwin method for calculating k_o is given by:

$$k_o = \frac{k(d_o - d_c)}{d_c} \qquad 23$$

where d_o is the overall d of the fixed effects model, k is the number of studies in the meta-analysis, and d_c is the critical value of d that has been chosen to be negligible.

Determining where a negligible level therapeutic effectiveness lies has the potential to raise ethical problems when this line of reasoning is applied to medicine, but it is possible to make some assumptions that might be less objectionable than others. Thus, we assumed that a negligible level of effectiveness is no effectiveness (i.e. a *d* of 0), and that the confidence limits of a meta-analysis conducted on any unpublished studies would have the same confidence limits that we report here. This means that the maximum statistically non-significant value for a negligible effect equals the upper confidence limit of these unpublished studies.

CONTROVERSY REGARDING PUBLICATION BIAS—Begg[958] has argued that the assumption that the results of missing studies are centered about a d of 0 is artificial (to this we add that our assumption in the Orwin method that the confidence limits of unpublished studies are equal to those we observed in our meta-analyses is equally artificial), and that the methods are weak because they are not influenced by bias in the data (e.g. by the shape of the funnel plot). It is

the conclusion of Begg as well as others[959] that statistical methods for assessing publication bias are still under development, and should not be widely used.

12.0 Appendix III: AHCPR Strength-of-Evidence Rating System

The Agency for Health Care Policy and Research strength-of-evidence rating system is as follows:[960]

Rating **A**
- Results of two or more randomized controlled clinical trials on ulcers in humans provide support.

Rating **B**
- Results of two or more controlled clinical trials on ulcers in humans provide support, or when appropriate, results of two or more controlled trials in an animal model provide indirect support.

Rating **C**
- This rating requires one or more of the following: (1) results of one controlled trials; (2) results of at least two case series/descriptive studies on ulcers in humans; or (3) expert opinion.

Evidence ratings are based on the number of studies (quantity), quality of research, number of replications, and consistency of findings.

13.0 Appendix IV: External Reviewer Comments

127-002

14.0 Citations

For your convenience, each citations is provided in its entirety each time it is referenced in the text of the report.

1. Weingarten MS. Advances in wound healing. In: Oloff LM. Musculoskeletal disorders of the lower extremities. Philadelphia: Saunders; 1994. p. 52-64.

2. Weingarten MS. Advances in wound healing. In: Oloff LM. Musculoskeletal disorders of the lower extremities. Philadelphia: Saunders; 1994. p. 52-64.

3. Weingarten MS. Advances in wound healing. In: Oloff LM. Musculoskeletal disorders of the lower extremities. Philadelphia: Saunders; 1994. p. 52-64.

4. Weingarten MS. Review: obstacles to wound healing. Wounds 1993 Sep-Oct;5(5):238-44.

5. Weingarten MS. Review: obstacles to wound healing. Wounds 1993 Sep-Oct;5(5):238-44.

6. Weingarten MS. Advances in wound healing. In: Oloff LM. Musculoskeletal disorders of the lower extremities. Philadelphia: Saunders; 1994. p. 52-64.

7. Cohen IK, Diegelmann RF, Lindblad WJ, editors. Wound healing: biochemical & clinical aspects. Philadelphia: Saunders; 1992. 630 p.

8. Consensus paper on venous leg ulcer. The Alexander House Group. J Dermatol Surg Oncol 1992 Jul;18(7):592-602.

9. Cohen IK, Diegelmann RF, Lindblad WJ, editors. Wound healing: biochemical & clinical aspects. Philadelphia: Saunders; 1992. 630 p.

10. Margolis DJ, Cohen JH. Management of chronic venous leg ulcers: a literature-guided approach. Clin Dermatol 1994 Jan-Mar;12(1):19-26.

11. Cohen IK, Diegelmann RF, Lindblad WJ, editors. Wound healing: biochemical & clinical aspects. Philadelphia: Saunders; 1992. 630 p.

12. Pressure ulcers prevalence, cost and risk assessment: consensus development conference statement-- The National Pressure Ulcer Advisory Panel. Decubitus 1989 May;2(2):24-8.

13. Pressure ulcers prevalence, cost and risk assessment: consensus development conference statement-- The National Pressure Ulcer Advisory Panel. Decubitus 1989 May;2(2):24-8.

14. Allman RM. Epidemiology of pressure sores in different populations. Decubitus 1989 May;2(2):30-3.

15. Pressure ulcers prevalence, cost and risk assessment: consensus development conference statement-- The National Pressure Ulcer Advisory Panel. Decubitus 1989 May;2(2):24-8.

16. Weingarten MS. Advances in wound healing. In: Oloff LM. Musculoskeletal disorders of the lower extremities. Philadelphia: Saunders; 1994. p. 52-64.

17. Agency for Health Care Policy and Research (AHCPR). Treatment of pressure ulcers. Rockville (MD): U.S. Department of Health and Human Services, Public Health Service, AHCPR; 1994 Dec. 154 p. AHCPR publication no. 95-0652. (Clinical practice guideline; no. 15).

18. Weingarten MS. Advances in wound healing. In: Oloff LM. Musculoskeletal disorders of the lower extremities. Philadelphia: Saunders; 1994. p. 52-64.

19. Weingarten MS. Advances in wound healing. In: Oloff LM. Musculoskeletal disorders of the lower extremities. Philadelphia: Saunders; 1994. p. 52-64.

20. Romanko KP. Pressure ulcers. Clin Podiatr Med Surg 1991 Oct;8(4):857-67.

21. Weingarten MS. Advances in wound healing. In: Oloff LM. Musculoskeletal disorders of the lower extremities. Philadelphia: Saunders; 1994. p. 52-64.

22. Agency for Health Care Policy and Research (AHCPR). Treatment of pressure ulcers. Rockville (MD): U.S. Department of Health and Human Services, Public Health Service, AHCPR; 1994 Dec. 154 p. AHCPR publication no. 95-0652. (Clinical practice guideline; no. 15).

23. Weingarten MS. Advances in wound healing. In: Oloff LM. Musculoskeletal disorders of the lower extremities. Philadelphia: Saunders; 1994. p. 52-64.

24. Agency for Health Care Policy and Research (AHCPR). Treatment of pressure ulcers. Rockville (MD): U.S. Department of Health and Human Services, Public Health Service, AHCPR; 1994 Dec. 154 p. AHCPR publication no. 95-0652. (Clinical practice guideline; no. 15).

25. Agency for Health Care Policy and Research (AHCPR). Treatment of pressure ulcers. Rockville (MD): U.S. Department of Health and Human Services, Public Health Service, AHCPR; 1994 Dec. 154 p. AHCPR publication no. 95-0652. (Clinical practice guideline; no. 15).

26. Romanko KP. Pressure ulcers. Clin Podiatr Med Surg 1991 Oct;8(4):857-67.

27. Romanko KP. Pressure ulcers. Clin Podiatr Med Surg 1991 Oct;8(4):857-67.

28. Agency for Health Care Policy and Research (AHCPR). Treatment of pressure ulcers. Rockville (MD): U.S. Department of Health and Human Services, Public Health Service, AHCPR; 1994 Dec. 154 p. AHCPR publication no. 95-0652. (Clinical practice guideline; no. 15).

29. Agency for Health Care Policy and Research (AHCPR). Treatment of pressure ulcers. Rockville (MD): U.S. Department of Health and Human Services, Public Health Service, AHCPR; 1994 Dec. 154 p. AHCPR publication no. 95-0652. (Clinical practice guideline; no. 15).

30. Weingarten MS. Advances in wound healing. In: Oloff LM. Musculoskeletal disorders of the lower extremities. Philadelphia: Saunders; 1994. p. 52-64.

31. Olejniczak S, Zielinski A. Low hyperbaric therapy in management of leg ulcers. Mich Med 1975 Nov;74(32):707-12.

32. Heng MC. Hyperbaric oxygen therapy for a foot ulcer in a patient with polyarteritis nodosa. Australas J Dermatol 1983 Dec;24(3):105-8.

33. Upson AV. Topical hyperbaric oxygenation in the treatment of recalcitrant open wounds. A clinical report. Phys Ther 1986 Sep;66(9):1408-12.

34. Richmond MN, Galbraith KA, Rogerson JT. Hyperbaric oxygen for a thalassaemic leg ulcer. J R Army Med Corps 1987 Feb;133(1):23-5.

35. Wattel F, Mathieu D, Coget JM, Billard V. Hyperbaric oxygen therapy in chronic vascular wound management. Angiology 1990 Jan;41(1):59-65.

36. Davis JC, Landeen JM, Levine RA. Pyoderma gangrenosum: skin grafting after preparation with hyperbaric oxygen. Plast Reconstr Surg 1987 Feb;79(2):200-7.

37. Gimmon Z, Wexler MR, Rachmilewitz EA. Juvenile leg ulceration in beta-thalassemia major and intermedia. Plast Reconstr Surg 1982 Feb;69(2):320-5.

38. Vassa N, Twardowski ZJ, Campbell J. Hyperbaric oxygen therapy in calciphylaxis-induced skin necrosis in a peritoneal dialysis patient. Am J Kidney Dis 1994 Jun;23(6):878-81.

39. Akman MN, Loubser PG, Fife CE, Donovan WH. Hyperbaric oxygen therapy: implications for spinal cord injury patients with intrathecal baclofen infusion pumps. Case report. Paraplegia 1994 Apr;32(4):281-4.

40. Wasserteil V, Bruce S, Sessoms SL, Guntupalli KK. Pyoderma gangrenosum treated with hyperbaric oxygen therapy. Int J Dermatol 1992 Aug;31(8):594-6.

41. Heng MC. Hyperbaric oxygen therapy for pyoderma gangrenosum. Aust N Z J Med 1984 Oct;14(5):618-21.

42. Diamond E, Forst MB, Hyman SA, Rand SA. The effect of hyperbaric oxygen on lower extremity ulcerations. J Am Podiatry Assoc 1982 Apr;72(4):180-5.

43. Fischer BH. Treatment of ulcers on the legs with hyperbaric oxygen. J Dermatol Surg 1975 Oct;1(3):55-8.

44. Sourifman HA, Thomas MP, Epstein DL. Hyperbaric oxygenation and ulcer treatment: a case report. J Am Podiatry Assoc 1981 Jul;71(7):381-5.

45. Hoffmann G. Improvement of wound healing in chronic ulcers by hyperbaric oxygenation and by waterfiltered ultrared A induced localized hyperthermia. Adv Exp Med Biol 1994;345:181-8.

46. Hammarlund C, Sundberg T. Hyperbaric oxygen reduced size of chronic leg ulcers: a randomized double-blind study. Plast Reconstr Surg 1994 Apr;93(4):829-33; discussion 834.

47. Baroni G, Porro T, Faglia E, Pizzi G, Mastropasqua A, Oriani G, Pedesini G, Favales F. Hyperbaric oxygen in diabetic gangrene treatment. Diabetes Care 1987 Jan-Feb;10(1):81-6.

48. Rosenthal AM, Schurman A. Hyperbaric treatment of pressure sores. Arch Phys Med Rehabil 1971 Sep;52(9):413-5, 433.

49. Fischer BH. Topical hyperbaric oxygen treatment of pressure sores and skin ulcers. Lancet 1969 Aug 23;2(617):405-9.

50. Agency for Health Care Policy and Research (AHCPR). Treatment of pressure ulcers. Rockville (MD): U.S. Department of Health and Human Services, Public Health Service, AHCPR; 1994 Dec. 154 p. AHCPR publication no. 95-0652. (Clinical practice guideline; no. 15).

51. Robson MC, Phillips LG, Thomason A, Altrock BW, Pence PC, Heggers JP, Johnston AF, McHugh TP, Anthony MS, Robson LE, et al. Recombinant human platelet-derived growth factor-BB for the treatment of chronic pressure ulcers. Ann Plast Surg 1992 Sep;29(3):193-201.

52. Mustoe TA, Cutler NR, Allman RM, Goode PS, Deuel TF, Prause JA, Bear M, Serdar CM, Pierce GF. A phase II study to evaluate recombinant platelet-derived growth factor-BB in the treatment of stage 3 and 4 pressure ulcers. Arch Surg 1994 Feb;129(2):213-9.

53. Robson MC, Phillips LG, Thomason A, Robson LE, Pierce GF. Platelet-derived growth factor BB for the treatment of chronic pressure ulcers. Lancet 1992 Jan 4;339(8784):23-5.

54. Pierce GF, Tarpley JE, Allman RM, Goode PS, Serdar CM, Morris B, Mustoe TA, Vande Berg J. Tissue repair processes in healing chronic pressure ulcers treated with recombinant platelet-derived growth factor BB. Am J Pathol 1994 Dec;145(6):1399-410.

55. Steed DL. Clinical evaluation of recombinant human platelet-derived growth factor for the treatment of lower extremity diabetic ulcers. Diabetic Ulcer Study Group. J Vasc Surg 1995 Jan;21(1):71-8; discussion 79-81.

56. Savage K, Siebert E, Swann D. The effect of platelet-derived growth factor on cell division and glycosaminoglycan synthesis by human skin and scar fibroblasts. J Invest Dermatol 1987 Jul;89(1):93-9.

57. Steed DL, Goslen JB, Holloway GA, Malone JM, Bunt TJ, Webster MW. Randomized prospective double-blind trial in healing chronic diabetic foot ulcers. CT-102 activated platelet supernatant, topical versus placebo. Diabetes Care 1992 Nov;15(11):1598-604.

58. Krupski WC, Reilly LM, Perez S, Moss KM, Crombleholme PA, Rapp JH. A prospective randomized trial of autologous platelet-derived wound healing factors for treatment of chronic nonhealing wounds: a preliminary report. J Vasc Surg 1991 Oct;14(4):526-32; discussion 532-6.

59. Knighton DR, Ciresi K, Fiegel VD, Schumerth S, Butler E, Cerra F. Stimulation of repair in chronic, nonhealing, cutaneous ulcers using platelet-derived wound healing formula. Surg Gynecol Obstet 1990 Jan;170(1):56-60.

60. Knighton DR, Ciresi KF, Fiegel VD, Austin LL, Butler EL. Classification and treatment of chronic nonhealing wounds. Successful treatment with autologous platelet-derived wound healing factors (PDWHF). Ann Surg 1986 Sep;204(3):322-9; discussion 329-30.

61. Sporn MB, Roberts AB, Wakefield LM, Assoian RK. Transforming growth factor-beta: biological function and chemical structure. Science 1986 Aug 1;233(4763):532-4.

62. Robson MC, Phillips LG, Lawrence WT, Bishop JB, Youngerman JS, Hayward PG, Broemeling LD, Heggers JP. The safety and effect of topically applied recombinant basic fibroblast growth factor on the healing of chronic pressure sores. Ann Surg 1992 Oct;216(4):401-6; discussion 406-8.

63. Richard JL, Parer-Richard C, Daures JP, Clouet S, Vannereau D, Bringer J, Rodier M, Jacob C, Comte-Bardonnet M. Effect of topical basic fibroblast growth factor on the healing of chronic diabetic neuropathic ulcer of the foot. A pilot, randomized, double-blind, placebo-controlled study. Diabetes Care 1995 Jan;18(1):64-9.

64. Falanga V, Eaglstein WH, Bucalo B, Katz MH, Harris B, Carson P. Topical use of human recombinant epidermal growth factor (h-EGF) in venous ulcers. J Dermatol Surg Oncol 1992 Jul;18(7):604-6.

65. Brown GL, Curtsinger L, Jurkiewicz MJ, Nahai F, Schultz G. Stimulation of healing of chronic wounds by epidermal growth factor. Plast Reconstr Surg 1991 Aug;88(2):189-94; discussion 195-6.

66. Agency for Health Care Policy and Research (AHCPR). Treatment of pressure ulcers. Rockville (MD): U.S. Department of Health and Human Services, Public Health Service, AHCPR; 1994 Dec. 154 p. AHCPR publication no. 95-0652. (Clinical practice guideline; no. 15).

67. ter Riet G, Kessels AG, Knipschild P. Randomised clinical trial of ultrasound treatment for pressure ulcers [published erratum appears in BMJ 1995 May 20;310(6990):1300]. BMJ 1995 Apr 22;310(6986):1040-1.

68. McDiarmid T, Burns PN, Lewith GT, Machin D. Ultrasound and the treatment of pressure sores. Physiotherapy 1985 Feb;71(2):66-70.

69. Lundeberg T, Nordstrom F, Brodda-Jansen G, Eriksson SV, Kjartansson J, Samuelson UE. Pulsed ultrasound does not improve healing of venous ulcers. Scand J Rehabil Med 1990;22(4):195-7.

70. Callam MJ, Harper DR, Dale JJ, Ruckley CV, Prescott RJ. A controlled trial of weekly ultrasound therapy in chronic leg ulceration. Lancet 1987 Jul 25;2(8552):204-6.

71. Dyson M, Franks C, Suckling J. Stimulation of healing of varicose ulcers by ultrasound. Ultrasonics 1976 Sep;14(5):232-6.

72. Nussbaum EL, Biemann I, Mustard B. Comparison of ultrasound/ultraviolet-C and laser for treatment of pressure ulcers in patients with spinal cord injury. Phys Ther 1994 Sep;74(9):812-23; discussion 824-5.

73. Gogia PP, Marquez RR. Effects of helium-neon laser on wound healing. Ostomy Wound Manage 1992 Jul-Aug;38(6):33, 36, 38-41.

74. Agency for Health Care Policy and Research (AHCPR). Treatment of pressure ulcers. Rockville (MD): U.S. Department of Health and Human Services, Public Health Service, AHCPR; 1994 Dec. 154 p. AHCPR publication no. 95-0652. (Clinical practice guideline; no. 15).

75. Frantz RA, Gardner S. Elderly skin care: principles of chronic wound care. J Gerontol Nurs 1994 Sep;20(9):35-44.

76. Wound, Ostomy and Continence Nurses Society (WOCN). Standards of care. Patients with dermal wounds: pressure ulcers. Costa Mesa (CA): WOCN; 1992. 40 p.

77. Wound, Ostomy and Continence Nurses Society (WOCN). Standards of care. Patients with dermal wounds: lower extremity ulcers. Costa Mesa (CA): WOCN; 1993. 50 p.

78. University Hospital Consortium (UHC), Technology Advancement Center. Guidelines for the use of pressure relief devices in the treatment and prevention of pressure ulcers. Oak Brook (IL): UHC; 1990. [various pagings].

79. Wound, Ostomy and Continence Nurses Society (WOCN). Standards of care. Patients with dermal wounds: lower extremity ulcers. Costa Mesa (CA): WOCN; 1993. 50 p.

80. Smith DM. Pressure ulcers in the nursing home. Ann Intern Med 1995 Sep 15;123(6):433-42.

81. Douglas WS, Simpson NB. Guidelines for the management of chronic venous leg ulceration. Report of a multidisciplinary workshop. British Association of Dermatologists and the Research Unit of the Royal College of Physicians. Br J Dermatol 1995 Mar;132(3):446-52.

82. Consensus paper on venous leg ulcer. The Alexander House Group. J Dermatol Surg Oncol 1992 Jul;18(7):592-602.

83. Agency for Health Care Policy and Research (AHCPR). Treatment of pressure ulcers. Rockville (MD): U.S. Department of Health and Human Services, Public Health Service, AHCPR; 1994 Dec. 154 p. AHCPR publication no. 95-0652. (Clinical practice guideline; no. 15).

84. Hotta SS, Holohan TV. Procuren: a platelet-derived wound healing formula. Rockville (MD): U.S. Department of Health and Human Services, Public Health Service, Agency for Health Care Policy and Research (AHCPR); 1992 Jul. 3 p. AHCPR publication no. 92-0065. (Health technology review; no. 2).

85. Roe BH, Griffiths JM, Kenrick M, Cullum NA, Hutton JL. Nursing treatment of patients with chronic leg ulcers in the community. J Clin Nurs 1994 May;3(3):159-68.

86. Margolis DJ, Cohen JH. Management of chronic venous leg ulcers: a literature-guided approach. Clin Dermatol 1994 Jan-Mar;12(1):19-26.

87. Frantz RA, Gardner S, Harvey P, Specht J. Adoption of research-based practice for treatment of pressure ulcers in long-term care. Decubitus 1992 Jan;5(1):44-5, 48-54.

88. Douglas WS, Simpson NB. Guidelines for the management of chronic venous leg ulceration. Report of a multidisciplinary workshop. British Association of Dermatologists and the Research Unit of the Royal College of Physicians. Br J Dermatol 1995 Mar;132(3):446-52.

89. Wound, Ostomy and Continence Nurses Society (WOCN). Standards of care. Patients with dermal wounds: pressure ulcers. Costa Mesa (CA): WOCN; 1992. 40 p.

90. Wound, Ostomy and Continence Nurses Society (WOCN). Standards of care. Patients with dermal wounds: lower extremity ulcers. Costa Mesa (CA): WOCN; 1993. 50 p.

91. Frantz RA, Gardner S. Elderly skin care: principles of chronic wound care. J Gerontol Nurs 1994 Sep;20(9):35-44.

92. University Hospital Consortium (UHC), Technology Advancement Center. Guidelines for the use of pressure relief devices in the treatment and prevention of pressure ulcers. Oak Brook (IL): UHC; 1990. [various pagings].

93. Smith DM. Pressure ulcers in the nursing home. Ann Intern Med 1995 Sep 15;123(6):433-42.

94. Wiseman DM, Rovee DT, Alvarez OM. Wound dressings: design and use. In: Cohen IK, Diegelmann RF, Lindblad WJ, editors. Wound healing: biochemical & clinical aspects. Philadelphia: Saunders; 1992. p. 562-80.

95. Edlich RF, Rodeheaver GT, Thacker JG. Surgical devices in wound healing management. In: Cohen IK, Diegelmann RF, Lindblad WJ, editors. Wound healing: biochemical & clinical aspects. Philadelphia: Saunders; 1992. p. 581-600.

96. Consensus paper on venous leg ulcer. The Alexander House Group. J Dermatol Surg Oncol 1992 Jul;18(7):592-602.

97. Rodeheaver G, Baharestani MM, Brabec ME, Byrd HJ, Salzberg CA, Scherer P, Vogelpohl TS. Wound healing and wound management: focus on debridement. An interdisciplinary round table, September 18, 1992, Jackson Hole, WY. Adv Wound Care 1994 Jan;7(1):22-4, 26-9, 32-6; quiz 37-9.

98. Agency for Health Care Policy and Research (AHCPR). Pressure ulcers in adults: prediction and prevention. Rockville (MD): U.S. Department of Health and Human Services, Public Health Service, AHCPR; 1992. 63 p. AHCPR publication no. 92-0047. (Clinical practice guideline; no. 3).

99. Agency for Health Care Policy and Research (AHCPR). Treatment of pressure ulcers. Rockville (MD): U.S. Department of Health and Human Services, Public Health Service, AHCPR; 1994 Dec. 154 p. AHCPR publication no. 95-0652. (Clinical practice guideline; no. 15).

100. Agency for Health Care Policy and Research (AHCPR). Pressure ulcers in adults: prediction and prevention. Rockville (MD): U.S. Department of Health and Human Services, Public Health Service, AHCPR; 1992. 63 p. AHCPR publication no. 92-0047. (Clinical practice guideline; no. 3).

101. Hotta SS, Holohan TV. Procuren: a platelet-derived wound healing formula. Rockville (MD): U.S. Department of Health and Human Services, Public Health Service, Agency for Health Care Policy and Research (AHCPR); 1992 Jul. 3 p. AHCPR publication no. 92-0065. (Health technology review; no. 2).

102. Sheps SB. Hyperbaric oxygen for osteomyelitis and osteoradionecrosis. Vancouver, British Columbia (Canada): British Columbia Office of Health Technology Assessment, Centre for Health Services & Policy Research; 1992 Oct. 21 p. (British Columbia Office of Health Technology Assessment discussion paper series).

103. National Center for Health Services Research (NCHSR). Public Health Service assessment of ultraviolet light treatment for decubitus ulcers, 1981. Rockville (MD): U.S. Department of Health and Human Services, Public Health Service, Office of the Assistant Secretary for Health, NCHSR; 1981. 8 p. (Health technology assessment series, 1981; no. 3).

104. National Center for Health Services Research (NCHSR). Public Health Service assessment of hydrotherapy (whirlpool) baths for treatment of decubitus ulcers, 1981. Rockville (MD): U.S. Department of Health and Human Services, Public Health Service, Office of the Assistant Secretary for Health, NCHSR; 1981. 5 p. (Health technology assessment series, 1981; no. 2).

105. Brandeis GH, Berlowitz DR, Hossain M, Morris JN. Pressure ulcers: the minimum data set and the resident assessment protocol. Adv Wound Care 1995 Nov-Dec;8(6):18-25.

106. Margolis DJ, Cohen JH. Management of chronic venous leg ulcers: a literature-guided approach. Clin Dermatol 1994 Jan-Mar;12(1):19-26.

107. Roe BH, Griffiths JM, Kenrick M, Cullum NA, Hutton JL. Nursing treatment of patients with chronic leg ulcers in the community. J Clin Nurs 1994 May;3(3):159-68.

108. Frantz RA, Gardner S, Harvey P, Specht J. Adoption of research-based practice for treatment of pressure ulcers in long-term care. Decubitus 1992 Jan;5(1):44-5, 48-54.

109. Dayton PD, Palladino SJ. Electrical stimulation of cutaneous ulcerations. A literature review. J Am Podiatr Med Assoc 1989 Jul;79(7):318-21.

110. ECRI. Electrical bone growth stimulation for the spine and lower leg [technology assessment report]. Plymouth Meeting (PA): ECRI; 1993 Oct. 106 p.

111. Dayton PD, Palladino SJ. Electrical stimulation of cutaneous ulcerations. A literature review. J Am Podiatr Med Assoc 1989 Jul;79(7):318-21.

112. Weiss DS, Kirsner R, Eaglstein WH. Electrical stimulation and wound healing. Arch Dermatol 1990 Feb;126(2):222-5.

113. Cheng N, Van Hoof H, Bockx E, Hoogmartens MJ, Mulier JC, De Dijcker FJ, Sansen WM, De Loecker W. The effects of electric currents on ATP generation, protein synthesis, and membrane transport of rat skin. Clin Orthop 1982 Nov-Dec;(171):264-72.

114. Korenstein R, Somjen D, Fischler H, Binderman I. Capacitative pulsed electric stimulation of bone cells. Induction of cyclic-AMP changes and DNA synthesis. Biochim Biophys Acta 1984 Apr 16;803(4):302-7.

115. Konikoff JJ. Electrical promotion of soft tissue repairs. Ann Biomed Eng 1976 Mar;4(1):1-5.

116. Reger SI, Hyodo A, Reyes ET, Browne EZ. Treatment of pressure ulcers by electrical stimulation. Rehabil Res Dev Prog Rep 1992;29:467-8.

117. Alvarez OM, Mertz PM, Smerbeck RV, Eaglstein WH. The healing of superficial skin wounds is stimulated by external electrical current. J Invest Dermatol 1983 Aug;81(2):144-8.

118. Bourguignon GJ, Bourguignon LY. Electric stimulation of protein and DNA synthesis in human fibroblasts. FASEB J 1987 Nov;1(5):398-402.

119. Raji AR, Bowden RE. Effects of high-peak pulsed electromagnetic field on the degeneration and regeneration of the common peroneal nerve in rats. J Bone Joint Surg Br 1983 Aug;65(4):478-92.

120. Jayakumar K, Rajagopalan T, Sambasivan M, Bai S. Effect of pulsed electromagnetic field (PEMF) in cerebral oedema. Neurol India 1986;34:241-7.

121. Szuminsky NJ, Albers AC, Unger P, Eddy JG. Effect of narrow, pulsed high voltages on bacterial viability. Phys Ther 1994 Jul;74(7):660-7.

122. Kincaid CB, Lavoie KH. Inhibition of bacterial growth in vitro following stimulation with high voltage, monophasic, pulsed current. Phys Ther 1989 Aug;69(8):651-5.

123. ECRI. Electrical bone growth stimulation for the spine and lower leg [technology assessment report]. Plymouth Meeting (PA): ECRI; 1993 Oct. 106 p.

124. ECRI. Electrical bone growth stimulation for the spine [technology assessment report]. Plymouth Meeting (PA): ECRI; 1993 Oct. 70 p.

125. ECRI. Electrical bone growth stimulation for the wrist [technology assessment report]. Plymouth Meeting (PA): ECRI; 1994 Apr. 88 p.

126. ECRI. Spinal cord (dorsal column) stimulation for chronic intractable pain [technology assessment report]. Plymouth Meeting (PA): ECRI; 1993 Oct. 87 p.

127. Masureik C, Eriksson C. Preliminary clinical evaluation of the effect of small electrical currents on the healing of jaw fractures. Clin Orthop 1977 May;(124):84-91.

128. Wilson DH. Comparison of short wave diathermy and pulsed electromagnetic energy in treatment of soft tissue injuries. Physiotherapy 1974 Oct;60(10):309-10.

129. Kiwerski J, Chrostowska T. [Clinical use of pulsating electromagnetic energy in the treatment of spinal cord injuries]. Chir Narzadow Ruchu Ortop Pol 1980;45(3):273-7. (Pol).

130. Hedenius P, Odeblad E, Wahlstrom L. Some preliminary investigations on the therapeutic effect of pulsed short waves in intermittent claudication. Curr Ther Res Clin Exp 1966 Jul;8(7):317-21.

131. Barclay V, Collier RJ, Jones A. Treatment of various hand injuries by pulsed electromagnetic energy (Diapulse). Physiotherapy 1983 Jun 10;69(6):186-8.

132. Sambasivan M. Pulsed electromagnetic field in management of head injuries. Neurol India 1993;41 Suppl:56-9.

133. Pennington GM, Danley DL, Sumko MH, Bucknell A, Nelson JH. Pulsed, non-thermal, high-frequency electromagnetic energy (DIAPULSE) in the treatment of grade I and grade II ankle sprains. Mil Med 1993 Feb;158(2):101-4.

134. Kaplan EG, Weinstock RE. Clinical evaluation of Diapulse as adjunctive therapy following foot surgery. J Am Podiatry Assoc 1968 May;58(5):218-21.

135. Aronofsky DH. Reduction of dental postsurgical symptoms using nonthermal pulsed high-peak-power electromagnetic energy. Oral Surg Oral Med Oral Pathol 1971 Nov;32(5):688-96.

136. Rhodes C. The adjunctive utilization of Diapulse therapy (pulsed high peak power electromagnetic energy) in accelerating tissue healing in oral surgery. The Quarterly, NDA 1981 Jul;39(4):166-75 contd.

137. Rhodes C. The adjunctive utilization of Diapulse therapy (pulsed high peak power electromagnetic energy) in accelerating tissue healing in oral surgery. The Quarterly, NDA 1981 Oct;40(1):4-11 concl.

138. Akers TK, Gabrielson AL. The effect of high voltage galvanic stimulation on the rate of healing of decubitus ulcers. Biomed Sci Instrum 1984;20:99-100.

139. Wolcott LE, Wheeler PC, Hardwicke HM, Rowley BA. Accelerated healing of skin ulcer by electrotherapy: preliminary clinical results. South Med J 1969 Jul;62(7):795-801.

140. Wood JM, Evans PE 3rd, Schallreuter KU, Jacobson WE, Sufit R, Newman J, White C, Jacobson M. A multicenter study on the use of pulsed low-intensity direct current for healing chronic stage II and stage III decubitus ulcers. Arch Dermatol 1993 Aug;129(8):999-1009.

141. Wood JM, Evans PE 3rd, Schallreuter KU, Jacobson WE, Sufit R, Newman J, White C, Jacobson M. A multicenter study on the use of pulsed low-intensity direct current for healing chronic stage II and stage III decubitus ulcers. Arch Dermatol 1993 Aug;129(8):999-1009.

142. Gogia PP, Marquez RR, Minerbo GM. Effects of high voltage galvanic stimulation on wound healing. Ostomy Wound Manage 1992 Jan-Feb;38(1):29-35.

143. Feedar JA, Kloth LC, Gentzkow GD. Chronic dermal ulcer healing enhanced with monophasic pulsed electrical stimulation. Phys Ther 1991 Sep;71(9):639-49.

144. Mulder GD. Treatment of open-skin wounds with electric stimulation. Arch Phys Med Rehabil 1991 May;72(6):375-7.

145. Weiss DS, Eaglstein WH, Falanga V. Exogenous electric current can reduce the formation of hypertrophic scars. J Dermatol Surg Oncol 1989 Dec;15(12):1272-5.

146. Feedar J, Kloth L, Gentzkow G. Chronic dermal ulcer healing enhanced with monophasic pulsed electrical stimulation [comment]. Phys Ther 1992 Jul;72(7):539.

147. Feedar JA, Kloth LC, Gentzkow GD. Chronic dermal ulcer healing enhanced with monophasic pulsed electrical stimulation. Phys Ther 1991 Sep;71(9):639-49.

148. Wood JM, Evans PE 3rd, Schallreuter KU, Jacobson WE, Sufit R, Newman J, White C, Jacobson M. A multicenter study on the use of pulsed low-intensity direct current for healing chronic stage II and stage III decubitus ulcers. Arch Dermatol 1993 Aug;129(8):999-1009.

149. Fitzgerald GK, Newsome D. Treatment of a large infected thoracic spine wound using high voltage pulsed monophasic current. Phys Ther 1993 Jun;73(6):355-60.

150. Gogia PP, Marquez RR, Minerbo GM. Effects of high voltage galvanic stimulation on wound healing. Ostomy Wound Manage 1992 Jan-Feb;38(1):29-35.

151. Griffin JW, Tooms RE, Mendius RA, Clifft JK, Vander Zwaag R, el-Zeky F. Efficacy of high voltage pulsed current for healing of pressure ulcers in patients with spinal cord injury. Phys Ther 1991 Jun;71(6):433-42; discussion 442-4.

152. Unger PG. A randomized clinical trial of the effect of HVPC on wound healing [abstract]. Phys Ther 1991 Jun;71(6 Suppl):S118.

153. Unger P, Eddy J, Raimastry S. A controlled study of the effect of high voltage pulse current (HVPC) on wound healing [abstract]. Phys Ther 1991 Jun;71(6 Suppl):S119.

154. Kloth LC, Feedar JA. Acceleration of wound healing with high voltage, monophasic, pulsed current [published erratum appears in Phys Ther 1989 Aug;69(8):702]. Phys Ther 1988 Apr;68(4):503-8.

155. Feedar JA, Kloth LC. Acceleration of wound healing with high voltage pulsating direct current [abstract]. Phys Ther 1985 May;65(5):741.

156. Griffin JW, Tooms RE, Mendius RA, Clifft JK, Vander Zwaag R, el-Zeky F. Efficacy of high voltage pulsed current for healing of pressure ulcers in patients with spinal cord injury. Phys Ther 1991 Jun;71(6):433-42; discussion 442-4.

157. Kloth LC, Feedar JA. Acceleration of wound healing with high voltage, monophasic, pulsed current [published erratum appears in Phys Ther 1989 Aug;69(8):702]. Phys Ther 1988 Apr;68(4):503-8.

158. Lundeberg TC, Eriksson SV, Malm M. Electrical nerve stimulation improves healing of diabetic ulcers. Ann Plast Surg 1992 Oct;29(4):328-31.

159. Lundeberg T, Kjartansson J, Samuelsson U. Effect of electrical nerve stimulation on healing of ischaemic skin flaps. Lancet 1988 Sep 24;2(8613):712-4.

160. Frantz RA. The effectiveness of transcutaneous electrical nerve stimulation (TENS) on decubitus ulcer healing in adult patients. In: Funk SG, Tornquist EM, Champagne MT, Copp LA, Wiese RA, editors. Key aspects of recovery: improving nutrition, rest, and mobility. New York: Springer; 1990. p. 197-205.

161. Kjartansson J, Lundeberg T. Effects of electrical nerve stimulation (ENS) in ischemic tissue. Scand J Plast Reconstr Surg Hand Surg 1990;24(2):129-34.

162. Kaada B, Emru M. Promoted healing of leprous ulcers by transcutaneous nerve stimulation. Acupunct Electrother Res 1988;13(4):165-76.

163. Alon G, Azaria M, Stein H. Diabetic ulcer healing using high voltage TENS [abstract]. Phys Ther 1986 May;66(5):775.

164. Barron JJ, Jacobson WE, Tidd G. Treatment of decubitus ulcers. A new approach. Minn Med 1985 Feb;68(2):103-6.

165. Kaada B. Promoted healing of chronic ulceration by transcutaneous nerve stimulation (TNS). Vasa 1983;12(3):262-9.

166. Westerhof W, Bos JD. Trigeminal trophic syndrome: a successful treatment with transcutaneous electrical stimulation. Br J Dermatol 1983 May;108(5):601-4.

167. Lundeberg TC, Eriksson SV, Malm M. Electrical nerve stimulation improves healing of diabetic ulcers. Ann Plast Surg 1992 Oct;29(4):328-31.

168. Frantz RA. The effectiveness of transcutaneous electrical nerve stimulation (TENS) on decubitus ulcer healing in adult patients. In: Funk SG, Tornquist EM, Champagne MT, Copp LA, Wiese RA, editors. Key aspects of recovery: improving nutrition, rest, and mobility. New York: Springer; 1990. p. 197-205.

169. Stefanovska A, Vodovnik L, Benko H, Turk R. Treatment of chronic wounds by means of electric and electromagnetic fields. Part 2. Value of FES parameters for pressure sore treatment. Med Biol Eng Comput 1993 May;31(3):213-20.

170. Karba R, Vodovnik L, Presern-Strukelj M, Klesnik M. Promoted healing of chronic wounds due to electrical stimulation. Wounds 1991 Jan-Feb;3(1):16-23.

171. Stefanovska A, Vodovnik L, Benko H, Turk R. Treatment of chronic wounds by means of electric and electromagnetic fields. Part 2. Value of FES parameters for pressure sore treatment. Med Biol Eng Comput 1993 May;31(3):213-20.

172. Stiller MJ, Pak GH, Shupack JL, Thaler S, Kenny C, Jondreau L. A portable pulsed electromagnetic field (PEMF) device to enhance healing of recalcitrant venous ulcers: a double-blind, placebo-controlled clinical trial. Br J Dermatol 1992 Aug;127(2):147-54.

173. Todd DJ, Heylings DJ, Allen GE, McMillin WP. Treatment of chronic varicose ulcers with pulsed electromagnetic fields: a controlled pilot study. Ir Med J 1991 Jun;84(2):54-5.

174. Ieran M, Zaffuto S, Bagnacani M, Annovi M, Moratti A, Cadossi R. Effect of low frequency pulsing electromagnetic fields on skin ulcers of venous origin in humans: a double-blind study. J Orthop Res 1990 Mar;8(2):276-82.

175. Jeran M, Zaffuto S, Moratti A, Bagnacani M, Cadossi R. PEMF stimulation of skin ulcers of venous origin in humans: preliminary report of a double blind study. J Bioelectr 1987;6(2):181-8.

176. Stiller MJ, Pak GH, Shupack JL, Thaler S, Kenny C, Jondreau L. A portable pulsed electromagnetic field (PEMF) device to enhance healing of recalcitrant venous ulcers: a double-blind, placebo-controlled clinical trial. Br J Dermatol 1992 Aug;127(2):147-54.

177. Salzberg CA, Cooper-Vastola SA, Perez F, Viehbeck MG, Byrne DW. The effects of non-thermal pulsed electromagnetic energy on wound healing of pressure ulcers in spinal cord-injured patients: a randomized, double-blind study. Ostomy Wound Manage 1995 Apr;41(3):42-4, 46, 48 passim.

178. Tung S, Khaski A, Milano E, Kay C. The application of Diapulse in the treatment of decubitus ulcers: case reports. Contemp Surg 1995 Jul;47(1):27-32.

179. Itoh M, Montemayor JS Jr, Matsumoto E, Eason A, Lee MH, Folk FS. Accelerated wound healing of pressure ulcers by pulsed high peak power electromagnetic energy (Diapulse). Decubitus 1991 Feb;4(1):24-5, 29-34.

180. Goldin JH, Broadbent NR, Nancarrow JD, Marshall T. The effects of Diapulse on the healing of wounds: a double-blind randomised controlled trial in man. Br J Plast Surg 1981 Jul;34(3):267-70.

181. ECRI. Spinal cord (dorsal column) stimulation for chronic intractable pain [technology assessment report]. Plymouth Meeting (PA): ECRI; 1993 Oct. 87 p.

182. Meglio M, Cioni B, Dal Lago A, De Santis M, Pola P, Serricchio M. Pain control and improvement of peripheral blood flow following epidural spinal cord stimulation: case report. J Neurosurg 1981 Jun;54(6):821-3.

183. Richardson RR, Cerullo LJ, Meyer PR. Autonomic hyper-reflexia modulated by percutaneous epidural neurostimulation: a preliminary report. Neurosurgery 1979 Jun;4(6):517-20.

184. Cook AW, Oygar A, Baggenstos P, Pacheco S, Kleriga E. Vascular disease of extremities. Electric stimulation of spinal cord and posterior roots. N Y State J Med 1976 Mar;76(3):366-8.

185. Graber JN, Lifson A. The use of spinal cord stimulation for severe limb-threatening ischemia: a preliminary report. Ann Vasc Surg 1987 Dec;1(5):578-81.

186. Jivegård L, Augustinsson LE, Carlsson CA, Holm J. Long-term results by epidural spinal electrical stimulation (ESES) in patients with inoperable severe lower limb ischaemia. Eur J Vasc Surg 1987 Oct;1(5):345-9.

187. ECRI. Spinal cord (dorsal column) stimulation for chronic intractable pain [technology assessment report]. Plymouth Meeting (PA): ECRI; 1993 Oct. 87 p.

188. Kloth LC. Physical modalities in wound management: UVC, therapeutic heating and electrical stimulation. Ostomy Wound Manage 1995 Jun;41(5):18-20, 22-4, 26-7.

189. Feedar JA, Kloth LC, Gentzkow GD. Chronic dermal ulcer healing enhanced with monophasic pulsed electrical stimulation. Phys Ther 1991 Sep;71(9):639-49.

190. Mulder GD. Treatment of open-skin wounds with electric stimulation. Arch Phys Med Rehabil 1991 May;72(6):375-7.

191. Gentzkow GD, Pollack SV, Kloth LC, Stubbs HA. Improved healing of pressure ulcers using Dermapulse, a new electrical stimulation device. Wounds 1991 Sep-Oct;3(5):158-70.

192. Griffin JW, Tooms RE, Mendius RA, Clifft JK, Vander Zwaag R, el-Zeky F. Efficacy of high voltage pulsed current for healing of pressure ulcers in patients with spinal cord injury. Phys Ther 1991 Jun;71(6):433-42; discussion 442-4.

193. Feedar JA, Kloth LC, Gentzkow GD. Chronic dermal ulcer healing enhanced with monophasic pulsed electrical stimulation. Phys Ther 1991 Sep;71(9):639-49.

194. Salzberg CA, Cooper-Vastola SA, Perez F, Viehbeck MG, Byrne DW. The effects of non-thermal pulsed electromagnetic energy on wound healing of pressure ulcers in spinal cord-injured patients: a randomized, double-blind study. Ostomy Wound Manage 1995 Apr;41(3):42-4, 46, 48 passim.

195. Stiller MJ, Pak GH, Shupack JL, Thaler S, Kenny C, Jondreau L. A portable pulsed electromagnetic field (PEMF) device to enhance healing of recalcitrant venous ulcers: a double-blind, placebo-controlled clinical trial. Br J Dermatol 1992 Aug;127(2):147-54.

196. Todd DJ, Heylings DJ, Allen GE, McMillin WP. Treatment of chronic varicose ulcers with pulsed electromagnetic fields: a controlled pilot study. Ir Med J 1991 Jun;84(2):54-5.

197. Itoh M, Montemayor JS Jr, Matsumoto E, Eason A, Lee MH, Folk FS. Accelerated wound healing of pressure ulcers by pulsed high peak power electromagnetic energy (Diapulse). Decubitus 1991 Feb;4(1):24-5, 29-34.

198. ECRI. Spinal cord (dorsal column) stimulation for chronic intractable pain [technology assessment report]. Plymouth Meeting (PA): ECRI; 1993 Oct. 87 p.

199. Carey LC, Lepley D Jr. Effect of continuous direct electric current on healing wounds. Surg Forum 1962;13:33-5.

200. Assimacopoulos D. Wound healing promotion by the use of negative electric current. Am Surg 1968 Jun;34(6):423-31.

201. Fenn JE. Effect of pulsed electromagnetic energy (Diapulse) on experimental hematomas. Can Med Assoc J 1969 Feb 1;100(5):251-4.

202. Barranco SD, Spadaro JA, Berger TJ, Becker RO. In vitro effect of weak direct current on Staphylococcus aureus. Clin Orthop 1974 May;(100):250-5.

203. Wilson DH, Jagadeesh P. Experimental regeneration in peripheral nerves and the spinal cord in laboratory animals exposed to a pulsed electromagnetic field. Paraplegia 1976 May;14(1):12-20.

204. Konikoff JJ. Electrical promotion of soft tissue repairs. Ann Biomed Eng 1976 Mar;4(1):1-5.

205. Cheng N, Van Hoof H, Bockx E, Hoogmartens MJ, Mulier JC, De Dijcker FJ, Sansen WM, De Loecker W. The effects of electric currents on ATP generation, protein synthesis, and membrane transport of rat skin. Clin Orthop 1982 Nov-Dec;(171):264-72.

206. Alvarez OM, Mertz PM, Smerbeck RV, Eaglstein WH. The healing of superficial skin wounds is stimulated by external electrical current. J Invest Dermatol 1983 Aug;81(2):144-8.

207. Raji AR, Bowden RE. Effects of high-peak pulsed electromagnetic field on the degeneration and regeneration of the common peroneal nerve in rats. J Bone Joint Surg Br 1983 Aug;65(4):478-92.

208. Foulds IS, Barker AT. Human skin battery potentials and their possible role in wound healing. Br J Dermatol 1983 Nov;109(5):515-22.

209. Korenstein R, Somjen D, Fischler H, Binderman I. Capacitative pulsed electric stimulation of bone cells. Induction of cyclic-AMP changes and DNA synthesis. Biochim Biophys Acta 1984 Apr 16;803(4):302-7.

210. Young W. Pulsed electromagnetic fields alter calcium in spinal cord injury. Presented at: The 75th Meeting of the Society of Neurological Surgeons; 1984 Apr 25-28; New York; [1984]. 2 p.

211. Murray JC, Farndale RW. Modulation of collagen production in cultured fibroblasts by a low-frequency, pulsed magnetic field. Biochim Biophys Acta 1985 Jan 28;838(1):98-105.

212. Jayakumar K, Rajagopalan T, Sambasivan M, Bai S. Effect of pulsed electromagnetic field (PEMF) in cerebral oedema. Neurol India 1986;34:241-7.

213. Bourguignon GJ, Bourguignon LY. Electric stimulation of protein and DNA synthesis in human fibroblasts. FASEB J 1987 Nov;1(5):398-402.

214. Kjartansson J, Lundeberg T, Samuelson UE, Dalsgaard CJ. Transcutaneous electrical nerve stimulation (TENS) increases survival of ischaemic musculocutaneous flaps. Acta Physiol Scand 1988 Sep;134(1):95-9.

215. Yen-Patton GP, Patton WF, Beer DM, Jacobson BS. Endothelial cell response to pulsed electromagnetic fields: stimulation of growth rate and angiogenesis in vitro. J Cell Physiol 1988 Jan;134(1):37-46.

216. Dunn MG, Doillon CJ, Berg RA, Olson RM, Silver FH. Wound healing using a collagen matrix: effect of DC electrical stimulation. J Biomed Mater Res 1988 Aug;22(A2 Suppl):191-206.

217. Politis MJ, Zanakis MF, Miller JE. Enhanced survival of full-thickness skin grafts following the application of DC electrical fields. Plast Reconstr Surg 1989 Aug;84(2):267-72.

218. Kincaid CB, Lavoie KH. Inhibition of bacterial growth in vitro following stimulation with high voltage, monophasic, pulsed current. Phys Ther 1989 Aug;69(8):651-5.

219. Reger SI, Hyodo A, Reyes ET, Browne EZ. Treatment of pressure ulcers by electrical stimulation. Rehabil Res Dev Prog Rep 1992;29:467-8.

220. Akai M, Wadano Y, Yabuki T, Oda H, Sirasaki Y, Tateishi T. [Effect of a direct electric current on modification of bone and ligament repair processes--experimental investigation of a rabbit model]. Nippon Seikeigeka Gakkai Zasshi 1991 Apr;65(4):196-206. (Jpn).

221. Szuminsky NJ, Albers AC, Unger P, Eddy JG. Effect of narrow, pulsed high voltages on bacterial viability. Phys Ther 1994 Jul;74(7):660-7.

222. Katelaris PM, Fletcher JP, Little JM, McEntyre RJ, Jeffcoate KW. Electrical stimulation in the treatment of chronic venous ulceration. Aust N Z J Surg 1987 Sep;57(9):605-7.

223. Carley PJ, Wainapel SF. Electrotherapy for acceleration of wound healing: low intensity direct current. Arch Phys Med Rehabil 1985 Jul;66(7):443-6.

224. Akers TK, Gabrielson AL. The effect of high voltage galvanic stimulation on the rate of healing of decubitus ulcers. Biomed Sci Instrum 1984;20:99-100.

225. Gault WR, Gatens PF Jr. Use of low intensity direct current in management of ischemic skin ulcers. Phys Ther 1976 Mar;56(3):265-9.

226. Wolcott LE, Wheeler PC, Hardwicke HM, Rowley BA. Accelerated healing of skin ulcer by electrotherapy: preliminary clinical results. South Med J 1969 Jul;62(7):795-801.

227. Assimacopoulos D. Low intensity negative electric current in the treatment of ulcers of the leg due to chronic venous insufficiency. Preliminary report of three cases. Am J Surg 1968 May;115(5):683-7.

228. Wood JM, Evans PE 3rd, Schallreuter KU, Jacobson WE, Sufit R, Newman J, White C, Jacobson M. A multicenter study on the use of pulsed low-intensity direct current for healing chronic stage II and stage III decubitus ulcers. Arch Dermatol 1993 Aug;129(8):999-1009.

229. Fitzgerald GK, Newsome D. Treatment of a large infected thoracic spine wound using high voltage pulsed monophasic current. Phys Ther 1993 Jun;73(6):355-60.

230. Gogia PP, Marquez RR, Minerbo GM. Effects of high voltage galvanic stimulation on wound healing. Ostomy Wound Manage 1992 Jan-Feb;38(1):29-35.

231. Gentzkow GD, Pollack SV, Kloth LC, Stubbs HA. Improved healing of pressure ulcers using Dermapulse, a new electrical stimulation device. Wounds 1991 Sep-Oct;3(5):158-70.

232. Griffin JW, Tooms RE, Mendius RA, Clifft JK, Vander Zwaag R, el-Zeky F. Efficacy of high voltage pulsed current for healing of pressure ulcers in patients with spinal cord injury. Phys Ther 1991 Jun;71(6):433-42; discussion 442-4.

233. Feedar JA, Kloth LC, Gentzkow GD. Chronic dermal ulcer healing enhanced with monophasic pulsed electrical stimulation. Phys Ther 1991 Sep;71(9):639-49.

234. Mulder GD. Treatment of open-skin wounds with electric stimulation. Arch Phys Med Rehabil 1991 May;72(6):375-7.

235. Unger PG. A randomized clinical trial of the effect of HVPC on wound healing [abstract]. Phys Ther 1991 Jun;71(6 Suppl):S118.

236. Unger P, Eddy J, Raimastry S. A controlled study of the effect of high voltage pulse current (HVPC) on wound healing [abstract]. Phys Ther 1991 Jun;71(6 Suppl):S119.

237. Weiss DS, Eaglstein WH, Falanga V. Exogenous electric current can reduce the formation of hypertrophic scars. J Dermatol Surg Oncol 1989 Dec;15(12):1272-5.

238. Kloth LC, Feedar JA. Acceleration of wound healing with high voltage, monophasic, pulsed current [published erratum appears in Phys Ther 1989 Aug;69(8):702]. Phys Ther 1988 Apr;68(4):503-8.

239. Feedar JA, Kloth LC. Acceleration of wound healing with high voltage pulsating direct current [abstract]. Phys Ther 1985 May;65(5):741.

240. Kesner, C.R. (DynaWave Corporation, Geneva, IL). Personal communication [letter]. 1996 Mar 16. 2 p.

241. Ross CR, Segal D. High voltage galvanic stimulation: an aid to post-operative healing. Curr Podiatry 1981;30(5):19-25.

242. Thurman BF, Christian EL. Response of a serious circulatory lesion to electrical stimulation. Phys Ther 1971 Oct;51(10):1107-10.

243. Stefanovska A, Vodovnik L, Benko H, Turk R. Treatment of chronic wounds by means of electric and electromagnetic fields. Part 2. Value of FES parameters for pressure sore treatment. Med Biol Eng Comput 1993 May;31(3):213-20.

244. Lundeberg TC, Eriksson SV, Malm M. Electrical nerve stimulation improves healing of diabetic ulcers. Ann Plast Surg 1992 Oct;29(4):328-31.

245. Karba R, Vodovnik L, Presern-Strukelj M, Klesnik M. Promoted healing of chronic wounds due to electrical stimulation. Wounds 1991 Jan-Feb;3(1):16-23.

246. Frantz RA. The effectiveness of transcutaneous electrical nerve stimulation (TENS) on decubitus ulcer healing in adult patients. In: Funk SG, Tornquist EM, Champagne MT, Copp LA, Wiese RA, editors. Key aspects of recovery: improving nutrition, rest, and mobility. New York: Springer; 1990. p. 197-205.

247. Kjartansson J, Lundeberg T. Effects of electrical nerve stimulation (ENS) in ischemic tissue. Scand J Plast Reconstr Surg Hand Surg 1990;24(2):129-34.

248. Kaada B, Emru M. Promoted healing of leprous ulcers by transcutaneous nerve stimulation. Acupunct Electrother Res 1988;13(4):165-76.

249. Lundeberg T, Kjartansson J, Samuelsson U. Effect of electrical nerve stimulation on healing of ischaemic skin flaps. Lancet 1988 Sep 24;2(8613):712-4.

250. Alon G, Azaria M, Stein H. Diabetic ulcer healing using high voltage TENS [abstract]. Phys Ther 1986 May;66(5):775.

251. Barron JJ, Jacobson WE, Tidd G. Treatment of decubitus ulcers. A new approach. Minn Med 1985 Feb;68(2):103-6.

252. Kaada B. Promoted healing of chronic ulceration by transcutaneous nerve stimulation (TNS). Vasa 1983;12(3):262-9.

253. Westerhof W, Bos JD. Trigeminal trophic syndrome: a successful treatment with transcutaneous electrical stimulation. Br J Dermatol 1983 May;108(5):601-4.

254. Salzberg CA, Cooper-Vastola SA, Perez F, Viehbeck MG, Byrne DW. The effects of non-thermal pulsed electromagnetic energy on wound healing of pressure ulcers in spinal cord-injured patients: a randomized, double-blind study. Ostomy Wound Manage 1995 Apr;41(3):42-4, 46, 48 passim.

255. Tung S, Khaski A, Milano E, Kay C. The application of Diapulse in the treatment of decubitus ulcers: case reports. Contemp Surg 1995 Jul;47(1):27-32.

256. Stiller MJ, Pak GH, Shupack JL, Thaler S, Kenny C, Jondreau L. A portable pulsed electromagnetic field (PEMF) device to enhance healing of recalcitrant venous ulcers: a double-blind, placebo-controlled clinical trial. Br J Dermatol 1992 Aug;127(2):147-54.

257. Todd DJ, Heylings DJ, Allen GE, McMillin WP. Treatment of chronic varicose ulcers with pulsed electromagnetic fields: a controlled pilot study. Ir Med J 1991 Jun;84(2):54-5.

258. Itoh M, Montemayor JS Jr, Matsumoto E, Eason A, Lee MH, Folk FS. Accelerated wound healing of pressure ulcers by pulsed high peak power electromagnetic energy (Diapulse). Decubitus 1991 Feb;4(1):24-5, 29-34.

259. Ieran M, Zaffuto S, Bagnacani M, Annovi M, Moratti A, Cadossi R. Effect of low frequency pulsing electromagnetic fields on skin ulcers of venous origin in humans: a double-blind study. J Orthop Res 1990 Mar;8(2):276-82.

260. Jeran M, Zaffuto S, Moratti A, Bagnacani M, Cadossi R. PEMF stimulation of skin ulcers of venous origin in humans: preliminary report of a double blind study. J Bioelectr 1987;6(2):181-8.

261. Goldin JH, Broadbent NR, Nancarrow JD, Marshall T. The effects of Diapulse on the healing of wounds: a double-blind randomised controlled trial in man. Br J Plast Surg 1981 Jul;34(3):267-70.

262. 3M Health Care, St. Paul, MN. 3M TENS Stimulators: treatment flexibility, quality and value for all your TENS patients [promotional material]. St. Paul (MN): 3M Health Care. 1992. 7 p.

263. 3M Health Care, St. Paul, MN. 3M TENS Stimulators: treatment flexibility, quality and value for all your TENS patients [promotional material]. St. Paul (MN): 3M Health Care. 1992. 7 p.

264. ECRI. Stimulators, electroanalgesic, transcutaneous electrical nerve. In: Healthcare product comparison system. Plymouth Meeting (PA): ECRI; 1994 May. 20 p.

265. AVRA Tronics Corp., Greenvale, NY. Model 770 GALVANATOR: a physical therapy stimulator instrument for pulsed galvanic stimulation of muscles and localized tissues [promotional material]. Greenvale (NY): AVRA Tronics. 2 p.

266. American Imex, Irvine, CA. A-TENS AI-86: a conservative and major step in pain management [promotional material]. Irvine (CA): American Imex. 2 p.

267. American Imex, Irvine, CA. TENS for conservative non-invasive pain management [promotional material]. Irvine (CA): American Imex. 2 p.

268. American Imex, Irvine, CA. MES iF microcurrent interferential [promotional material]. Irvine (CA): American Imex. 2 p.

269. American Imex, Irvine, CA. TENS for conservative non-invasive pain management [promotional material]. Irvine (CA): American Imex. 2 p.

270. American Imex, Irvine, CA. ULTIMA Xs microampere current: clinical microcurrent therapy on a personal scale [promotional material]. Irvine (CA): American Imex. 2 p.

271. ECRI. Ultrasound units, physical therapy; ultrasound units/neuromuscular stimulators, physical therapy. In: Healthcare product comparison system. Plymouth Meeting (PA): ECRI; 1994 Oct. 19 p.

272. ECRI. Ultrasound units, physical therapy; ultrasound units/neuromuscular stimulators, physical therapy. In: Healthcare product comparison system. Plymouth Meeting (PA): ECRI; 1994 Oct. 19 p.

273. ECRI. Ultrasound units, physical therapy; ultrasound units/neuromuscular stimulators, physical therapy. In: Healthcare product comparison system. Plymouth Meeting (PA): ECRI; 1994 Oct. 19 p.

274. ECRI. Ultrasound units, physical therapy; ultrasound units/neuromuscular stimulators, physical therapy. In: Healthcare product comparison system. Plymouth Meeting (PA): ECRI; 1994 Oct. 19 p.

275. [Biomedical Life Systems, Inc., Vista, CA]. BioMed and Systems TENS series [promotional material]. Scarborough, Ontario (Canada): Canadian Medical Products Ltd. 1 p.

276. [Biomedical Life Systems, Inc., Vista, CA]. EMS 2000 [promotional material]. Scarborough, Ontario (Canada): Canadian Medical Products Ltd. 1 p.

277. ECRI. Stimulators, electroanalgesic, transcutaneous electrical nerve. In: Healthcare product comparison system. Plymouth Meeting (PA): ECRI; 1994 May. 20 p.

278. [Biomedical Life Systems, Inc., Vista, CA]. BioMed and Systems TENS series [promotional material]. Scarborough, Ontario (Canada): Canadian Medical Products Ltd. 1 p.

279. [Biomedical Life Systems, Inc., Vista, CA]. BioMed and Systems TENS series [promotional material]. Scarborough, Ontario (Canada): Canadian Medical Products Ltd. 1 p.

280. Biorem Elettromedicali, Agropoli, Italy. TopLine COMPACT 100 electrotherapy low and medium frequency BRT/100 [promotional material]. Agropoli (Italy): Biorem. 2 p.

281. Biorem Elettromedicali, Agropoli, Italy. TopLine ERGON electrotherapy medium frequency [promotional material]. Agropoli (Italy): Biorem. 2 p.

282. Biorem Elettromedicali, Agropoli, Italy. TopLine EXPERT electrotherapy low and medium frequency BRT/70 [promotional material]. Agropoli (Italy): Biorem. 2 p.

283. Biorem Elettromedicali, Agropoli, Italy. TopLine EXPERT Mini electrotherapy low and medium frequency BRT/8 [promotional material]. Agropoli (Italy): Biorem. 2 p.

284. Biorem Elettromedicali, Agropoli, Italy. TopLine EXPERT Plus low and medium frequency expert system in electrotherapy [promotional material]. Agropoli (Italy): Biorem. 2 p.

285. Bloomex International, Inc., Elmwood Park, NJ. [Bloomex product catalog]. Elmwood Park (NJ): Bloomex. 14 p.

286. Bloomex International, Inc., Elmwood Park, NJ. [Bloomex product catalog]. Elmwood Park (NJ): Bloomex. 14 p.

287. Bloomex International, Inc., Elmwood Park, NJ. [Bloomex product catalog]. Elmwood Park (NJ): Bloomex. 14 p.

288. Bloomex International, Inc., Elmwood Park, NJ. [Bloomex product catalog]. Elmwood Park (NJ): Bloomex. 14 p.

289. ECRI. Stimulators, electroanalgesic, transcutaneous electrical nerve. In: Healthcare product comparison system. Plymouth Meeting (PA): ECRI; 1994 May. 20 p.

290. ECRI. Stimulators, electroanalgesic, transcutaneous electrical nerve. In: Healthcare product comparison system. Plymouth Meeting (PA): ECRI; 1994 May. 20 p.

291. ECRI. Stimulators, electroanalgesic, transcutaneous electrical nerve. In: Healthcare product comparison system. Plymouth Meeting (PA): ECRI; 1994 May. 20 p.

292. ECRI. Stimulators, electroanalgesic, transcutaneous electrical nerve. In: Healthcare product comparison system. Plymouth Meeting (PA): ECRI; 1994 May. 20 p.

293. ECRI. Stimulators, electroanalgesic, transcutaneous electrical nerve. In: Healthcare product comparison system. Plymouth Meeting (PA): ECRI; 1994 May. 20 p.

294. Carin Electromedicarin, S.A., Barcelona, Spain. Carin Electromedicarin, S.A. [product catalog]. Barcelona (Spain): Carin. 20 p.

295. Carin Electromedicarin, S.A., Barcelona, Spain. Carin Electromedicarin, S.A. [product catalog]. Barcelona (Spain): Carin. 20 p.

296. Carin Electromedicarin, S.A., Barcelona, Spain. Carin Electromedicarin, S.A. [product catalog]. Barcelona (Spain): Carin. 20 p.

297. Carin Electromedicarin, S.A., Barcelona, Spain. Carin Electromedicarin, S.A. [product catalog]. Barcelona (Spain): Carin. 20 p.

298. Cefar medical products ab, Lund, Sweden. Sensory electrostimulation [product catalog]. Lund (Sweden): Cefar. 14 p.

299. Cefar medical products ab, Lund, Sweden. Sensory electrostimulation [product catalog]. Lund (Sweden): Cefar. 14 p.

300. Cefar medical products ab, Lund, Sweden. Sensory electrostimulation [product catalog]. Lund (Sweden): Cefar. 14 p.

301. Cefar medical products ab, Lund, Sweden. Sensory electrostimulation [product catalog]. Lund (Sweden): Cefar. 14 p.

302. Cefar medical products ab, Lund, Sweden. Sensory electrostimulation [product catalog]. Lund (Sweden): Cefar. 14 p.

303. Cefar medical products ab, Lund, Sweden. Sensory electrostimulation [product catalog]. Lund (Sweden): Cefar. 14 p.

304. Cefar medical products ab, Lund, Sweden. Sensory electrostimulation [product catalog]. Lund (Sweden): Cefar. 14 p.

305. T.H. Charters, Inc., Beaverton, OR. ElectroBLOC [promotional material]. Beaverton (OR): T.H. Charters. 2 p.

306. T.H. Charters, Inc., Beaverton, OR. EXER-STIM Single Channel Muscle Stimulator [promotional material]. Beaverton (OR): T.H. Charters. 2 p.

307. T.H. Charters, Inc., Beaverton, OR. EXER-STIM 2 Dual Channel Muscle Stimulator [promotional material]. Beaverton (OR): T.H. Charters. 2 p.

308. T.H. Charters, Inc., Beaverton, OR. MINI-1 TENS [promotional material]. Beaverton (OR): T.H. Charters. 1 p.

309. T.H. Charters, Inc., Beaverton, OR. Myopulse Stimulator relieves muscle fatigue spasm [promotional material]. Beaverton (OR): T.H. Charters. 2 p.

310. T.H. Charters, Inc., Beaverton, OR. NeuroPulser 2+ TENS [promotional material]. Beaverton (OR): T.H. Charters. 1991. 2 p.

311. Chattanooga Group, Inc., Hixson, TN. Forte ES450 Electrotherapy System: a new world of flexibility and simplicity for today and tomorrow [promotional material]. Hixson (TN): Chattanooga Group. 1994. 2 p.

312. Chattanooga Group, Inc., Hixson, TN. Intelect 150 High Voltage Stimulator: the portable, affordable high voltage system [promotional material]. Hixson (TN): Chattanooga Group. 1994. 2 p.

313. Chattanooga Group, Inc., Hixson, TN. Intelect 500 S High Voltage Stimulator: versatility in treatment parameters [promotional material]. Hixson (TN): Chattanooga Group. 1990. 2 p.

314. ECRI. Stimulators, electroanalgesic, transcutaneous electrical nerve. In: Healthcare product comparison system. Plymouth Meeting (PA): ECRI; 1994 May. 20 p.

315. Comfort Technologies Inc., Pittstown, NJ. Transcutaneous electrical nerve stimulators (T.E.N.S.) for drug-free pain relief [product brochure]. Pittstown (NJ): Comfort Technologies. 2 p.

316. Comfort Technologies Inc., Pittstown, NJ. Transcutaneous electrical nerve stimulators (T.E.N.S.) for drug-free pain relief [product brochure]. Pittstown (NJ): Comfort Technologies. 2 p.

317. Comfort Technologies Inc., Pittstown, NJ. Transcutaneous electrical nerve stimulators (T.E.N.S.) for drug-free pain relief [product brochure]. Pittstown (NJ): Comfort Technologies. 2 p.

318. Comfort Technologies Inc., Pittstown, NJ. Transcutaneous electrical nerve stimulators (T.E.N.S.) for drug-free pain relief [product brochure]. Pittstown (NJ): Comfort Technologies. 2 p.

319. Comfort Technologies Inc., Pittstown, NJ. Transcutaneous electrical nerve stimulators (T.E.N.S.) for drug-free pain relief [product brochure]. Pittstown (NJ): Comfort Technologies. 2 p.

320. Comfort Technologies Inc., Pittstown, NJ. Transcutaneous electrical nerve stimulators (T.E.N.S.) for drug-free pain relief [product brochure]. Pittstown (NJ): Comfort Technologies. 2 p.

321. danmeter, Odense, Denmark. AUTOMOVE AM 706: electro myographic controlled stimulation for improved rehabilitation after stroke [promotional material]. Odense (Denmark): danmeter. 4 p.

322. danmeter, Odense, Denmark. elpha 2000 Muscle and Pain Stimulator [promotional material]. Odense (Denmark): danmeter. 4 p.

323. danmeter, Odense, Denmark. Effective pain and muscle stimulator TS 6000 [promotional material]. Odense (Denmark): danmeter. 4 p.

324. Diter-Elektronikka Oy, Turku, Finland. Diter electrotherapy & ultrasoundtherapy devices [product catalog]. Turku (Finland): Diter. 18 p.

325. Diter-Elektronikka Oy, Turku, Finland. Diter electrotherapy & ultrasoundtherapy devices [product catalog]. Turku (Finland): Diter. 18 p.

326. Diter-Elektronikka Oy, Turku, Finland. Diter electrotherapy & ultrasoundtherapy devices [product catalog]. Turku (Finland): Diter. 18 p.

327. Diter-Elektronikka Oy, Turku, Finland. Diter electrotherapy & ultrasoundtherapy devices [product catalog]. Turku (Finland): Diter. 18 p.

328. Dynatronics, Salt Lake City, UT. Dynatron 400: interferential therapy [promotional material]. Salt Lake City (UT): Dynatronics. 1992. 2 p.

329. Dynatronics, Salt Lake City, UT. Dynatron 500PLUS: interferential, microcurrent and muscle stimulation [promotional material]. Salt Lake City (UT): Dynatronics. 1993. 2 p.

330. Dynatronics, Salt Lake City, UT. Dynatron 800: combination therapy [promotional material]. Salt Lake City (UT): Dynatronics. 1993. 2 p.

331. Dynatronics, Salt Lake City, UT. The Dynatron 50 Series: a quantum leap in portable electrotherapy and ultrasound technology [promotional material]. Salt Lake City (UT): Dynatronics. 1994. 2 p.

332. DynaWave Corporation, Geneva, IL. DynaLator: the ultimate combination [promotional material]. Geneva (IL): DynaWave. 2 p.

333. DynaWave Corporation, Geneva, IL. DynaWave Model 12 [promotional material]. Geneva (IL): DynaWave. 2 p.

334. N H Eastwood & Son Ltd., Hertfordshire, England. Mini-Tens: range of transcutaneous electrical nerve stimulators [promotional material]. Hertfordshire (England): N H Eastwood & Son. 4 p.

335. N H Eastwood & Son Ltd., Hertfordshire, England. Mini-Tens: range of transcutaneous electrical nerve stimulators [promotional material]. Hertfordshire (England): N H Eastwood & Son. 4 p.

336. N H Eastwood & Son Ltd., Hertfordshire, England. Mini-Tens: range of transcutaneous electrical nerve stimulators [promotional material]. Hertfordshire (England): N H Eastwood & Son. 4 p.

337. N H Eastwood & Son Ltd., Hertfordshire, England. Mini-Tens: range of transcutaneous electrical nerve stimulators [promotional material]. Hertfordshire (England): N H Eastwood & Son. 4 p.

338. N H Eastwood & Son Ltd., Hertfordshire, England. Mini-Tens: range of transcutaneous electrical nerve stimulators [promotional material]. Hertfordshire (England): N H Eastwood & Son. 4 p.

339. [Electro Therapeutics Devices, Inc., Markham, Ontario, Canada]. ACCU-O-MATIC VM2 advanced transcutaneous electro therapy device: puts effective pain management capabilities in your hands [promotional material]. [Markham, Ontario (Canada): Electro Therapeutic Devices]. 1988 Jan. 2 p.

340. ECRI. Stimulators, electroanalgesic, transcutaneous electrical nerve. In: Healthcare product comparison system. Plymouth Meeting (PA): ECRI; 1994 May. 20 p.

341. ECRI. Stimulators, electroanalgesic, transcutaneous electrical nerve. In: Healthcare product comparison system. Plymouth Meeting (PA): ECRI; 1994 May. 20 p.

342. ECRI. Stimulators, electroanalgesic, transcutaneous electrical nerve. In: Healthcare product comparison system. Plymouth Meeting (PA): ECRI; 1994 May. 20 p.

343. Electro-Med Health Industries, Inc., (EMHI), North Miami, FL. Model 300 High Voltage Pulsed Galvanic Stimulator [promotional material]. North Miami (FL): EMHI. 1986 Jan. 2 p.

344. Electro-Med Health Industries, Inc., (EMHI), North Miami, FL. EGS 100-2S High Voltage Pulsed Galvanic Stimulator [promotional material]. North Miami (FL): EMHI. 1986 Apr. 2 p.

345. Electro-Med Health Industries, Inc., (EMHI), North Miami, FL. EGS-100SL includes the micro-current component! [promotional material]. North Miami (FL): EMHI. 1992 Jan. 1 p.

346. Electro-Med Health Industries, Inc., (EMHI), North Miami, FL. Introducing the latest in versatility: VeraStim 380 Medium Frequency Neuro-muscular Stimulator [promotional material]. North Miami (FL): EMHI. 1987 Feb. 2 p.

347. Electro-Medical Supplies (Greenham) Limited (EMS), Wantage, Oxfordshire, England. The new EMS 950: cost effective interferential therapy [promotional material]. Wantage, Oxfordshire (England): EMS. 2 p.

348. Electro-Medical Supplies (Greenham) Limited (EMS), Wantage, Oxfordshire, England. MEDI-LINK Electro-Therapy System [promotional material]. Wantage, Oxfordshire (England): EMS. 7 p.

349. ELMED Incorporated, Addison, IL. ELMED HVG 500 [promotional material]. Addison (IL): ELMED. 2 p.

350. EMPI, Inc., St. Paul, MN. ComfortPulse: the portable, medium frequency stimulator that reduces the pain of pain relief [promotional material]. St. Paul (MN): EMPI. 1993 Dec. 4 p.

351. ECRI. Stimulators, electroanalgesic, transcutaneous electrical nerve. In: Healthcare product comparison system. Plymouth Meeting (PA): ECRI; 1994 May. 20 p.

352. EMPI, Inc., St. Paul, MN. Eclipse+. Raise your patient's comfort level. And yours [promotional material]. St. Paul (MN): EMPI. 1993 Aug. 4 p.

353. EMPI, Inc., St. Paul, MN. EPIX XL: advancing the limits of TENS technology [promotional material]. St. Paul (MN): EMPI. 1988. 4 p.

354. EMPI, Inc., St. Paul, MN. For the best in neuromuscular stimulation, you have to have a FOCUS [promotional material]. St. Paul (MN): EMPI. 2 p.

355. EMPI, Inc., St. Paul, MN. Respond Select Neuromuscular Stimulator [promotional material]. St. Paul (MN): EMPI. 1994 Jan. 4 p.

356. Excel Tech Ltd., Oakville, Ontario, Canada. Excel Ultra III. Accurately control the total energy transferred to your patient with the world's most advanced combination therapy system [promotional material]. Timonium (MD): Alan G. Day Corporation. 3 p.

357. ECRI. Stimulators, electroanalgesic, transcutaneous electrical nerve. In: Healthcare product comparison system. Plymouth Meeting (PA): ECRI; 1994 May. 20 p.

358. General Physiotherapy, Inc., St. Louis, MO. Porta-Puls II Muscle Stimulator: product bulletin [promotional material]. St. Louis (MO): General Physiotherapy. 2 p.

359. ECRI. Stimulators, electroanalgesic, transcutaneous electrical nerve. In: Healthcare product comparison system. Plymouth Meeting (PA): ECRI; 1994 May. 20 p.

360. ECRI. Stimulators, electroanalgesic, transcutaneous electrical nerve. In: Healthcare product comparison system. Plymouth Meeting (PA): ECRI; 1994 May. 20 p.

361. ECRI. Stimulators, electroanalgesic, transcutaneous electrical nerve. In: Healthcare product comparison system. Plymouth Meeting (PA): ECRI; 1994 May. 20 p.

362. ECRI. Stimulators, electroanalgesic, transcutaneous electrical nerve. In: Healthcare product comparison system. Plymouth Meeting (PA): ECRI; 1994 May. 20 p.

363. ECRI. Stimulators, electroanalgesic, transcutaneous electrical nerve. In: Healthcare product comparison system. Plymouth Meeting (PA): ECRI; 1994 May. 20 p.

364. ECRI. Stimulators, electroanalgesic, transcutaneous electrical nerve. In: Healthcare product comparison system. Plymouth Meeting (PA): ECRI; 1994 May. 20 p.

365. ECRI. Stimulators, electroanalgesic, transcutaneous electrical nerve. In: Healthcare product comparison system. Plymouth Meeting (PA): ECRI; 1994 May. 20 p.

366. ECRI. Stimulators, electroanalgesic, transcutaneous electrical nerve. In: Healthcare product comparison system. Plymouth Meeting (PA): ECRI; 1994 May. 20 p.

367. ECRI. Stimulators, electroanalgesic, transcutaneous electrical nerve. In: Healthcare product comparison system. Plymouth Meeting (PA): ECRI; 1994 May. 20 p.

368. ECRI. Stimulators, electroanalgesic, transcutaneous electrical nerve. In: Healthcare product comparison system. Plymouth Meeting (PA): ECRI; 1994 May. 20 p.

369. ECRI. Stimulators, electroanalgesic, transcutaneous electrical nerve. In: Healthcare product comparison system. Plymouth Meeting (PA): ECRI; 1994 May. 20 p.

370. ECRI. Stimulators, electroanalgesic, transcutaneous electrical nerve. In: Healthcare product comparison system. Plymouth Meeting (PA): ECRI; 1994 May. 20 p.

371. ECRI. Stimulators, electroanalgesic, transcutaneous electrical nerve. In: Healthcare product comparison system. Plymouth Meeting (PA): ECRI; 1994 May. 20 p.

372. ECRI. Stimulators, electroanalgesic, transcutaneous electrical nerve. In: Healthcare product comparison system. Plymouth Meeting (PA): ECRI; 1994 May. 20 p.

373. Henley International, Inc., Sugar Land, TX. Team*mate TRI-STIM: 3 modalities in one [promotional material]. Sugar Land (TX): Henley. 1994. 2 p.

374. ITO Co., Ltd., Tokyo, Japan. Stimulators, electroanalgesic, transcutaneous electrical nerve [table]. Tokyo (Japan): ITO. 1 p.

375. ITO Co., Ltd., Tokyo, Japan. Dual-Channel TENS Model 120Z [promotional material]. Tokyo (Japan): ITO. 1 p.

376. ITO Co., Ltd., Tokyo, Japan. Stimulators, electroanalgesic, transcutaneous electrical nerve [table]. Tokyo (Japan): ITO. 1 p.

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382. ECRI. Stimulators, electroanalgesic, transcutaneous electrical nerve. In: Healthcare product comparison system. Plymouth Meeting (PA): ECRI; 1994 May. 20 p.

383. Medical Devices, Inc., St. Paul, MN. FasTENS [promotional material]. St. Paul (MN): Medical Devices. 1987. 1 p.

384. Medical Devices, Inc., St. Paul, MN. FasTENS 30 [promotional material]. St. Paul (MN): Medical Devices. 1987. 1 p.

385. Medical Devices, Inc., St. Paul, MN. GV II High Voltage Pulsed Galvanic Stimulator...electromedical technology from Medical Devices, Inc. [promotional material]. St. Paul (MN): Medical Devices. 1990. 2 p.

386. Medical Devices, Inc., St. Paul, MN. IF II Interferential Stimulator...electromedical technology from Medical Devices, Inc. [promotional material]. St. Paul (MN): Medical Devices. 1989. 2 p.

387. Medical Devices, Inc., St. Paul, MN. Matrix I Programmed TENS [promotional material]. St. Paul (MN): Medical Devices. 1990. 8 p.

388. Medical Devices, Inc., St. Paul, MN. MC II Microcurrent Stimulator...electromedical technology from Medical Devices, Inc. [promotional material]. St. Paul (MN): Medical Devices. 1990. 2 p.

389. Medical Devices, Inc., St. Paul, MN. MediMOD [promotional material]. St. Paul (MN): Medical Devices. 1989. 2 p.

390. Medical Devices, Inc., St. Paul, MN. MENTOR 159 [promotional material]. St. Paul (MN): Medical Devices. 1988. 1 p.

391. Medical Devices, Inc., St. Paul, MN. MENTOR 259 [promotional material]. St. Paul (MN): Medical Devices. 1988. 1 p.

392. Medical Devices, Inc., St. Paul, MN. ULTRAPAC II SX [promotional material]. St. Paul (MN): Medical Devices. 1986. 1 p.

393. Medical Devices, Inc., St. Paul, MN. ULTRAPAC II SX PLUS [promotional material]. St. Paul (MN): Medical Devices. 1987. 1 p.

394. Mettler Electronics Corp., Anaheim, CA. Sonicator Plus: get it together [promotional material]. Anaheim (CA): Mettler Electronics. 1993 Oct. 2 p.

395. Mettler Electronics Corp., Anaheim, CA. Sys*Stim 206: the very affordable, portable stimulator [promotional material]. Anaheim (CA): Mettler Electronics. 1994 May. 2 p.

396. Mettler Electronics Corp., Anaheim, CA. Sys*Stim 206A: our proven performer now brings more flexibility and control to the table [promotional material]. Anaheim (CA): Mettler Electronics. 1994 Mar. 2 p.

397. Mettler Electronics Corp., Anaheim, CA. Sys*Stim 207A: the stimulator famous for its extra muscle now packs a one-two punch [promotional material]. Anaheim (CA): Mettler Electronics. 1994 Mar. 2 p.

398. Mettler Electronics Corp., Anaheim, CA. Sys*Stim 220: it's never been easier to get the beat... with full-featured interferential therapy from Mettler [promotional material]. Anaheim (CA): Mettler Electronics. 1994 Mar. 2 p.

399. OMS Medical Supplies. OMS new products supplement and price list for 1992-93 catalog; 1995 Jan. p. 14.

400. OMS Medical Supplies. OMS Medical Supplies 1992-93 catalog; p. 36-9.

401. OMS Medical Supplies. OMS Medical Supplies 1992-93 catalog; p. 36-9.

402. OMS Medical Supplies. OMS Medical Supplies 1992-93 catalog; p. 36-9.

403. J A Preston Corp. [Preston product catalog]. Jackson (MI): Preston; Ultramax III H.V.P.G.S.; p. 164.

404. J A Preston Corp. [Preston product catalog]. Jackson (MI): Preston; Ultramax III H.V.P.G.S.; p. 164.

405. J A Preston Corp. [Preston product catalog]. Jackson (MI): Preston; Ultramax III H.V.P.G.S.; p. 164.

406. PTI, Topeka, KS. PTI Omnistim 500 Portable/Clinical Multi-Modality Electrotherapy and Rehabilitation System [promotional material]. Topeka (KS): PTI. 1993 Mar. 4 p.

407. PTI, Topeka, KS. PTI Omnisound Combination Therapy 2500C System [promotional material]. Topeka (KS): PTI. 1993 Jul. 6 p.

408. Rich-Mar Corporation, [Inola, OK]. Rich-Mar III and III-G: economical and portable low volt stimulators [promotional material]. [Inola (OK)]: Rich-Mar. 2 p.

409. Rich-Mar Corporation, [Inola, OK]. Rich-Mar III and III-G: economical and portable low volt stimulators [promotional material]. [Inola (OK)]: Rich-Mar. 2 p.

410. Rich-Mar Corporation, [Inola, OK]. Rich-Mar III and III-G: economical and portable low volt stimulators [promotional material]. [Inola (OK)]: Rich-Mar. 2 p.

411. Rich-Mar Corporation, [Inola, OK]. Rich-Mar Theratouch 3.3: a new twist in electrotherapy [promotional material]. [Inola (OK)]: Rich-Mar. 1994. 2 p.

412. Rich-Mar Corporation, [Inola, OK]. Rich-Mar Theratouch 4.7: a stimulator that actually improves with age [promotional material]. [Inola (OK)]: Rich-Mar. 1994. 2 p.

413. Sale & Service, S.L., Electromedicina, Spain. TENS 3002 Pro - multifunción: transcutaneous electrical nerve stimulator (dual channel) [promotional material]. Spain: Sale & Service. 2 p.

414. ST - Electromedicina, S.A., Barcelona, Spain. Sarria ST-110: electrotherapy unit [promotional material]. Barcelona (Spain): ST. 2 p.

415. ST - Electromedicina, S.A., Barcelona, Spain. Sarria ST-120: electrotherapy unit [promotional material]. Barcelona (Spain): ST. 2 p.

416. Staodyn, Inc., Longmont, CO. Dermapulse for accelerated healing [promotional material]. Longmont (CO): Staodyn. 1994. 4 p.

417. Staodyn, Inc., Longmont, CO. EMS+2 Neuromuscular Stimulator. EMS+2 puts you in control [promotional material]. Longmont (CO): Staodyn. 2 p.

418. Staodyn, Inc., Longmont, CO. Maxima II TENS: a powerful multi-mode unit that's easy to use [promotional material]. Longmont (CO): Staodyn. 2 p.

419. Staodyn, Inc., Longmont, CO. Advanced TENS products [promotional material]. Longmont (CO): Staodyn. 1990. 6 p.

420. Staodyn, Inc., Longmont, CO. Maxima III: reflex sympathetic dystrophy syndrome. TENS clinical guidelines. Longmont (CO): Staodyn. 1990. 4 p.

421. Staodyn, Inc., Longmont, CO. Advanced TENS products [promotional material]. Longmont (CO): Staodyn. 1990. 6 p.

422. Staodyn, Inc., Longmont, CO. Maxima III TENS: strength duration modulation combined with intelligence [promotional material]. Longmont (CO): Staodyn. 1990. 2 p.

423. Staodyn, Inc., Longmont, CO. NUWAVE: the unconventional pain management modality [promotional material]. Longmont (CO): Staodyn. 1992. 2 p.

424. Staodyn, Inc., Longmont, CO. Advanced TENS products [promotional material]. Longmont (CO): Staodyn. 1990. 6 p.

425. Staodyn, Inc., Longmont, CO. Introducing TUWAVE the 2 in one modality [promotional material]. Longmont (CO): Staodyn. 1992. 4 p.

426. Titan Electronics Ltd., Tiberias, Israel. Compact-TENS: a compact system for pain relief [promotional material]. Tiberias (Israel): Titan. 3 p.

427. Titan Electronics Ltd., Tiberias, Israel. Wave away menstrual pain with TiCi-EL [promotional material]. Tiberias (Israel): Titan. 15 p.

428. Ultraschall Dr. Born GmbH, Frankfurt, Germany. Ultraschall press release. Two in one therapy unit: ultrasonic and stimulus current [promotional material]. Frankfurt (Germany): Ultraschall. 1993 Nov. 3 p.

429. Universal Technology Systems, Inc., (UTS), Jacksonville, FL. Therapy through new technology: introducing the PGS-3000 Portable Pulsed Galvanic Stimulator [promotional material]. Jacksonville (FL): UTS. 2 p.

430. Verimed, Fort Lauderdale, FL. Introducing the Veristim II: the ultimate hand held, combination surface EMG - neuro muscular electrical stimulator [promotional material]. Fort Lauderdale (FL): Verimed. 2 p.

431. Verimed, Fort Lauderdale, FL. Phyaction 780 series has it all...and then some! [promotional material]. Fort Lauderdale (FL): Verimed. 2 p.

432. Biorem Elettromedicali, Agropoli, Italy. TopLine MAXIMA Magnetic Field B20-1/2 programmable magnetotherapy [promotional material]. Agropoli (Italy): Biorem. 2 p.

433. Biorem Elettromedicali, Agropoli, Italy. TopLine MICRA magnetotherapy [promotional material]. Agropoli (Italy): Biorem. 2 p.

434. Ross, Jesse, D.Sci. (Diapulse Corporation of America, Great Neck, NY). Personal communication [letter]. 1996 Mar 15. 16 p.

435. [Electropharmacology, Pompano Beach, FL]. sofPulse [package insert]. Pompano Beach (FL): Magnetic Resonance Therapeutics, Inc. 2 p.

436. AVRA Tronics Corp., Greenvale, NY. Model 770 GALVANATOR: a physical therapy stimulator instrument for pulsed galvanic stimulation of muscles and localized tissues [promotional material]. Greenvale (NY): AVRA Tronics. 2 p.

437. Chattanooga Group, Inc., Hixson, TN. Intelect 500 S High Voltage Stimulator: versatility in treatment parameters [promotional material]. Hixson (TN): Chattanooga Group. 1990. 2 p.

438. DynaWave Corporation, Geneva, IL. DynaWave Model 12 [promotional material]. Geneva (IL): DynaWave. 2 p.

439. EMPI, Inc., St. Paul, MN. Eclipse+. Raise your patient's comfort level. And yours [promotional material]. St. Paul (MN): EMPI. 1993 Aug. 4 p.

440. ECRI. Stimulators, electroanalgesic, transcutaneous electrical nerve. In: Healthcare product comparison system. Plymouth Meeting (PA): ECRI; 1994 May. 20 p.

441. Staodyn, Inc., Longmont, CO. Dermapulse for accelerated healing [promotional material]. Longmont (CO): Staodyn. 1994. 4 p.

442. Universal Technology Systems, Inc., (UTS), Jacksonville, FL. Therapy through new technology: introducing the PGS-3000 Portable Pulsed Galvanic Stimulator [promotional material]. Jacksonville (FL): UTS. 2 p.

443. Ross, Jesse, D.Sci. (Diapulse Corporation of America, Great Neck, NY). Personal communication [letter]. 1996 Mar 15. 16 p.

444. Fakhri O, Amin MA. The effect of low-voltage electric therapy on the healing of resistant skin burns. J Burn Care Rehabil 1987 Jan-Feb;8(1):15-8.

445. Mawson AR, Siddiqui FH, Connolly BJ, Sharp CJ, Stewart GW, Summer WR, Biundo JJ Jr. Effect of high voltage pulsed galvanic stimulation on sacral transcutaneous oxygen tension levels in the spinal cord injured. Paraplegia 1993 May;31(5):311-9.

446. Finsen V, Persen L, Lovlien M, Veslegaard EK, Simensen M, Gasvann AK, Benum P. Transcutaneous electrical nerve stimulation after major amputation. J Bone Joint Surg Br 1988 Jan;70(1):109-12.

447. Kjartansson J, Lundeberg T. Effects of electrical nerve stimulation (ENS) in ischemic tissue. Scand J Plast Reconstr Surg Hand Surg 1990;24(2):129-34.

448. Lundeberg T, Kjartansson J, Samuelsson U. Effect of electrical nerve stimulation on healing of ischaemic skin flaps. Lancet 1988 Sep 24;2(8613):712-4.

449. Goldin JH, Broadbent NR, Nancarrow JD, Marshall T. The effects of Diapulse on the healing of wounds: a double-blind randomised controlled trial in man. Br J Plast Surg 1981 Jul;34(3):267-70.

450. Wilson DH. Treatment of soft-tissue injuries by pulsed electrical energy. Br Med J 1972 Apr 29;2(808):269-70.

451. Jivegård LE, Augustinsson LE, Holm J, Risberg B, Ortenwall P. Effects of spinal cord stimulation (SCS) in patients with inoperable severe lower limb ischaemia: a prospective randomised controlled study. Eur J Vasc Endovasc Surg 1995 May;9(4):421-5.

452. Weingarten MS. Advances in wound healing. In: Oloff LM. Musculoskeletal disorders of the lower extremities. Philadelphia: Saunders; 1994. p. 52-64.

453. Knighton DR, Loss L. Design and implementation of clinical studies in chronic nonhealing wounds. Prog Clin Biol Res 1991;365:67-76.

454. Weingarten MS. Review: obstacles to wound healing. Wounds 1993 Sep-Oct;5(5):238-44.

455. Weingarten MS. Review: obstacles to wound healing. Wounds 1993 Sep-Oct;5(5):238-44.

456. Weingarten MS. Advances in wound healing. In: Oloff LM. Musculoskeletal disorders of the lower extremities. Philadelphia: Saunders; 1994. p. 52-64.

457. Kaada B, Emru M. Promoted healing of leprous ulcers by transcutaneous nerve stimulation. Acupunct Electrother Res 1988;13(4):165-76.

458. Resch CS, Kerner E, Robson MC, Heggers JP, Scherer M, Boertman JA, Schileru R. Pressure sore volume measurement. A technique to document and record wound healing. J Am Geriatr Soc 1988 May;36(5):444-6.

459. Vodovnik L, Karba R. Treatment of chronic wounds by means of electric and electromagnetic fields. Part 1. Literature review. Med Biol Eng Comput 1992 May;30(3):257-66.

460. Weingarten MS. Review: obstacles to wound healing. Wounds 1993 Sep-Oct;5(5):238-44.

461. Piérard GE, Piérard-Franchimont C. Planimetry of the healing rate of leg ulcers. Eur J Dermatol 1995 Apr-May;5(3):257-62.

462. Katelaris PM, Fletcher JP, Little JM, McEntyre RJ, Jeffcoate KW. Electrical stimulation in the treatment of chronic venous ulceration. Aust N Z J Surg 1987 Sep;57(9):605-7.

463. Carley PJ, Wainapel SF. Electrotherapy for acceleration of wound healing: low intensity direct current. Arch Phys Med Rehabil 1985 Jul;66(7):443-6.

464. Akers TK, Gabrielson AL. The effect of high voltage galvanic stimulation on the rate of healing of decubitus ulcers. Biomed Sci Instrum 1984;20:99-100.

465. Wood JM, Evans PE 3rd, Schallreuter KU, Jacobson WE, Sufit R, Newman J, White C, Jacobson M. A multicenter study on the use of pulsed low-intensity direct current for healing chronic stage II and stage III decubitus ulcers. Arch Dermatol 1993 Aug;129(8):999-1009.

466. Gogia PP, Marquez RR, Minerbo GM. Effects of high voltage galvanic stimulation on wound healing. Ostomy Wound Manage 1992 Jan-Feb;38(1):29-35.

467. Gentzkow GD, Pollack SV, Kloth LC, Stubbs HA. Improved healing of pressure ulcers using Dermapulse, a new electrical stimulation device. Wounds 1991 Sep-Oct;3(5):158-70.

468. Griffin JW, Tooms RE, Mendius RA, Clifft JK, Vander Zwaag R, el-Zeky F. Efficacy of high voltage pulsed current for healing of pressure ulcers in patients with spinal cord injury. Phys Ther 1991 Jun;71(6):433-42; discussion 442-4.

469. Feedar JA, Kloth LC, Gentzkow GD. Chronic dermal ulcer healing enhanced with monophasic pulsed electrical stimulation. Phys Ther 1991 Sep;71(9):639-49.

470. Mulder GD. Treatment of open-skin wounds with electric stimulation. Arch Phys Med Rehabil 1991 May;72(6):375-7.

471. Unger P, Eddy J, Raimastry S. A controlled study of the effect of high voltage pulse current (HVPC) on wound healing [abstract]. Phys Ther 1991 Jun;71(6 Suppl):S119.

472. Kloth LC, Feedar JA. Acceleration of wound healing with high voltage, monophasic, pulsed current [published erratum appears in Phys Ther 1989 Aug;69(8):702]. Phys Ther 1988 Apr;68(4):503-8.

473. Feedar JA, Kloth LC. Acceleration of wound healing with high voltage pulsating direct current [abstract]. Phys Ther 1985 May;65(5):741.

474. Stefanovska A, Vodovnik L, Benko H, Turk R. Treatment of chronic wounds by means of electric and electromagnetic fields. Part 2. Value of FES parameters for pressure sore treatment. Med Biol Eng Comput 1993 May;31(3):213-20.

475. Lundeberg TC, Eriksson SV, Malm M. Electrical nerve stimulation improves healing of diabetic ulcers. Ann Plast Surg 1992 Oct;29(4):328-31.

476. Salzberg CA, Cooper-Vastola SA, Perez F, Viehbeck MG, Byrne DW. The effects of non-thermal pulsed electromagnetic energy on wound healing of pressure ulcers in spinal cord-injured patients: a randomized, double-blind study. Ostomy Wound Manage 1995 Apr;41(3):42-4, 46, 48 passim.

477. Stiller MJ, Pak GH, Shupack JL, Thaler S, Kenny C, Jondreau L. A portable pulsed electromagnetic field (PEMF) device to enhance healing of recalcitrant venous ulcers: a double-blind, placebo-controlled clinical trial. Br J Dermatol 1992 Aug;127(2):147-54.

478. Todd DJ, Heylings DJ, Allen GE, McMillin WP. Treatment of chronic varicose ulcers with pulsed electromagnetic fields: a controlled pilot study. Ir Med J 1991 Jun;84(2):54-5.

479. Ieran M, Zaffuto S, Bagnacani M, Annovi M, Moratti A, Cadossi R. Effect of low frequency pulsing electromagnetic fields on skin ulcers of venous origin in humans: a double-blind study. J Orthop Res 1990 Mar;8(2):276-82.

480. Jeran M, Zaffuto S, Moratti A, Bagnacani M, Cadossi R. PEMF stimulation of skin ulcers of venous origin in humans: preliminary report of a double blind study. J Bioelectr 1987;6(2):181-8.

481. Katelaris PM, Fletcher JP, Little JM, McEntyre RJ, Jeffcoate KW. Electrical stimulation in the treatment of chronic venous ulceration. Aust N Z J Surg 1987 Sep;57(9):605-7.

482. Carley PJ, Wainapel SF. Electrotherapy for acceleration of wound healing: low intensity direct current. Arch Phys Med Rehabil 1985 Jul;66(7):443-6.

483. Akers TK, Gabrielson AL. The effect of high voltage galvanic stimulation on the rate of healing of decubitus ulcers. Biomed Sci Instrum 1984;20:99-100.

484. Gault WR, Gatens PF Jr. Use of low intensity direct current in management of ischemic skin ulcers. Phys Ther 1976 Mar;56(3):265-9.

485. Wolcott LE, Wheeler PC, Hardwicke HM, Rowley BA. Accelerated healing of skin ulcer by electrotherapy: preliminary clinical results. South Med J 1969 Jul;62(7):795-801.

486. Fakhri O, Amin MA. The effect of low-voltage electric therapy on the healing of resistant skin burns. J Burn Care Rehabil 1987 Jan-Feb;8(1):15-8.

487. Assimacopoulos D. Low intensity negative electric current in the treatment of ulcers of the leg due to chronic venous insufficiency. Preliminary report of three cases. Am J Surg 1968 May;115(5):683-7.

488. Wood JM, Evans PE 3rd, Schallreuter KU, Jacobson WE, Sufit R, Newman J, White C, Jacobson M. A multicenter study on the use of pulsed low-intensity direct current for healing chronic stage II and stage III decubitus ulcers. Arch Dermatol 1993 Aug;129(8):999-1009.

489. Gogia PP, Marquez RR, Minerbo GM. Effects of high voltage galvanic stimulation on wound healing. Ostomy Wound Manage 1992 Jan-Feb;38(1):29-35.

490. Gentzkow GD, Pollack SV, Kloth LC, Stubbs HA. Improved healing of pressure ulcers using Dermapulse, a new electrical stimulation device. Wounds 1991 Sep-Oct;3(5):158-70.

491. Griffin JW, Tooms RE, Mendius RA, Clifft JK, Vander Zwaag R, el-Zeky F. Efficacy of high voltage pulsed current for healing of pressure ulcers in patients with spinal cord injury. Phys Ther 1991 Jun;71(6):433-42; discussion 442-4.

492. Feedar JA, Kloth LC, Gentzkow GD. Chronic dermal ulcer healing enhanced with monophasic pulsed electrical stimulation. Phys Ther 1991 Sep;71(9):639-49.

493. Mulder GD. Treatment of open-skin wounds with electric stimulation. Arch Phys Med Rehabil 1991 May;72(6):375-7.

494. Unger P, Eddy J, Raimastry S. A controlled study of the effect of high voltage pulse current (HVPC) on wound healing [abstract]. Phys Ther 1991 Jun;71(6 Suppl):S119.

495. Kloth LC, Feedar JA. Acceleration of wound healing with high voltage, monophasic, pulsed current [published erratum appears in Phys Ther 1989 Aug;69(8):702]. Phys Ther 1988 Apr;68(4):503-8.

496. Feedar JA, Kloth LC. Acceleration of wound healing with high voltage pulsating direct current [abstract]. Phys Ther 1985 May;65(5):741.

497. Fitzgerald GK, Newsome D. Treatment of a large infected thoracic spine wound using high voltage pulsed monophasic current. Phys Ther 1993 Jun;73(6):355-60.

498. Weiss DS, Eaglstein WH, Falanga V. Exogenous electric current can reduce the formation of hypertrophic scars. J Dermatol Surg Oncol 1989 Dec;15(12):1272-5.

499. Unger PG. A randomized clinical trial of the effect of HVPC on wound healing [abstract]. Phys Ther 1991 Jun;71 (6 Suppl):S118.

500. Mawson AR, Siddiqui FH, Connolly BJ, Sharp CJ, Stewart GW, Summer WR, Biundo JJ Jr. Effect of high voltage pulsed galvanic stimulation on sacral transcutaneous oxygen tension levels in the spinal cord injured. Paraplegia 1993 May;31(5):311-9.

501. Ross CR, Segal D. High voltage galvanic stimulation: an aid to post-operative healing. Curr Podiatry 1981;30(5):19-25.

502. Thurman BF, Christian EL. Response of a serious circulatory lesion to electrical stimulation. Phys Ther 1971 Oct;51(10):1107-10.

503. Stefanovska A, Vodovnik L, Benko H, Turk R. Treatment of chronic wounds by means of electric and electromagnetic fields. Part 2. Value of FES parameters for pressure sore treatment. Med Biol Eng Comput 1993 May;31(3):213-20.

504. Lundeberg TC, Eriksson SV, Malm M. Electrical nerve stimulation improves healing of diabetic ulcers. Ann Plast Surg 1992 Oct;29(4):328-31.

505. Karba R, Vodovnik L, Presern-Strukelj M, Klesnik M. Promoted healing of chronic wounds due to electrical stimulation. Wounds 1991 Jan-Feb;3(1):16-23.

506. Frantz RA. The effectiveness of transcutaneous electrical nerve stimulation (TENS) on decubitus ulcer healing in adult patients. In: Funk SG, Tornquist EM, Champagne MT, Copp LA, Wiese RA, editors. Key aspects of recovery: improving nutrition, rest, and mobility. New York: Springer; 1990. p. 197-205.

507. Kaada B, Emru M. Promoted healing of leprous ulcers by transcutaneous nerve stimulation. Acupunct Electrother Res 1988;13(4):165-76.

508. Alon G, Azaria M, Stein H. Diabetic ulcer healing using high voltage TENS [abstract]. Phys Ther 1986 May;66(5):775.

509. Barron JJ, Jacobson WE, Tidd G. Treatment of decubitus ulcers. A new approach. Minn Med 1985 Feb;68(2):103-6.

510. Finsen V, Persen L, Lovlien M, Veslegaard EK, Simensen M, Gasvann AK, Benum P. Transcutaneous electrical nerve stimulation after major amputation. J Bone Joint Surg Br 1988 Jan;70(1):109-12.

511. Lundeberg T, Kjartansson J, Samuelsson U. Effect of electrical nerve stimulation on healing of ischaemic skin flaps. Lancet 1988 Sep 24;2(8613):712-4.

512. Kjartansson J, Lundeberg T. Effects of electrical nerve stimulation (ENS) in ischemic tissue. Scand J Plast Reconstr Surg Hand Surg 1990;24(2):129-34.

513. Kaada B. Promoted healing of chronic ulceration by transcutaneous nerve stimulation (TNS). Vasa 1983;12(3):262-9.

514. Westerhof W, Bos JD. Trigeminal trophic syndrome: a successful treatment with transcutaneous electrical stimulation. Br J Dermatol 1983 May;108(5):601-4.

515. Salzberg CA, Cooper-Vastola SA, Perez F, Viehbeck MG, Byrne DW. The effects of non-thermal pulsed electromagnetic energy on wound healing of pressure ulcers in spinal cord-injured patients: a randomized, double-blind study. Ostomy Wound Manage 1995 Apr;41(3):42-4, 46, 48 passim.

516. Stiller MJ, Pak GH, Shupack JL, Thaler S, Kenny C, Jondreau L. A portable pulsed electromagnetic field (PEMF) device to enhance healing of recalcitrant venous ulcers: a double-blind, placebo-controlled clinical trial. Br J Dermatol 1992 Aug;127(2):147-54.

517. Todd DJ, Heylings DJ, Allen GE, McMillin WP. Treatment of chronic varicose ulcers with pulsed electromagnetic fields: a controlled pilot study. Ir Med J 1991 Jun;84(2):54-5.

518. Itoh M, Montemayor JS Jr, Matsumoto E, Eason A, Lee MH, Folk FS. Accelerated wound healing of pressure ulcers by pulsed high peak power electromagnetic energy (Diapulse). Decubitus 1991 Feb;4(1):24-5, 29-34.

519. Ieran M, Zaffuto S, Bagnacani M, Annovi M, Moratti A, Cadossi R. Effect of low frequency pulsing electromagnetic fields on skin ulcers of venous origin in humans: a double-blind study. J Orthop Res 1990 Mar;8(2):276-82.

520. Jeran M, Zaffuto S, Moratti A, Bagnacani M, Cadossi R. PEMF stimulation of skin ulcers of venous origin in humans: preliminary report of a double blind study. J Bioelectr 1987;6(2):181-8.

521. Wilson DH. Treatment of soft-tissue injuries by pulsed electrical energy. Br Med J 1972 Apr 29;2(808):269-70.

522. Tung S, Khaski A, Milano E, Kay C. The application of Diapulse in the treatment of decubitus ulcers: case reports. Contemp Surg 1995 Jul;47(1):27-32.

523. Goldin JH, Broadbent NR, Nancarrow JD, Marshall T. The effects of Diapulse on the healing of wounds: a double-blind randomised controlled trial in man. Br J Plast Surg 1981 Jul;34(3):267-70.

524. Assimacopoulos D. Low intensity negative electric current in the treatment of ulcers of the leg due to chronic venous insufficiency. Preliminary report of three cases. Am J Surg 1968 May;115(5):683-7.

525. Wolcott LE, Wheeler PC, Hardwicke HM, Rowley BA. Accelerated healing of skin ulcer by electrotherapy: preliminary clinical results. South Med J 1969 Jul;62(7):795-801.

526. Gault WR, Gatens PF Jr. Use of low intensity direct current in management of ischemic skin ulcers. Phys Ther 1976 Mar;56(3):265-9.

527. Fakhri O, Amin MA. The effect of low-voltage electric therapy on the healing of resistant skin burns. J Burn Care Rehabil 1987 Jan-Feb;8(1):15-8.

528. Wolcott LE, Wheeler PC, Hardwicke HM, Rowley BA. Accelerated healing of skin ulcer by electrotherapy: preliminary clinical results. South Med J 1969 Jul;62(7):795-801.

529. Gault WR, Gatens PF Jr. Use of low intensity direct current in management of ischemic skin ulcers. Phys Ther 1976 Mar;56(3):265-9.

530. Akers TK, Gabrielson AL. The effect of high voltage galvanic stimulation on the rate of healing of decubitus ulcers. Biomed Sci Instrum 1984;20:99-100.

531. Carley PJ, Wainapel SF. Electrotherapy for acceleration of wound healing: low intensity direct current. Arch Phys Med Rehabil 1985 Jul;66(7):443-6.

532. Katelaris PM, Fletcher JP, Little JM, McEntyre RJ, Jeffcoate KW. Electrical stimulation in the treatment of chronic venous ulceration. Aust N Z J Surg 1987 Sep;57(9):605-7.

533. Thurman BF, Christian EL. Response of a serious circulatory lesion to electrical stimulation. Phys Ther 1971 Oct;51(10):1107-10.

534. Ross CR, Segal D. High voltage galvanic stimulation: an aid to post-operative healing. Curr Podiatry 1981;30(5):19-25.

535. Weiss DS, Eaglstein WH, Falanga V. Exogenous electric current can reduce the formation of hypertrophic scars. J Dermatol Surg Oncol 1989 Dec;15(12):1272-5.

536. Unger PG. A randomized clinical trial of the effect of HVPC on wound healing [abstract]. Phys Ther 1991 Jun;71 (6 Suppl):S118.

537. Fitzgerald GK, Newsome D. Treatment of a large infected thoracic spine wound using high voltage pulsed monophasic current. Phys Ther 1993 Jun;73(6):355-60.

538. Mawson AR, Siddiqui FH, Connolly BJ, Sharp CJ, Stewart GW, Summer WR, Biundo JJ Jr. Effect of high voltage pulsed galvanic stimulation on sacral transcutaneous oxygen tension levels in the spinal cord injured. Paraplegia 1993 May;31(5):311-9.

539. Feedar JA, Kloth LC. Acceleration of wound healing with high voltage pulsating direct current [abstract]. Phys Ther 1985 May;65(5):741.

540. Kloth LC, Feedar JA. Acceleration of wound healing with high voltage, monophasic, pulsed current [published erratum appears in Phys Ther 1989 Aug;69(8):702]. Phys Ther 1988 Apr;68(4):503-8.

541. Unger P, Eddy J, Raimastry S. A controlled study of the effect of high voltage pulse current (HVPC) on wound healing [abstract]. Phys Ther 1991 Jun;71(6 Suppl):S119.

542. Feedar JA, Kloth LC, Gentzkow GD. Chronic dermal ulcer healing enhanced with monophasic pulsed electrical stimulation. Phys Ther 1991 Sep;71(9):639-49.

543. Mulder GD. Treatment of open-skin wounds with electric stimulation. Arch Phys Med Rehabil 1991 May;72(6):375-7.

544. Griffin JW, Tooms RE, Mendius RA, Clifft JK, Vander Zwaag R, el-Zeky F. Efficacy of high voltage pulsed current for healing of pressure ulcers in patients with spinal cord injury. Phys Ther 1991 Jun;71(6):433-42; discussion 442-4.

545. Gentzkow GD, Pollack SV, Kloth LC, Stubbs HA. Improved healing of pressure ulcers using Dermapulse, a new electrical stimulation device. Wounds 1991 Sep-Oct;3(5):158-70.

546. Gogia PP, Marquez RR, Minerbo GM. Effects of high voltage galvanic stimulation on wound healing. Ostomy Wound Manage 1992 Jan-Feb;38(1):29-35.

547. Wood JM, Evans PE 3rd, Schallreuter KU, Jacobson WE, Sufit R, Newman J, White C, Jacobson M. A multicenter study on the use of pulsed low-intensity direct current for healing chronic stage II and stage III decubitus ulcers. Arch Dermatol 1993 Aug;129(8):999-1009.

548. Westerhof W, Bos JD. Trigeminal trophic syndrome: a successful treatment with transcutaneous electrical stimulation. Br J Dermatol 1983 May;108(5):601-4.

549. Kaada B. Promoted healing of chronic ulceration by transcutaneous nerve stimulation (TNS). Vasa 1983;12(3):262-9.

550. Barron JJ, Jacobson WE, Tidd G. Treatment of decubitus ulcers. A new approach. Minn Med 1985 Feb;68(2):103-6.

551. Alon G, Azaria M, Stein H. Diabetic ulcer healing using high voltage TENS [abstract]. Phys Ther 1986 May;66(5):775.

552. Kaada B, Emru M. Promoted healing of leprous ulcers by transcutaneous nerve stimulation. Acupunct Electrother Res 1988;13(4):165-76.

553. Frantz RA. The effectiveness of transcutaneous electrical nerve stimulation (TENS) on decubitus ulcer healing in adult patients. In: Funk SG, Tornquist EM, Champagne MT, Copp LA, Wiese RA, editors. Key aspects of recovery: improving nutrition, rest, and mobility. New York: Springer; 1990. p. 197-205.

554. Karba R, Vodovnik L, Presern-Strukelj M, Klesnik M. Promoted healing of chronic wounds due to electrical stimulation. Wounds 1991 Jan-Feb;3(1):16-23.

555. Finsen V, Persen L, Lovlien M, Veslegaard EK, Simensen M, Gasvann AK, Benum P. Transcutaneous electrical nerve stimulation after major amputation. J Bone Joint Surg Br 1988 Jan;70(1):109-12.

556. Lundeberg T, Kjartansson J, Samuelsson U. Effect of electrical nerve stimulation on healing of ischaemic skin flaps. Lancet 1988 Sep 24;2(8613):712-4.

557. Kjartansson J, Lundeberg T. Effects of electrical nerve stimulation (ENS) in ischemic tissue. Scand J Plast Reconstr Surg Hand Surg 1990;24(2):129-34.

558. Frantz RA. The effectiveness of transcutaneous electrical nerve stimulation (TENS) on decubitus ulcer healing in adult patients. In: Funk SG, Tornquist EM, Champagne MT, Copp LA, Wiese RA, editors. Key aspects of recovery: improving nutrition, rest, and mobility. New York: Springer; 1990. p. 197-205.

559. Lundeberg TC, Eriksson SV, Malm M. Electrical nerve stimulation improves healing of diabetic ulcers. Ann Plast Surg 1992 Oct;29(4):328-31.

560. Stefanovska A, Vodovnik L, Benko H, Turk R. Treatment of chronic wounds by means of electric and electromagnetic fields. Part 2. Value of FES parameters for pressure sore treatment. Med Biol Eng Comput 1993 May;31(3):213-20.

561. Itoh M, Montemayor JS Jr, Matsumoto E, Eason A, Lee MH, Folk FS. Accelerated wound healing of pressure ulcers by pulsed high peak power electromagnetic energy (Diapulse). Decubitus 1991 Feb;4(1):24-5, 29-34.

562. Tung S, Khaski A, Milano E, Kay C. The application of Diapulse in the treatment of decubitus ulcers: case reports. Contemp Surg 1995 Jul;47(1):27-32.

563. Wilson DH. Treatment of soft-tissue injuries by pulsed electrical energy. Br Med J 1972 Apr 29;2(808):269-70.

564. Goldin JH, Broadbent NR, Nancarrow JD, Marshall T. The effects of Diapulse on the healing of wounds: a double-blind randomised controlled trial in man. Br J Plast Surg 1981 Jul;34(3):267-70.

565. Jeran M, Zaffuto S, Moratti A, Bagnacani M, Cadossi R. PEMF stimulation of skin ulcers of venous origin in humans: preliminary report of a double blind study. J Bioelectr 1987;6(2):181-8.

566. Ieran M, Zaffuto S, Bagnacani M, Annovi M, Moratti A, Cadossi R. Effect of low frequency pulsing electromagnetic fields on skin ulcers of venous origin in humans: a double-blind study. J Orthop Res 1990 Mar;8(2):276-82.

567. Todd DJ, Heylings DJ, Allen GE, McMillin WP. Treatment of chronic varicose ulcers with pulsed electromagnetic fields: a controlled pilot study. Ir Med J 1991 Jun;84(2):54-5.

568. Stiller MJ, Pak GH, Shupack JL, Thaler S, Kenny C, Jondreau L. A portable pulsed electromagnetic field (PEMF) device to enhance healing of recalcitrant venous ulcers: a double-blind, placebo-controlled clinical trial. Br J Dermatol 1992 Aug;127(2):147-54.

569. Salzberg CA, Cooper-Vastola SA, Perez F, Viehbeck MG, Byrne DW. The effects of non-thermal pulsed electromagnetic energy on wound healing of pressure ulcers in spinal cord-injured patients: a randomized, double-blind study. Ostomy Wound Manage 1995 Apr;41(3):42-4, 46, 48 passim.

570. Cook AW, Oygar A, Baggenstos P, Pacheco S, Kleriga E. Vascular disease of extremities. Electric stimulation of spinal cord and posterior roots. N Y State J Med 1976 Mar;76(3):366-8.

571. Richardson RR, Cerullo LJ, Meyer PR. Autonomic hyper-reflexia modulated by percutaneous epidural neurostimulation: a preliminary report. Neurosurgery 1979 Jun;4(6):517-20.

572. Meglio M, Cioni B, Dal Lago A, De Santis M, Pola P, Serricchio M. Pain control and improvement of peripheral blood flow following epidural spinal cord stimulation: case report. J Neurosurg 1981 Jun;54(6):821-3.

573. Graber JN, Lifson A. The use of spinal cord stimulation for severe limb-threatening ischemia: a preliminary report. Ann Vasc Surg 1987 Dec;1(5):578-81.

574. Jivegård L, Augustinsson LE, Carlsson CA, Holm J. Long-term results by epidural spinal electrical stimulation (ESES) in patients with inoperable severe lower limb ischaemia. Eur J Vasc Surg 1987 Oct;1(5):345-9.

575. Jivegård LE, Augustinsson LE, Holm J, Risberg B, Ortenwall P. Effects of spinal cord stimulation (SCS) in patients with inoperable severe lower limb ischaemia: a prospective randomised controlled study. Eur J Vasc Endovasc Surg 1995 May;9(4):421-5.

576. [Electrical stimulation for wound healing]. Federal Research in Progress [database online]. Springfield (VA): National Technical Information Service; [cited 1995 Dec 14]. [36 references]. Available from Knight-Ridder Information, Inc., Mountain View, CA.

577. Katelaris PM, Fletcher JP, Little JM, McEntyre RJ, Jeffcoate KW. Electrical stimulation in the treatment of chronic venous ulceration. Aust N Z J Surg 1987 Sep;57(9):605-7.

578. Carley PJ, Wainapel SF. Electrotherapy for acceleration of wound healing: low intensity direct current. Arch Phys Med Rehabil 1985 Jul;66(7):443-6.

579. Akers TK, Gabrielson AL. The effect of high voltage galvanic stimulation on the rate of healing of decubitus ulcers. Biomed Sci Instrum 1984;20:99-100.

580. Gault WR, Gatens PF Jr. Use of low intensity direct current in management of ischemic skin ulcers. Phys Ther 1976 Mar;56(3):265-9.

581. Wolcott LE, Wheeler PC, Hardwicke HM, Rowley BA. Accelerated healing of skin ulcer by electrotherapy: preliminary clinical results. South Med J 1969 Jul;62(7):795-801.

582. Assimacopoulos D. Low intensity negative electric current in the treatment of ulcers of the leg due to chronic venous insufficiency. Preliminary report of three cases. Am J Surg 1968 May;115(5):683-7.

583. Fakhri O, Amin MA. The effect of low-voltage electric therapy on the healing of resistant skin burns. J Burn Care Rehabil 1987 Jan-Feb;8(1):15-8.

584. Wood JM, Evans PE 3rd, Schallreuter KU, Jacobson WE, Sufit R, Newman J, White C, Jacobson M. A multicenter study on the use of pulsed low-intensity direct current for healing chronic stage II and stage III decubitus ulcers. Arch Dermatol 1993 Aug;129(8):999-1009.

585. Fitzgerald GK, Newsome D. Treatment of a large infected thoracic spine wound using high voltage pulsed monophasic current. Phys Ther 1993 Jun;73(6):355-60.

586. Gogia PP, Marquez RR, Minerbo GM. Effects of high voltage galvanic stimulation on wound healing. Ostomy Wound Manage 1992 Jan-Feb;38(1):29-35.

587. Gentzkow GD, Pollack SV, Kloth LC, Stubbs HA. Improved healing of pressure ulcers using Dermapulse, a new electrical stimulation device. Wounds 1991 Sep-Oct;3(5):158-70.

588. Griffin JW, Tooms RE, Mendius RA, Clifft JK, Vander Zwaag R, el-Zeky F. Efficacy of high voltage pulsed current for healing of pressure ulcers in patients with spinal cord injury. Phys Ther 1991 Jun;71(6):433-42; discussion 442-4.

589. Feedar JA, Kloth LC, Gentzkow GD. Chronic dermal ulcer healing enhanced with monophasic pulsed electrical stimulation. Phys Ther 1991 Sep;71(9):639-49.

590. Mulder GD. Treatment of open-skin wounds with electric stimulation. Arch Phys Med Rehabil 1991 May;72(6):375-7.

591. Unger P, Eddy J, Raimastry S. A controlled study of the effect of high voltage pulse current (HVPC) on wound healing [abstract]. Phys Ther 1991 Jun;71(6 Suppl):S119.

592. Unger PG. A randomized clinical trial of the effect of HVPC on wound healing [abstract]. Phys Ther 1991 Jun;71 (6 Suppl):S118.

593. Kloth LC, Feedar JA. Acceleration of wound healing with high voltage, monophasic, pulsed current [published erratum appears in Phys Ther 1989 Aug;69(8):702]. Phys Ther 1988 Apr;68(4):503-8.

594. Feedar JA, Kloth LC. Acceleration of wound healing with high voltage pulsating direct current [abstract]. Phys Ther 1985 May;65(5):741.

595. Thurman BF, Christian EL. Response of a serious circulatory lesion to electrical stimulation. Phys Ther 1971 Oct;51(10):1107-10.

596. Ross CR, Segal D. High voltage galvanic stimulation: an aid to post-operative healing. Curr Podiatry 1981;30(5):19-25.

597. Weiss DS, Eaglstein WH, Falanga V. Exogenous electric current can reduce the formation of hypertrophic scars. J Dermatol Surg Oncol 1989 Dec;15(12):1272-5.

598. Mawson AR, Siddiqui FH, Connolly BJ, Sharp CJ, Stewart GW, Summer WR, Biundo JJ Jr. Effect of high voltage pulsed galvanic stimulation on sacral transcutaneous oxygen tension levels in the spinal cord injured. Paraplegia 1993 May;31(5):311-9.

599. Stefanovska A, Vodovnik L, Benko H, Turk R. Treatment of chronic wounds by means of electric and electromagnetic fields. Part 2. Value of FES parameters for pressure sore treatment. Med Biol Eng Comput 1993 May;31(3):213-20.

600. Lundeberg TC, Eriksson SV, Malm M. Electrical nerve stimulation improves healing of diabetic ulcers. Ann Plast Surg 1992 Oct;29(4):328-31.

601. Karba R, Vodovnik L, Presern-Strukelj M, Klesnik M. Promoted healing of chronic wounds due to electrical stimulation. Wounds 1991 Jan-Feb;3(1):16-23.

602. Frantz RA. The effectiveness of transcutaneous electrical nerve stimulation (TENS) on decubitus ulcer healing in adult patients. In: Funk SG, Tornquist EM, Champagne MT, Copp LA, Wiese RA, editors. Key aspects of recovery: improving nutrition, rest, and mobility. New York: Springer; 1990. p. 197-205.

603. Kaada B, Emru M. Promoted healing of leprous ulcers by transcutaneous nerve stimulation. Acupunct Electrother Res 1988;13(4):165-76.

604. Alon G, Azaria M, Stein H. Diabetic ulcer healing using high voltage TENS [abstract]. Phys Ther 1986 May;66(5):775.

605. Barron JJ, Jacobson WE, Tidd G. Treatment of decubitus ulcers. A new approach. Minn Med 1985 Feb;68(2):103-6.

606. Kaada B. Promoted healing of chronic ulceration by transcutaneous nerve stimulation (TNS). Vasa 1983;12(3):262-9.

607. Westerhof W, Bos JD. Trigeminal trophic syndrome: a successful treatment with transcutaneous electrical stimulation. Br J Dermatol 1983 May;108(5):601-4.

608. Lundeberg T, Kjartansson J, Samuelsson U. Effect of electrical nerve stimulation on healing of ischaemic skin flaps. Lancet 1988 Sep 24;2(8613):712-4.

609. Kjartansson J, Lundeberg T. Effects of electrical nerve stimulation (ENS) in ischemic tissue. Scand J Plast Reconstr Surg Hand Surg 1990;24(2):129-34.

610. Finsen V, Persen L, Lovlien M, Veslegaard EK, Simensen M, Gasvann AK, Benum P. Transcutaneous electrical nerve stimulation after major amputation. J Bone Joint Surg Br 1988 Jan;70(1):109-12.

611. Salzberg CA, Cooper-Vastola SA, Perez F, Viehbeck MG, Byrne DW. The effects of non-thermal pulsed electromagnetic energy on wound healing of pressure ulcers in spinal cord-injured patients: a randomized, double-blind study. Ostomy Wound Manage 1995 Apr;41(3):42-4, 46, 48 passim.

612. Tung S, Khaski A, Milano E, Kay C. The application of Diapulse in the treatment of decubitus ulcers: case reports. Contemp Surg 1995 Jul;47(1):27-32.

613. Stiller MJ, Pak GH, Shupack JL, Thaler S, Kenny C, Jondreau L. A portable pulsed electromagnetic field (PEMF) device to enhance healing of recalcitrant venous ulcers: a double-blind, placebo-controlled clinical trial. Br J Dermatol 1992 Aug;127(2):147-54.

614. Todd DJ, Heylings DJ, Allen GE, McMillin WP. Treatment of chronic varicose ulcers with pulsed electromagnetic fields: a controlled pilot study. Ir Med J 1991 Jun;84(2):54-5.

615. Itoh M, Montemayor JS Jr, Matsumoto E, Eason A, Lee MH, Folk FS. Accelerated wound healing of pressure ulcers by pulsed high peak power electromagnetic energy (Diapulse). Decubitus 1991 Feb;4(1):24-5, 29-34.

616. Ieran M, Zaffuto S, Bagnacani M, Annovi M, Moratti A, Cadossi R. Effect of low frequency pulsing electromagnetic fields on skin ulcers of venous origin in humans: a double-blind study. J Orthop Res 1990 Mar;8(2):276-82.

617. Jeran M, Zaffuto S, Moratti A, Bagnacani M, Cadossi R. PEMF stimulation of skin ulcers of venous origin in humans: preliminary report of a double blind study. J Bioelectr 1987;6(2):181-8.

618. Goldin JH, Broadbent NR, Nancarrow JD, Marshall T. The effects of Diapulse on the healing of wounds: a double-blind randomised controlled trial in man. Br J Plast Surg 1981 Jul;34(3):267-70.

619. Wilson DH. Treatment of soft-tissue injuries by pulsed electrical energy. Br Med J 1972 Apr 29;2(808):269-70.

620. Jivegård L, Augustinsson LE, Carlsson CA, Holm J. Long-term results by epidural spinal electrical stimulation (ESES) in patients with inoperable severe lower limb ischaemia. Eur J Vasc Surg 1987 Oct;1(5):345-9.

621. Graber JN, Lifson A. The use of spinal cord stimulation for severe limb-threatening ischemia: a preliminary report. Ann Vasc Surg 1987 Dec;1(5):578-81.

622. Meglio M, Cioni B, Dal Lago A, De Santis M, Pola P, Serricchio M. Pain control and improvement of peripheral blood flow following epidural spinal cord stimulation: case report. J Neurosurg 1981 Jun;54(6):821-3.

623. Richardson RR, Cerullo LJ, Meyer PR. Autonomic hyper-reflexia modulated by percutaneous epidural neurostimulation: a preliminary report. Neurosurgery 1979 Jun;4(6):517-20.

624. Cook AW, Oygar A, Baggenstos P, Pacheco S, Kleriga E. Vascular disease of extremities. Electric stimulation of spinal cord and posterior roots. N Y State J Med 1976 Mar;76(3):366-8.

625. Jivegård LE, Augustinsson LE, Holm J, Risberg B, Ortenwall P. Effects of spinal cord stimulation (SCS) in patients with inoperable severe lower limb ischaemia: a prospective randomised controlled study. Eur J Vasc Endovasc Surg 1995 May;9(4):421-5.

626. [Electrical stimulation for wound healing]. Federal Research in Progress [database online]. Springfield (VA): National Technical Information Service; [cited 1995 Dec 14]. [36 references]. Available from Knight-Ridder Information, Inc., Mountain View, CA.

627. Piérard GE, Piérard-Franchimont C. Planimetry of the healing rate of leg ulcers. Eur J Dermatol 1995 Apr-May;5(3):257-62.

628. Feedar JA, Kloth LC, Gentzkow GD. Chronic dermal ulcer healing enhanced with monophasic pulsed electrical stimulation. Phys Ther 1991 Sep;71(9):639-49.

629. Griffin JW, Tooms RE, Mendius RA, Clifft JK, Vander Zwaag R, el-Zeky F. Efficacy of high voltage pulsed current for healing of pressure ulcers in patients with spinal cord injury. Phys Ther 1991 Jun;71(6):433-42; discussion 442-4.

630. Gentzkow GD, Pollack SV, Kloth LC, Stubbs HA. Improved healing of pressure ulcers using Dermapulse, a new electrical stimulation device. Wounds 1991 Sep-Oct;3(5):158-70.

631. Gogia PP, Marquez RR, Minerbo GM. Effects of high voltage galvanic stimulation on wound healing. Ostomy Wound Manage 1992 Jan-Feb;38(1):29-35.

632. Wood JM, Evans PE 3rd, Schallreuter KU, Jacobson WE, Sufit R, Newman J, White C, Jacobson M. A multicenter study on the use of pulsed low-intensity direct current for healing chronic stage II and stage III decubitus ulcers. Arch Dermatol 1993 Aug;129(8):999-1009.

633. Karba R, Vodovnik L, Presern-Strukelj M, Klesnik M. Promoted healing of chronic wounds due to electrical stimulation. Wounds 1991 Jan-Feb;3(1):16-23.

634. Kaada B, Emru M. Promoted healing of leprous ulcers by transcutaneous nerve stimulation. Acupunct Electrother Res 1988;13(4):165-76.

635. Karba R, Vodovnik L, Presern-Strukelj M, Klesnik M. Promoted healing of chronic wounds due to electrical stimulation. Wounds 1991 Jan-Feb;3(1):16-23.

636. Stefanovska A, Vodovnik L, Benko H, Turk R. Treatment of chronic wounds by means of electric and electromagnetic fields. Part 2. Value of FES parameters for pressure sore treatment. Med Biol Eng Comput 1993 May;31(3):213-20.

637. Wood JM, Evans PE 3rd, Schallreuter KU, Jacobson WE, Sufit R, Newman J, White C, Jacobson M. A multicenter study on the use of pulsed low-intensity direct current for healing chronic stage II and stage III decubitus ulcers. Arch Dermatol 1993 Aug;129(8):999-1009.

638. Feedar JA, Kloth LC, Gentzkow GD. Chronic dermal ulcer healing enhanced with monophasic pulsed electrical stimulation. Phys Ther 1991 Sep;71(9):639-49.

639. Katelaris PM, Fletcher JP, Little JM, McEntyre RJ, Jeffcoate KW. Electrical stimulation in the treatment of chronic venous ulceration. Aust N Z J Surg 1987 Sep;57(9):605-7.

640. Carley PJ, Wainapel SF. Electrotherapy for acceleration of wound healing: low intensity direct current. Arch Phys Med Rehabil 1985 Jul;66(7):443-6.

641. Gogia PP, Marquez RR, Minerbo GM. Effects of high voltage galvanic stimulation on wound healing. Ostomy Wound Manage 1992 Jan-Feb;38(1):29-35.

642. Gentzkow GD, Pollack SV, Kloth LC, Stubbs HA. Improved healing of pressure ulcers using Dermapulse, a new electrical stimulation device. Wounds 1991 Sep-Oct;3(5):158-70.

643. Griffin JW, Tooms RE, Mendius RA, Clifft JK, Vander Zwaag R, el-Zeky F. Efficacy of high voltage pulsed current for healing of pressure ulcers in patients with spinal cord injury. Phys Ther 1991 Jun;71(6):433-42; discussion 442-4.

644. Feedar JA, Kloth LC, Gentzkow GD. Chronic dermal ulcer healing enhanced with monophasic pulsed electrical stimulation. Phys Ther 1991 Sep;71(9):639-49.

645. Stefanovska A, Vodovnik L, Benko H, Turk R. Treatment of chronic wounds by means of electric and electromagnetic fields. Part 2. Value of FES parameters for pressure sore treatment. Med Biol Eng Comput 1993 May;31(3):213-20.

646. Lundeberg TC, Eriksson SV, Malm M. Electrical nerve stimulation improves healing of diabetic ulcers. Ann Plast Surg 1992 Oct;29(4):328-31.

647. Itoh M, Montemayor JS Jr, Matsumoto E, Eason A, Lee MH, Folk FS. Accelerated wound healing of pressure ulcers by pulsed high peak power electromagnetic energy (Diapulse). Decubitus 1991 Feb;4(1):24-5, 29-34.

648. Todd DJ, Heylings DJ, Allen GE, McMillin WP. Treatment of chronic varicose ulcers with pulsed electromagnetic fields: a controlled pilot study. Ir Med J 1991 Jun;84(2):54-5.

649. Salzberg CA, Cooper-Vastola SA, Perez F, Viehbeck MG, Byrne DW. The effects of non-thermal pulsed electromagnetic energy on wound healing of pressure ulcers in spinal cord-injured patients: a randomized, double-blind study. Ostomy Wound Manage 1995 Apr;41(3):42-4, 46, 48 passim.

650. Stiller MJ, Pak GH, Shupack JL, Thaler S, Kenny C, Jondreau L. A portable pulsed electromagnetic field (PEMF) device to enhance healing of recalcitrant venous ulcers: a double-blind, placebo-controlled clinical trial. Br J Dermatol 1992 Aug;127(2):147-54.

651. Hedges LV, Olkin I. Statistical methods for meta-analysis. Boston: Academic Press; 1985. 369 p.

652. Hedges LV, Olkin I. Statistical methods for meta-analysis. Boston: Academic Press; 1985. 369 p.

653. Hedges LV, Olkin I. Statistical methods for meta-analysis. Boston: Academic Press; 1985. 369 p.

654. Petitti DB. Meta-analysis, decision analysis, and cost-effectiveness analysis: methods for quantitative synthesis in medicine. New York: Oxford University Press; 1994. Chapter 8, Other statistical issues in meta-analysis; p. 115-30. (Monographs in epidemiology and biostatistices; vol. 24).

655. Hedges LV, Olkin I. Statistical methods for meta-analysis. Boston: Academic Press; 1985. 369 p.

656. Fleiss JL, Gross AJ. Meta-analysis in epidemiology, with special reference to studies of the association between exposure to environmental tobacco smoke and lung cancer: a critique. J Clin Epidemiol 1991;44(2):127-39.

657. Bailey KR. Inter-study differences: how should they influence the interpretation and analysis of results? Stat Med 1987 Apr-May;6(3):351-60.

658. Demets DL. Methods for combining randomized clinical trials: strengths and limitations. Stat Med 1987 Apr-May;6(3):341-50.

659. Katelaris PM, Fletcher JP, Little JM, McEntyre RJ, Jeffcoate KW. Electrical stimulation in the treatment of chronic venous ulceration. Aust N Z J Surg 1987 Sep;57(9):605-7.

660. Gentzkow GD, Pollack SV, Kloth LC, Stubbs HA. Improved healing of pressure ulcers using Dermapulse, a new electrical stimulation device. Wounds 1991 Sep-Oct;3(5):158-70.

661. Salzberg CA, Cooper-Vastola SA, Perez F, Viehbeck MG, Byrne DW. The effects of non-thermal pulsed electromagnetic energy on wound healing of pressure ulcers in spinal cord-injured patients: a randomized, double-blind study. Ostomy Wound Manage 1995 Apr;41(3):42-4, 46, 48 passim.

662. Rosenthal R. Meta-analytic procedures for social research. Rev. ed. Newbury Park (CA): Sage Publications; 1991. Chapter 4, Comparing and combining research results; p. 59-88. (Applied social research methods series; vol. 6).

663. Salzberg CA, Cooper-Vastola SA, Perez F, Viehbeck MG, Byrne DW. The effects of non-thermal pulsed electromagnetic energy on wound healing of pressure ulcers in spinal cord-injured patients: a randomized, double-blind study. Ostomy Wound Manage 1995 Apr;41(3):42-4, 46, 48 passim.

664. Kloth LC, Feedar JA. Acceleration of wound healing with high voltage, monophasic, pulsed current [published erratum appears in Phys Ther 1989 Aug;69(8):702]. Phys Ther 1988 Apr;68(4):503-8.

665. Wood JM, Evans PE 3rd, Schallreuter KU, Jacobson WE, Sufit R, Newman J, White C, Jacobson M. A multicenter study on the use of pulsed low-intensity direct current for healing chronic stage II and stage III decubitus ulcers. Arch Dermatol 1993 Aug;129(8):999-1009.

666. Kloth LC, Feedar JA. Acceleration of wound healing with high voltage, monophasic, pulsed current [published erratum appears in Phys Ther 1989 Aug;69(8):702]. Phys Ther 1988 Apr;68(4):503-8.

667. Rosenthal R. Meta-analytic procedures for social research. Rev. ed. Newbury Park (CA): Sage Publications; 1991. Chapter 5, Combining probabilities; p. 89-109. (Applied social research methods series; vol. 6).

668. Orwin RG. A fail-safe N for effect size in meta-analysis. J Educ Stat 1983 Summer;8(2):157-9.

669. Hedges LV, Olkin I. Statistical methods for meta-analysis. Boston: Academic Press; 1985. 369 p.

670. Wood JM, Evans PE 3rd, Schallreuter KU, Jacobson WE, Sufit R, Newman J, White C, Jacobson M. A multicenter study on the use of pulsed low-intensity direct current for healing chronic stage II and stage III decubitus ulcers. Arch Dermatol 1993 Aug;129(8):999-1009.

671. Feedar JA, Kloth LC, Gentzkow GD. Chronic dermal ulcer healing enhanced with monophasic pulsed electrical stimulation. Phys Ther 1991 Sep;71(9):639-49.

672. Katelaris PM, Fletcher JP, Little JM, McEntyre RJ, Jeffcoate KW. Electrical stimulation in the treatment of chronic venous ulceration. Aust N Z J Surg 1987 Sep;57(9):605-7.

673. Carley PJ, Wainapel SF. Electrotherapy for acceleration of wound healing: low intensity direct current. Arch Phys Med Rehabil 1985 Jul;66(7):443-6.

674. Akers TK, Gabrielson AL. The effect of high voltage galvanic stimulation on the rate of healing of decubitus ulcers. Biomed Sci Instrum 1984;20:99-100.

675. Gault WR, Gatens PF Jr. Use of low intensity direct current in management of ischemic skin ulcers. Phys Ther 1976 Mar;56(3):265-9.

676. Wolcott LE, Wheeler PC, Hardwicke HM, Rowley BA. Accelerated healing of skin ulcer by electrotherapy: preliminary clinical results. South Med J 1969 Jul;62(7):795-801.

677. Wood JM, Evans PE 3rd, Schallreuter KU, Jacobson WE, Sufit R, Newman J, White C, Jacobson M. A multicenter study on the use of pulsed low-intensity direct current for healing chronic stage II and stage III decubitus ulcers. Arch Dermatol 1993 Aug;129(8):999-1009.

678. Gogia PP, Marquez RR, Minerbo GM. Effects of high voltage galvanic stimulation on wound healing. Ostomy Wound Manage 1992 Jan-Feb;38(1):29-35.

679. Gentzkow GD, Pollack SV, Kloth LC, Stubbs HA. Improved healing of pressure ulcers using Dermapulse, a new electrical stimulation device. Wounds 1991 Sep-Oct;3(5):158-70.

680. Griffin JW, Tooms RE, Mendius RA, Clifft JK, Vander Zwaag R, el-Zeky F. Efficacy of high voltage pulsed current for healing of pressure ulcers in patients with spinal cord injury. Phys Ther 1991 Jun;71(6):433-42; discussion 442-4.

681. Feedar JA, Kloth LC, Gentzkow GD. Chronic dermal ulcer healing enhanced with monophasic pulsed electrical stimulation. Phys Ther 1991 Sep;71(9):639-49.

682. Unger P, Eddy J, Raimastry S. A controlled study of the effect of high voltage pulse current (HVPC) on wound healing [abstract]. Phys Ther 1991 Jun;71(6 Suppl):S119.

683. Unger PG. A randomized clinical trial of the effect of HVPC on wound healing [abstract]. Phys Ther 1991 Jun;71 (6 Suppl):S118.

684. Kloth LC, Feedar JA. Acceleration of wound healing with high voltage, monophasic, pulsed current [published erratum appears in Phys Ther 1989 Aug;69(8):702]. Phys Ther 1988 Apr;68(4):503-8.

685. Feedar JA, Kloth LC. Acceleration of wound healing with high voltage pulsating direct current [abstract]. Phys Ther 1985 May;65(5):741.

686. Mulder GD. Treatment of open-skin wounds with electric stimulation. Arch Phys Med Rehabil 1991 May;72(6):375-7.

687. Stefanovska A, Vodovnik L, Benko H, Turk R. Treatment of chronic wounds by means of electric and electromagnetic fields. Part 2. Value of FES parameters for pressure sore treatment. Med Biol Eng Comput 1993 May;31(3):213-20.

688. Lundeberg TC, Eriksson SV, Malm M. Electrical nerve stimulation improves healing of diabetic ulcers. Ann Plast Surg 1992 Oct;29(4):328-31.

689. Karba R, Vodovnik L, Presern-Strukelj M, Klesnik M. Promoted healing of chronic wounds due to electrical stimulation. Wounds 1991 Jan-Feb;3(1):16-23.

690. Frantz RA. The effectiveness of transcutaneous electrical nerve stimulation (TENS) on decubitus ulcer healing in adult patients. In: Funk SG, Tornquist EM, Champagne MT, Copp LA, Wiese RA, editors. Key aspects of recovery: improving nutrition, rest, and mobility. New York: Springer; 1990. p. 197-205.

691. Kaada B, Emru M. Promoted healing of leprous ulcers by transcutaneous nerve stimulation. Acupunct Electrother Res 1988;13(4):165-76.

692. Alon G, Azaria M, Stein H. Diabetic ulcer healing using high voltage TENS [abstract]. Phys Ther 1986 May;66(5):775.

693. Barron JJ, Jacobson WE, Tidd G. Treatment of decubitus ulcers. A new approach. Minn Med 1985 Feb;68(2):103-6.

694. Salzberg CA, Cooper-Vastola SA, Perez F, Viehbeck MG, Byrne DW. The effects of non-thermal pulsed electromagnetic energy on wound healing of pressure ulcers in spinal cord-injured patients: a randomized, double-blind study. Ostomy Wound Manage 1995 Apr;41(3):42-4, 46, 48 passim.

695. Stiller MJ, Pak GH, Shupack JL, Thaler S, Kenny C, Jondreau L. A portable pulsed electromagnetic field (PEMF) device to enhance healing of recalcitrant venous ulcers: a double-blind, placebo-controlled clinical trial. Br J Dermatol 1992 Aug;127(2):147-54.

696. Todd DJ, Heylings DJ, Allen GE, McMillin WP. Treatment of chronic varicose ulcers with pulsed electromagnetic fields: a controlled pilot study. Ir Med J 1991 Jun;84(2):54-5.

697. Itoh M, Montemayor JS Jr, Matsumoto E, Eason A, Lee MH, Folk FS. Accelerated wound healing of pressure ulcers by pulsed high peak power electromagnetic energy (Diapulse). Decubitus 1991 Feb;4(1):24-5, 29-34.

698. Ieran M, Zaffuto S, Bagnacani M, Annovi M, Moratti A, Cadossi R. Effect of low frequency pulsing electromagnetic fields on skin ulcers of venous origin in humans: a double-blind study. J Orthop Res 1990 Mar;8(2):276-82.

699. Jeran M, Zaffuto S, Moratti A, Bagnacani M, Cadossi R. PEMF stimulation of skin ulcers of venous origin in humans: preliminary report of a double blind study. J Bioelectr 1987;6(2):181-8.

700. Katelaris PM, Fletcher JP, Little JM, McEntyre RJ, Jeffcoate KW. Electrical stimulation in the treatment of chronic venous ulceration. Aust N Z J Surg 1987 Sep;57(9):605-7.

701. Stiller MJ, Pak GH, Shupack JL, Thaler S, Kenny C, Jondreau L. A portable pulsed electromagnetic field (PEMF) device to enhance healing of recalcitrant venous ulcers: a double-blind, placebo-controlled clinical trial. Br J Dermatol 1992 Aug;127(2):147-54.

702. Todd DJ, Heylings DJ, Allen GE, McMillin WP. Treatment of chronic varicose ulcers with pulsed electromagnetic fields: a controlled pilot study. Ir Med J 1991 Jun;84(2):54-5.

703. Ieran M, Zaffuto S, Bagnacani M, Annovi M, Moratti A, Cadossi R. Effect of low frequency pulsing electromagnetic fields on skin ulcers of venous origin in humans: a double-blind study. J Orthop Res 1990 Mar;8(2):276-82.

704. Jeran M, Zaffuto S, Moratti A, Bagnacani M, Cadossi R. PEMF stimulation of skin ulcers of venous origin in humans: preliminary report of a double blind study. J Bioelectr 1987;6(2):181-8.

705. Akers TK, Gabrielson AL. The effect of high voltage galvanic stimulation on the rate of healing of decubitus ulcers. Biomed Sci Instrum 1984;20:99-100.

706. Stefanovska A, Vodovnik L, Benko H, Turk R. Treatment of chronic wounds by means of electric and electromagnetic fields. Part 2. Value of FES parameters for pressure sore treatment. Med Biol Eng Comput 1993 May;31(3):213-20.

707. Wood JM, Evans PE 3rd, Schallreuter KU, Jacobson WE, Sufit R, Newman J, White C, Jacobson M. A multicenter study on the use of pulsed low-intensity direct current for healing chronic stage II and stage III decubitus ulcers. Arch Dermatol 1993 Aug;129(8):999-1009.

708. Gentzkow GD, Pollack SV, Kloth LC, Stubbs HA. Improved healing of pressure ulcers using Dermapulse, a new electrical stimulation device. Wounds 1991 Sep-Oct;3(5):158-70.

709. Griffin JW, Tooms RE, Mendius RA, Clifft JK, Vander Zwaag R, el-Zeky F. Efficacy of high voltage pulsed current for healing of pressure ulcers in patients with spinal cord injury. Phys Ther 1991 Jun;71(6):433-42; discussion 442-4.

710. Unger P, Eddy J, Raimastry S. A controlled study of the effect of high voltage pulse current (HVPC) on wound healing [abstract]. Phys Ther 1991 Jun;71(6 Suppl):S119.

711. Kloth LC, Feedar JA. Acceleration of wound healing with high voltage, monophasic, pulsed current [published erratum appears in Phys Ther 1989 Aug;69(8):702]. Phys Ther 1988 Apr;68(4):503-8.

712. Feedar JA, Kloth LC. Acceleration of wound healing with high voltage pulsating direct current [abstract]. Phys Ther 1985 May;65(5):741.

713. Stefanovska A, Vodovnik L, Benko H, Turk R. Treatment of chronic wounds by means of electric and electromagnetic fields. Part 2. Value of FES parameters for pressure sore treatment. Med Biol Eng Comput 1993 May;31(3):213-20.

714. Salzberg CA, Cooper-Vastola SA, Perez F, Viehbeck MG, Byrne DW. The effects of non-thermal pulsed electromagnetic energy on wound healing of pressure ulcers in spinal cord-injured patients: a randomized, double-blind study. Ostomy Wound Manage 1995 Apr;41(3):42-4, 46, 48 passim.

715. Lundeberg TC, Eriksson SV, Malm M. Electrical nerve stimulation improves healing of diabetic ulcers. Ann Plast Surg 1992 Oct;29(4):328-31.

716. Carley PJ, Wainapel SF. Electrotherapy for acceleration of wound healing: low intensity direct current. Arch Phys Med Rehabil 1985 Jul;66(7):443-6.

717. Gault WR, Gatens PF Jr. Use of low intensity direct current in management of ischemic skin ulcers. Phys Ther 1976 Mar;56(3):265-9.

718. Wolcott LE, Wheeler PC, Hardwicke HM, Rowley BA. Accelerated healing of skin ulcer by electrotherapy: preliminary clinical results. South Med J 1969 Jul;62(7):795-801.

719. Gogia PP, Marquez RR, Minerbo GM. Effects of high voltage galvanic stimulation on wound healing. Ostomy Wound Manage 1992 Jan-Feb;38(1):29-35.

720. Feedar JA, Kloth LC, Gentzkow GD. Chronic dermal ulcer healing enhanced with monophasic pulsed electrical stimulation. Phys Ther 1991 Sep;71(9):639-49.

721. Katelaris PM, Fletcher JP, Little JM, McEntyre RJ, Jeffcoate KW. Electrical stimulation in the treatment of chronic venous ulceration. Aust N Z J Surg 1987 Sep;57(9):605-7.

722. Kloth LC, Feedar JA. Acceleration of wound healing with high voltage, monophasic, pulsed current [published erratum appears in Phys Ther 1989 Aug;69(8):702]. Phys Ther 1988 Apr;68(4):503-8.

723. Gentzkow GD, Pollack SV, Kloth LC, Stubbs HA. Improved healing of pressure ulcers using Dermapulse, a new electrical stimulation device. Wounds 1991 Sep-Oct;3(5):158-70.

724. Griffin JW, Tooms RE, Mendius RA, Clifft JK, Vander Zwaag R, el-Zeky F. Efficacy of high voltage pulsed current for healing of pressure ulcers in patients with spinal cord injury. Phys Ther 1991 Jun;71(6):433-42; discussion 442-4.

725. Lundeberg TC, Eriksson SV, Malm M. Electrical nerve stimulation improves healing of diabetic ulcers. Ann Plast Surg 1992 Oct;29(4):328-31.

726. Stiller MJ, Pak GH, Shupack JL, Thaler S, Kenny C, Jondreau L. A portable pulsed electromagnetic field (PEMF) device to enhance healing of recalcitrant venous ulcers: a double-blind, placebo-controlled clinical trial. Br J Dermatol 1992 Aug;127(2):147-54.

727. Stefanovska A, Vodovnik L, Benko H, Turk R. Treatment of chronic wounds by means of electric and electromagnetic fields. Part 2. Value of FES parameters for pressure sore treatment. Med Biol Eng Comput 1993 May;31(3):213-20.

728. Wood JM, Evans PE 3rd, Schallreuter KU, Jacobson WE, Sufit R, Newman J, White C, Jacobson M. A multicenter study on the use of pulsed low-intensity direct current for healing chronic stage II and stage III decubitus ulcers. Arch Dermatol 1993 Aug;129(8):999-1009.

729. Salzberg CA, Cooper-Vastola SA, Perez F, Viehbeck MG, Byrne DW. The effects of non-thermal pulsed electromagnetic energy on wound healing of pressure ulcers in spinal cord-injured patients: a randomized, double-blind study. Ostomy Wound Manage 1995 Apr;41(3):42-4, 46, 48 passim.

730. Rosenthal R. Meta-analytic procedures for social research. Rev. ed. Newbury Park (CA): Sage Publications; 1991. Chapter 2, Defining research results; p. 13-35. (Applied social research methods series; vol. 6).

731. Katelaris PM, Fletcher JP, Little JM, McEntyre RJ, Jeffcoate KW. Electrical stimulation in the treatment of chronic venous ulceration. Aust N Z J Surg 1987 Sep;57(9):605-7.

732. Kloth LC, Feedar JA. Acceleration of wound healing with high voltage, monophasic, pulsed current [published erratum appears in Phys Ther 1989 Aug;69(8):702]. Phys Ther 1988 Apr;68(4):503-8.

733. Ieran M, Zaffuto S, Bagnacani M, Annovi M, Moratti A, Cadossi R. Effect of low frequency pulsing electromagnetic fields on skin ulcers of venous origin in humans: a double-blind study. J Orthop Res 1990 Mar;8(2):276-82.

734. Griffin JW, Tooms RE, Mendius RA, Clifft JK, Vander Zwaag R, el-Zeky F. Efficacy of high voltage pulsed current for healing of pressure ulcers in patients with spinal cord injury. Phys Ther 1991 Jun;71(6):433-42; discussion 442-4.

735. Todd DJ, Heylings DJ, Allen GE, McMillin WP. Treatment of chronic varicose ulcers with pulsed electromagnetic fields: a controlled pilot study. Ir Med J 1991 Jun;84(2):54-5.

736. Unger P, Eddy J, Raimastry S. A controlled study of the effect of high voltage pulse current (HVPC) on wound healing [abstract]. Phys Ther 1991 Jun;71(6 Suppl):S119.

737. Lundeberg TC, Eriksson SV, Malm M. Electrical nerve stimulation improves healing of diabetic ulcers. Ann Plast Surg 1992 Oct;29(4):328-31.

738. Wood JM, Evans PE 3rd, Schallreuter KU, Jacobson WE, Sufit R, Newman J, White C, Jacobson M. A multicenter study on the use of pulsed low-intensity direct current for healing chronic stage II and stage III decubitus ulcers. Arch Dermatol 1993 Aug;129(8):999-1009.

739. Salzberg CA, Cooper-Vastola SA, Perez F, Viehbeck MG, Byrne DW. The effects of non-thermal pulsed electromagnetic energy on wound healing of pressure ulcers in spinal cord-injured patients: a randomized, double-blind study. Ostomy Wound Manage 1995 Apr;41(3):42-4, 46, 48 passim.

740. Rosenthal R. Meta-analytic procedures for social research. Rev. ed. Newbury Park (CA): Sage Publications; 1991. Chapter 2, Defining research results; p. 13-35. (Applied social research methods series; vol. 6).

741. Rosenthal R. Meta-analytic procedures for social research. Rev. ed. Newbury Park (CA): Sage Publications; 1991. Chapter 2, Defining research results; p. 13-35. (Applied social research methods series; vol. 6).

742. Stiller MJ, Pak GH, Shupack JL, Thaler S, Kenny C, Jondreau L. A portable pulsed electromagnetic field (PEMF) device to enhance healing of recalcitrant venous ulcers: a double-blind, placebo-controlled clinical trial. Br J Dermatol 1992 Aug;127(2):147-54.

743. Todd DJ, Heylings DJ, Allen GE, McMillin WP. Treatment of chronic varicose ulcers with pulsed electromagnetic fields: a controlled pilot study. Ir Med J 1991 Jun;84(2):54-5.

744. Ieran M, Zaffuto S, Bagnacani M, Annovi M, Moratti A, Cadossi R. Effect of low frequency pulsing electromagnetic fields on skin ulcers of venous origin in humans: a double-blind study. J Orthop Res 1990 Mar;8(2):276-82.

745. Jeran M, Zaffuto S, Moratti A, Bagnacani M, Cadossi R. PEMF stimulation of skin ulcers of venous origin in humans: preliminary report of a double blind study. J Bioelectr 1987;6(2):181-8.

746. Stiller MJ, Pak GH, Shupack JL, Thaler S, Kenny C, Jondreau L. A portable pulsed electromagnetic field (PEMF) device to enhance healing of recalcitrant venous ulcers: a double-blind, placebo-controlled clinical trial. Br J Dermatol 1992 Aug;127(2):147-54.

747. Todd DJ, Heylings DJ, Allen GE, McMillin WP. Treatment of chronic varicose ulcers with pulsed electromagnetic fields: a controlled pilot study. Ir Med J 1991 Jun;84(2):54-5.

748. Ieran M, Zaffuto S, Bagnacani M, Annovi M, Moratti A, Cadossi R. Effect of low frequency pulsing electromagnetic fields on skin ulcers of venous origin in humans: a double-blind study. J Orthop Res 1990 Mar;8(2):276-82.

749. Wood JM, Evans PE 3rd, Schallreuter KU, Jacobson WE, Sufit R, Newman J, White C, Jacobson M. A multicenter study on the use of pulsed low-intensity direct current for healing chronic stage II and stage III decubitus ulcers. Arch Dermatol 1993 Aug;129(8):999-1009.

750. Stefanovska A, Vodovnik L, Benko H, Turk R. Treatment of chronic wounds by means of electric and electromagnetic fields. Part 2. Value of FES parameters for pressure sore treatment. Med Biol Eng Comput 1993 May;31(3):213-20.

751. Gentzkow GD, Pollack SV, Kloth LC, Stubbs HA. Improved healing of pressure ulcers using Dermapulse, a new electrical stimulation device. Wounds 1991 Sep-Oct;3(5):158-70.

752. Griffin JW, Tooms RE, Mendius RA, Clifft JK, Vander Zwaag R, el-Zeky F. Efficacy of high voltage pulsed current for healing of pressure ulcers in patients with spinal cord injury. Phys Ther 1991 Jun;71(6):433-42; discussion 442-4.

753. Kloth LC, Feedar JA. Acceleration of wound healing with high voltage, monophasic, pulsed current [published erratum appears in Phys Ther 1989 Aug;69(8):702]. Phys Ther 1988 Apr;68(4):503-8.

754. Salzberg CA, Cooper-Vastola SA, Perez F, Viehbeck MG, Byrne DW. The effects of non-thermal pulsed electromagnetic energy on wound healing of pressure ulcers in spinal cord-injured patients: a randomized, double-blind study. Ostomy Wound Manage 1995 Apr;41(3):42-4, 46, 48 passim.

755. Unger P, Eddy J, Raimastry S. A controlled study of the effect of high voltage pulse current (HVPC) on wound healing [abstract]. Phys Ther 1991 Jun;71(6 Suppl):S119.

756. Feedar JA, Kloth LC. Acceleration of wound healing with high voltage pulsating direct current [abstract]. Phys Ther 1985 May;65(5):741.

757. Wood JM, Evans PE 3rd, Schallreuter KU, Jacobson WE, Sufit R, Newman J, White C, Jacobson M. A multicenter study on the use of pulsed low-intensity direct current for healing chronic stage II and stage III decubitus ulcers. Arch Dermatol 1993 Aug;129(8):999-1009.

758. Stefanovska A, Vodovnik L, Benko H, Turk R. Treatment of chronic wounds by means of electric and electromagnetic fields. Part 2. Value of FES parameters for pressure sore treatment. Med Biol Eng Comput 1993 May;31(3):213-20.

759. Gentzkow GD, Pollack SV, Kloth LC, Stubbs HA. Improved healing of pressure ulcers using Dermapulse, a new electrical stimulation device. Wounds 1991 Sep-Oct;3(5):158-70.

760. Griffin JW, Tooms RE, Mendius RA, Clifft JK, Vander Zwaag R, el-Zeky F. Efficacy of high voltage pulsed current for healing of pressure ulcers in patients with spinal cord injury. Phys Ther 1991 Jun;71(6):433-42; discussion 442-4.

761. Kloth LC, Feedar JA. Acceleration of wound healing with high voltage, monophasic, pulsed current [published erratum appears in Phys Ther 1989 Aug;69(8):702]. Phys Ther 1988 Apr;68(4):503-8.

762. Salzberg CA, Cooper-Vastola SA, Perez F, Viehbeck MG, Byrne DW. The effects of non-thermal pulsed electromagnetic energy on wound healing of pressure ulcers in spinal cord-injured patients: a randomized, double-blind study. Ostomy Wound Manage 1995 Apr;41(3):42-4, 46, 48 passim.

763. Bowszyc J, Bowszyc-Dmochowska M, Kazmierowski M, Ben-Amer HM, Garbowska T, Harding E. Comparison of two dressings in the treatment of venous leg ulcers. J Wound Care 1995 Mar;4(3):106-10.

764. Ohlsson P, Larsson K, Lindholm C, Moller M. A cost-effectiveness study of leg ulcer treatment in primary care. Comparison of saline-gauze and hydrocolloid treatment in a prospective, randomized study. Scand J Prim Health Care 1994 Dec;12(4):295-9.

765. Werner-Schlenzka H, Kuhlmann RK. Treatment of venous leg ulcers with topical iloprost: a placebo controlled study. Vasa 1994;23(2):145-50.

766. Greguric S, Budimcic D, Soldo-Belic A, Tudoric M, Baricevic B, Cajkovac V, Dobric I. Hydrocolloid dressing versus a conventional dressing using magnesium sulphate paste in the management of venous leg ulcers. Acta Derm Venereol 1994;2(2):65-71.

767. Smith BA. The dressing makes the difference. Trial of two modern dressings on venous ulcers. Prof Nurse 1994 Feb;9(5):348, 350-2.

768. Arnold TE, Stanley JC, Fellows EP, Moncada GA, Allen R, Hutchinson JJ, Swartz WM, Bolton LL, Vickers CF, Kerstein MD. Prospective, multicenter study of managing lower extremity venous ulcers. Ann Vasc Surg 1994 Jul;8(4):356-62.

769. McCulloch JM, Marler KC, Neal MB, Phifer TJ. Intermittent pneumatic compression improves venous ulcer healing. Adv Wound Care 1994 Jul;7(4):22-4, 26.

770. Layton AM, Ibbotson SH, Davies JA, Goodfield MJ. Randomised trial of oral aspirin for chronic venous leg ulcers. Lancet 1994 Jul 16;344(8916):164-5.

771. Huovinen S, Kotilainen P, Jarvinen H, Malanin K, Sarna S, Helander I, Huovinen P. Comparison of ciprofloxacin or trimethoprim therapy for venous leg ulcers: results of a pilot study. J Am Acad Dermatol 1994 Aug;31(2 Pt 1):279-81.

772. Nikolova K. Treatment of post-phlebitic syndrome and venous leg ulcers with flunarizine. Methods Find Exp Clin Pharmacol 1994 Oct;16(8):609-13.

773. Teepe RG, Roseeuw DI, Hermans J, Koebrugge EJ, Altena T, de Coninck A, Ponec M, Vermeer BJ. Randomized trial comparing cryopreserved cultured epidermal allografts with hydrocolloid dressings in healing chronic venous ulcers. J Am Acad Dermatol 1993 Dec;29(6):982-8.

774. Cordts PR, Hanrahan LM, Rodriguez AA, Woodson J, LaMorte WW, Menzoian JO. A prospective, randomized trial of Unna's boot versus Duoderm CGF hydroactive dressing plus compression in the management of venous leg ulcers. J Vasc Surg 1992 Mar;15(3):480-6.

775. Barbarino C. Pentoxifylline in the treatment of venous leg ulcers. Curr Med Res Opin 1992;12(9):547-51.

776. Davis LB, McCulloch JM, Neal MB. The effectiveness of Unna Boot and semipermeable film vs. Unna Boot alone in the healing of venous ulcers. A pilot report. Ostomy Wound Manage 1992 Jan-Feb;38(1):19-21.

777. Bishop JB, Phillips LG, Mustoe TA, VanderZee AJ, Wiersema L, Roach DE, Heggers JP, Hill DP Jr, Taylor EL, Robson MC. A prospective randomized evaluator-blinded trial of two potential wound healing agents for the treatment of venous stasis ulcers. J Vasc Surg 1992 Aug;16(2):251-7.

778. Brandrup F, Menné T, Ågren MS, Strömberg HE, Holst R, Frisén M. A randomized trial of two occlusive dressings in the treatment of leg ulcers. Acta Derm Venereol 1990;70(3):231-5.

779. Colgan MP, Dormandy JA, Jones PW, Schraibman IG, Shanik DG, Young RA. Oxpentifylline treatment of venous ulcers of the leg. BMJ 1990 Apr 14;300(6730):972-5.

780. Rubin JR, Alexander J, Plecha EJ, Marman C. Unna's boot vs polyurethane foam dressings for the treatment of venous ulceration. A randomized prospective study. Arch Surg 1990 Apr;125(4):489-90.

781. Queral LA, Criado FJ, Lilly MP, Rudolphi D. The role of sclerotherapy as an adjunct to Unna's boot for treating venous ulcers: a prospective study. J Vasc Surg 1990 Apr;11(4):572-5.

782. Smith PC, Sarin S, Hasty J, Scurr JH. Sequential gradient pneumatic compression enhances venous ulcer healing: a randomized trial. Surgery 1990 Nov;108(5):871-5.

783. Valtonen V, Karppinen L, Kariniemi AL. A comparative study of ciprofloxacin and conventional therapy in the treatment of patients with chronic lower leg ulcers infected with Pseudomonas aeruginosa or other gram-negative rods. Scand J Infect Dis Suppl 1989;60:79-83.

784. Roelens P. Double-blind placebo-controlled study with topical 2% ketanserin ointment in the treatment of venous ulcers. Dermatologica 1989;178(2):98-102.

785. Rudofsky G. Intravenous prostaglandin E1 in the treatment of venous ulcers--a double-blind, placebo-controlled trial. Vasa Suppl 1989;28:39-43.

786. Holloway GA Jr, Johansen KH, Barnes RW, Pierce GE. Multicenter trial of cadexomer iodine to treat venous stasis ulcer. West J Med 1989 Jul;151(1):35-8.

787. Hillström L. Iodosorb compared to standard treatment in chronic venous leg ulcers--a multicenter study. Acta Chir Scand Suppl 1988;544:53-5; discussion 55-6.

788. Kikta MJ, Schuler JJ, Meyer JP, Durham JR, Eldrup-Jorgensen J, Schwarcz TH, Flanigan DP. A prospective, randomized trial of Unna's boots versus hydroactive dressing in the treatment of venous stasis ulcers. J Vasc Surg 1988 Mar;7(3):478-86.

789. Handfield-Jones SE, Grattan CE, Simpson RA, Kennedy CT. Comparison of a hydrocolloid dressing and paraffin gauze in the treatment of venous ulcers. Br J Dermatol 1988 Mar;118(3):425-7.

790. Blair SD, Wright DD, Backhouse CM, Riddle E, McCollum CN. Sustained compression and healing of chronic venous ulcers [published erratum appears in BMJ 1988 Dec 10;297(6662):1500]. BMJ 1988 Nov 5;297(6657):1159-61.

791. Laudanska H, Gustavson B. In-patient treatment of chronic varicose venous ulcers. A randomized trial of cadexomer iodine versus standard dressings. J Int Med Res 1988 Nov-Dec;16(6):428-35.

792. Poskitt KR, James AH, Lloyd-Davies ER, Walton J, McCollum C. Pinch skin grafting or porcine dermis in venous ulcers: a randomised clinical trial. Br Med J (Clin Res Ed) 1987 Mar 14;294(6573):674-6.

793. Backhouse CM, Blair SD, Savage AP, Walton J, McCollum CN. Controlled trial of occlusive dressings in healing chronic venous ulcers. Br J Surg 1987 Jul;74(7):626-7.

794. Eriksson G. Comparison of two occlusive bandages in the treatment of venous leg ulcers. Br J Dermatol 1986 Feb;114(2):227-30.

795. Alinovi A, Bassissi P, Pini M. Systemic administration of antibiotics in the management of venous ulcers. A randomized clinical trial. J Am Acad Dermatol 1986 Aug;15(2 Pt 1):186-91.

796. Stillwell GK. Therapeutic heat and cold. In: Krusen FH, editor. Handbook of physical medicine and rehabilitation. 2nd ed. Philadelphia: Saunders; 1971. p. 259-72.

797. Biland L, Hürlimann F, Goor W, Körner WF, Kündig A, Madar G, Widmer LK, Ziegler WJ. Treatment of venous ulcers. A multi-center randomized double-blind study. Vasa 1985;14(4):383-9.

798. Ormiston MC, Seymour MT, Venn GE, Cohen RI, Fox JA. Controlled trial of Iodosorb in chronic venous ulcers. Br Med J (Clin Res Ed) 1985 Aug 3;291(6491):308-10.

799. Mann RJ. A double blind trial of oral O. B-hydroxyethyl rutosides for stasis leg ulcers. Br J Clin Pract 1981 Feb;35(2):79-81.

800. Phillips A, Davidson M, Greaves MW. Venous leg ulceration: evaluation of zinc treatment, serum zinc and rate of healing. Clin Exp Dermatol 1977 Dec;2(4):395-9.

801. Hallbook T, Lanner E. Serum-zinc and healing of venous leg ulcers. Lancet 1972 Oct 14;2(781):780-2.

802. Greaves MW, Ive FA. Double-blind trial of zinc sulphate in the treatment of chronic venous leg ulceration. Br J Dermatol 1972 Dec;87(6):632-4.

803. Stiller MJ, Pak GH, Shupack JL, Thaler S, Kenny C, Jondreau L. A portable pulsed electromagnetic field (PEMF) device to enhance healing of recalcitrant venous ulcers: a double-blind, placebo-controlled clinical trial. Br J Dermatol 1992 Aug;127(2):147-54.

804. Todd DJ, Heylings DJ, Allen GE, McMillin WP. Treatment of chronic varicose ulcers with pulsed electromagnetic fields: a controlled pilot study. Ir Med J 1991 Jun;84(2):54-5.

805. Ieran M, Zaffuto S, Bagnacani M, Annovi M, Moratti A, Cadossi R. Effect of low frequency pulsing electromagnetic fields on skin ulcers of venous origin in humans: a double-blind study. J Orthop Res 1990 Mar;8(2):276-82.

806. Rasmussen LH, Avnstorp C, Karlsmark T, Peters K, Horslev-Petersen K. Dose-response study of human growth hormone in venous ulcers: influence on healing and synthesis of collagen types I and III. Phlebology 1994;9(3):92-8.

807. Falanga V, Eaglstein WH, Bucalo B, Katz MH, Harris B, Carson P. Topical use of human recombinant epidermal growth factor (h-EGF) in venous ulcers. J Dermatol Surg Oncol 1992 Jul;18(7):604-6.

808. Rasmussen LH, Karlsmark T, Avnstorp C, Peters K, Jorgensen M, Jensen LT. Topical human growth hormone treatment of chronic leg ulcers. Phlebology 1991;6(1):23-30.

809. Burgos H, Herd A, Bennett JP. Placental angiogenic and growth factors in the treatment of chronic varicose ulcers: preliminary communication. J R Soc Med 1989 Oct;82(10):598-9.

810. Eriksson SV, Lundeberg T, Malm M. A placebo controlled trial of ultrasound therapy in chronic leg ulceration. Scand J Rehabil Med 1991;23(4):211-3.

811. Lundeberg T, Nordstrom F, Brodda-Jansen G, Eriksson SV, Kjartansson J, Samuelson UE. Pulsed ultrasound does not improve healing of venous ulcers. Scand J Rehabil Med 1990;22(4):195-7.

812. Callam MJ, Harper DR, Dale JJ, Ruckley CV, Prescott RJ. A controlled trial of weekly ultrasound therapy in chronic leg ulceration. Lancet 1987 Jul 25;2(8552):204-6.

813. Dyson M, Franks C, Suckling J. Stimulation of healing of varicose ulcers by ultrasound. Ultrasonics 1976 Sep;14(5):232-6.

814. Malm M, Lundeberg T. Effect of low power gallium arsenide laser on healing of venous ulcers. Scand J Plast Reconstr Surg Hand Surg 1991;25(3):249-51.

815. Lundeberg T, Malm M. Low-power HeNe laser treatment of venous leg ulcers. Ann Plast Surg 1991 Dec;27(6):537-9.

816. Stiller MJ, Pak GH, Shupack JL, Thaler S, Kenny C, Jondreau L. A portable pulsed electromagnetic field (PEMF) device to enhance healing of recalcitrant venous ulcers: a double-blind, placebo-controlled clinical trial. Br J Dermatol 1992 Aug;127(2):147-54.

817. Todd DJ, Heylings DJ, Allen GE, McMillin WP. Treatment of chronic varicose ulcers with pulsed electromagnetic fields: a controlled pilot study. Ir Med J 1991 Jun;84(2):54-5.

818. Ieran M, Zaffuto S, Bagnacani M, Annovi M, Moratti A, Cadossi R. Effect of low frequency pulsing electromagnetic fields on skin ulcers of venous origin in humans: a double-blind study. J Orthop Res 1990 Mar;8(2):276-82.

819. Day A, Dombranski S, Farkas C, Foster C, Godin J, Moody M, Morrison M, Tamer C. Managing sacral pressure ulcers with hydrocolloid dressings: results of a controlled, clinical study. Ostomy Wound Manage 1995 Mar;41(2):52-4, 56, 58 passim.

820. Hondé C, Derks C, Tudor D. Local treatment of pressure sores in the elderly: amino acid copolymer membrane versus hydrocolloid dressing. J Am Geriatr Soc 1994 Nov;42(11):1180-3.

821. Colwell JC, Foreman MD, Trotter JP. A comparison of the efficacy and cost-effectiveness of two methods of managing pressure ulcers. Decubitus 1993 Jul;6(4):28-36.

822. Kraft MR, Lawson L, Pohlmann B, Reid-Lokos C, Barder L. A comparison of Epi-Lock and saline dressings in the treatment of pressure ulcers. Decubitus 1993 Nov;6(6):42-4, 46, 48.

823. Xakellis GC, Chrischilles EA. Hydrocolloid versus saline-gauze dressings in treating pressure ulcers: a cost-effectiveness analysis. Arch Phys Med Rehabil 1992 May;73(5):463-9.

824. LeVasseur SA, Helme RD. A double-blind clinical trial to compare the efficacy of an active based cream F14001 against a placebo non-active based cream for the treatment of pressure ulcers in a population of elderly subjects. J Adv Nurs 1991 Aug;16(8):952-6.

825. Darkovich SL, Brown-Etris M, Spencer M. Biofilm hydrogel dressing: a clinical evaluation in the treatment of pressure sores. Ostomy Wound Manage 1990 Jul-Aug;29:47-60.

826. Alm A, Hornmark AM, Fall PA, Linder L, Bergstrand B, Ehrnebo M, Madsen SM, Setterberg G. Care of pressure sores: a controlled study of the use of a hydrocolloid dressing compared with wet saline gauze compresses. Acta Derm Venereol Suppl (Stockh) 1989;149:1-10.

827. Neill KM, Conforti C, Kedas A, Burris JF. Pressure sore response to a new hydrocolloid dressing. Wounds 1989 Nov;1(3):173-85.

828. Gorse GJ, Messner RL. Improved pressure sore healing with hydrocolloid dressings. Arch Dermatol 1987 Jun;123(6):766-71.

829. Allman RM, Walker JM, Hart MK, Laprade CA, Noel LB, Smith CR. Air-fluidized beds or conventional therapy for pressure sores. A randomized trial. Ann Intern Med 1987 Nov;107(5):641-8.

830. Oleske DM, Smith XP, White P, Pottage J, Donovan MI. A randomized clinical trial of two dressing methods for the treatment of low-grade pressure ulcers. J Enterostomal Ther 1986 May-Jun;13(3):90-8.

831. Sebern MD. Pressure ulcer management in home health care: efficacy and cost effectiveness of moisture vapor permeable dressing. Arch Phys Med Rehabil 1986 Oct;67(10):726-9.

832. Ågren MS, Strömberg HE. Topical treatment of pressure ulcers. A randomized comparative trial of Varidase and zinc oxide. Scand J Plast Reconstr Surg 1985;19(1):97-100.

833. Moberg S, Hoffman L, Grennert ML, Holst A. A randomized trial of cadexomer iodine in decubitus ulcers. J Am Geriatr Soc 1983 Aug;31(8):462-5.

834. Taylor TV, Rimmer S, Day B, Butcher J, Dymock IW. Ascorbic acid supplementation in the treatment of pressure-sores. Lancet 1974 Sep 7;2(7880):544-6.

835. Wood JM, Evans PE 3rd, Schallreuter KU, Jacobson WE, Sufit R, Newman J, White C, Jacobson M. A multicenter study on the use of pulsed low-intensity direct current for healing chronic stage II and stage III decubitus ulcers. Arch Dermatol 1993 Aug;129(8):999-1009.

836. Stefanovska A, Vodovnik L, Benko H, Turk R. Treatment of chronic wounds by means of electric and electromagnetic fields. Part 2. Value of FES parameters for pressure sore treatment. Med Biol Eng Comput 1993 May;31(3):213-20.

837. Gentzkow GD, Pollack SV, Kloth LC, Stubbs HA. Improved healing of pressure ulcers using Dermapulse, a new electrical stimulation device. Wounds 1991 Sep-Oct;3(5):158-70.

838. Griffin JW, Tooms RE, Mendius RA, Clifft JK, Vander Zwaag R, el-Zeky F. Efficacy of high voltage pulsed current for healing of pressure ulcers in patients with spinal cord injury. Phys Ther 1991 Jun;71(6):433-42; discussion 442-4.

839. Kloth LC, Feedar JA. Acceleration of wound healing with high voltage, monophasic, pulsed current [published erratum appears in Phys Ther 1989 Aug;69(8):702]. Phys Ther 1988 Apr;68(4):503-8.

840. Salzberg CA, Cooper-Vastola SA, Perez F, Viehbeck MG, Byrne DW. The effects of non-thermal pulsed electromagnetic energy on wound healing of pressure ulcers in spinal cord-injured patients: a randomized, double-blind study. Ostomy Wound Manage 1995 Apr;41(3):42-4, 46, 48 passim.

841. Mustoe TA, Cutler NR, Allman RM, Goode PS, Deuel TF, Prause JA, Bear M, Serdar CM, Pierce GF. A phase II study to evaluate recombinant platelet-derived growth factor-BB in the treatment of stage 3 and 4 pressure ulcers. Arch Surg 1994 Feb;129(2):213-9.

842. Robson MC, Phillips LG, Thomason A, Altrock BW, Pence PC, Heggers JP, Johnston AF, McHugh TP, Anthony MS, Robson LE, et al. Recombinant human platelet-derived growth factor-BB for the treatment of chronic pressure ulcers. Ann Plast Surg 1992 Sep;29(3):193-201.

843. Robson MC, Phillips LG, Lawrence WT, Bishop JB, Youngerman JS, Hayward PG, Broemeling LD, Heggers JP. The safety and effect of topically applied recombinant basic fibroblast growth factor on the healing of chronic pressure sores. Ann Surg 1992 Oct;216(4):401-6; discussion 406-8.

844. ter Riet G, Kessels AG, Knipschild P. Randomised clinical trial of ultrasound treatment for pressure ulcers [published erratum appears in BMJ 1995 May 20;310(6990):1300]. BMJ 1995 Apr 22;310(6986):1040-1.

845. Nussbaum EL, Biemann I, Mustard B. Comparison of ultrasound/ultraviolet-C and laser for treatment of pressure ulcers in patients with spinal cord injury. Phys Ther 1994 Sep;74(9):812-23; discussion 824-5.

846. McDiarmid T, Burns PN, Lewith GT, Machin D. Ultrasound and the treatment of pressure sores. Physiotherapy 1985 Feb;71(2):66-70.

847. Wills EE, Anderson TW, Beattie BL, Scott A. A randomized placebo-controlled trial of ultraviolet light in the treatment of superficial pressure sores. J Am Geriatr Soc 1983 Mar;31(3):131-3.

848. Wood JM, Evans PE 3rd, Schallreuter KU, Jacobson WE, Sufit R, Newman J, White C, Jacobson M. A multicenter study on the use of pulsed low-intensity direct current for healing chronic stage II and stage III decubitus ulcers. Arch Dermatol 1993 Aug;129(8):999-1009.

849. Stefanovska A, Vodovnik L, Benko H, Turk R. Treatment of chronic wounds by means of electric and electromagnetic fields. Part 2. Value of FES parameters for pressure sore treatment. Med Biol Eng Comput 1993 May;31(3):213-20.

850. Gentzkow GD, Pollack SV, Kloth LC, Stubbs HA. Improved healing of pressure ulcers using Dermapulse, a new electrical stimulation device. Wounds 1991 Sep-Oct;3(5):158-70.

851. Griffin JW, Tooms RE, Mendius RA, Clifft JK, Vander Zwaag R, el-Zeky F. Efficacy of high voltage pulsed current for healing of pressure ulcers in patients with spinal cord injury. Phys Ther 1991 Jun;71(6):433-42; discussion 442-4.

852. Kloth LC, Feedar JA. Acceleration of wound healing with high voltage, monophasic, pulsed current [published erratum appears in Phys Ther 1989 Aug;69(8):702]. Phys Ther 1988 Apr;68(4):503-8.

853. Salzberg CA, Cooper-Vastola SA, Perez F, Viehbeck MG, Byrne DW. The effects of non-thermal pulsed electromagnetic energy on wound healing of pressure ulcers in spinal cord-injured patients: a randomized, double-blind study. Ostomy Wound Manage 1995 Apr;41(3):42-4, 46, 48 passim.

854. Sacks H, Chalmers TC, Smith H Jr. Randomized versus historical controls for clinical trials. Am J Med 1982 Feb;72(2):233-40.

855. Stiller MJ, Pak GH, Shupack JL, Thaler S, Kenny C, Jondreau L. A portable pulsed electromagnetic field (PEMF) device to enhance healing of recalcitrant venous ulcers: a double-blind, placebo-controlled clinical trial. Br J Dermatol 1992 Aug;127(2):147-54.

856. Cordts PR, Hanrahan LM, Rodriguez AA, Woodson J, LaMorte WW, Menzoian JO. A prospective, randomized trial of Unna's boot versus Duoderm CGF hydroactive dressing plus compression in the management of venous leg ulcers. J Vasc Surg 1992 Mar;15(3):480-6.

857. Callam MJ, Harper DR, Dale JJ, Ruckley CV, Prescott RJ. A controlled trial of weekly ultrasound therapy in chronic leg ulceration. Lancet 1987 Jul 25;2(8552):204-6.

858. Unger P, Eddy J, Raimastry S. A controlled study of the effect of high voltage pulse current (HVPC) on wound healing [abstract]. Phys Ther 1991 Jun;71(6 Suppl):S119.

859. Feedar JA, Kloth LC. Acceleration of wound healing with high voltage pulsating direct current [abstract]. Phys Ther 1985 May;65(5):741.

860. Gentzkow GD, Pollack SV, Kloth LC, Stubbs HA. Improved healing of pressure ulcers using Dermapulse, a new electrical stimulation device. Wounds 1991 Sep-Oct;3(5):158-70.

861. Griffin JW, Tooms RE, Mendius RA, Clifft JK, Vander Zwaag R, el-Zeky F. Efficacy of high voltage pulsed current for healing of pressure ulcers in patients with spinal cord injury. Phys Ther 1991 Jun;71(6):433-42; discussion 442-4.

862. Stefanovska A, Vodovnik L, Benko H, Turk R. Treatment of chronic wounds by means of electric and electromagnetic fields. Part 2. Value of FES parameters for pressure sore treatment. Med Biol Eng Comput 1993 May;31(3):213-20.

863. Salzberg CA, Cooper-Vastola SA, Perez F, Viehbeck MG, Byrne DW. The effects of non-thermal pulsed electromagnetic energy on wound healing of pressure ulcers in spinal cord-injured patients: a randomized, double-blind study. Ostomy Wound Manage 1995 Apr;41(3):42-4, 46, 48 passim.

864. Wood JM, Evans PE 3rd, Schallreuter KU, Jacobson WE, Sufit R, Newman J, White C, Jacobson M. A multicenter study on the use of pulsed low-intensity direct current for healing chronic stage II and stage III decubitus ulcers. Arch Dermatol 1993 Aug;129(8):999-1009.

865. Stefanovska A, Vodovnik L, Benko H, Turk R. Treatment of chronic wounds by means of electric and electromagnetic fields. Part 2. Value of FES parameters for pressure sore treatment. Med Biol Eng Comput 1993 May;31(3):213-20.

866. Kloth LC, Feedar JA. Acceleration of wound healing with high voltage, monophasic, pulsed current [published erratum appears in Phys Ther 1989 Aug;69(8):702]. Phys Ther 1988 Apr;68(4):503-8.

867. Ohlsson P, Larsson K, Lindholm C, Moller M. A cost-effectiveness study of leg ulcer treatment in primary care. Comparison of saline-gauze and hydrocolloid treatment in a prospective, randomized study. Scand J Prim Health Care 1994 Dec;12(4):295-9.

868. Werner-Schlenzka H, Kuhlmann RK. Treatment of venous leg ulcers with topical loprost: a placebo controlled study. Vasa 1994;23(2):145-50.

869. Smith BA. The dressing makes the difference. Trial of two modern dressings on venous ulcers. Prof Nurse 1994 Feb;9(5):348, 350-2.

870. Layton AM, Ibbotson SH, Davies JA, Goodfield MJ. Randomised trial of oral aspirin for chronic venous leg ulcers. Lancet 1994 Jul 16;344(8916):164-5.

871. Huovinen S, Kotilainen P, Jarvinen H, Malanin K, Sarna S, Helander I, Huovinen P. Comparison of ciprofloxacin or trimethoprim therapy for venous leg ulcers: results of a pilot study. J Am Acad Dermatol 1994 Aug;31(2 Pt 1):279-81.

872. Nikolova K. Treatment of post-phlebitic syndrome and venous leg ulcers with flunarizine. Methods Find Exp Clin Pharmacol 1994 Oct;16(8):609-13.

873. Teepe RG, Roseeuw DI, Hermans J, Koebrugge EJ, Altena T, de Coninck A, Ponec M, Vermeer BJ. Randomized trial comparing cryopreserved cultured epidermal allografts with hydrocolloid dressings in healing chronic venous ulcers. J Am Acad Dermatol 1993 Dec;29(6):982-8.

874. Cordts PR, Hanrahan LM, Rodriguez AA, Woodson J, LaMorte WW, Menzoian JO. A prospective, randomized trial of Unna's boot versus Duoderm CGF hydroactive dressing plus compression in the management of venous leg ulcers. J Vasc Surg 1992 Mar;15(3):480-6.

875. Barbarino C. Pentoxifylline in the treatment of venous leg ulcers. Curr Med Res Opin 1992;12(9):547-51.

876. Bishop JB, Phillips LG, Mustoe TA, VanderZee AJ, Wiersema L, Roach DE, Heggers JP, Hill DP Jr, Taylor EL, Robson MC. A prospective randomized evaluator-blinded trial of two potential wound healing agents for the treatment of venous stasis ulcers. J Vasc Surg 1992 Aug;16(2):251-7.

877. Brandrup F, Menné T, Ågren MS, Strömberg HE, Holst R, Frisén M. A randomized trial of two occlusive dressings in the treatment of leg ulcers. Acta Derm Venereol 1990;70(3):231-5.

878. Smith PC, Sarin S, Hasty J, Scurr JH. Sequential gradient pneumatic compression enhances venous ulcer healing: a randomized trial. Surgery 1990 Nov;108(5):871-5.

879. Holloway GA Jr, Johansen KH, Barnes RW, Pierce GE. Multicenter trial of cadexomer iodine to treat venous stasis ulcer. West J Med 1989 Jul;151(1):35-8.

880. Hillström L. Iodosorb compared to standard treatment in chronic venous leg ulcers--a multicenter study. Acta Chir Scand Suppl 1988;544:53-5; discussion 55-6.

881. Laudanska H, Gustavson B. In-patient treatment of chronic varicose venous ulcers. A randomized trial of cadexomer iodine versus standard dressings. J Int Med Res 1988 Nov-Dec;16(6):428-35.

882. Backhouse CM, Blair SD, Savage AP, Walton J, McCollum CN. Controlled trial of occlusive dressings in healing chronic venous ulcers. Br J Surg 1987 Jul;74(7):626-7.

883. Alinovi A, Bassissi P, Pini M. Systemic administration of antibiotics in the management of venous ulcers. A randomized clinical trial. J Am Acad Dermatol 1986 Aug;15(2 Pt 1):186-91.

884. Stillwell GK. Therapeutic heat and cold. In: Krusen FH, editor. Handbook of physical medicine and rehabilitation. 2nd ed. Philadelphia: Saunders; 1971. p. 259-72.

885. Ormiston MC, Seymour MT, Venn GE, Cohen RI, Fox JA. Controlled trial of Iodosorb in chronic venous ulcers. Br Med J (Clin Res Ed) 1985 Aug 3;291(6491):308-10.

886. Mann RJ. A double blind trial of oral O. B-hydroxyethyl rutosides for stasis leg ulcers. Br J Clin Pract 1981 Feb;35(2):79-81.

887. Hallbook T, Lanner E. Serum-zinc and healing of venous leg ulcers. Lancet 1972 Oct 14;2(781):780-2.

888. Stiller MJ, Pak GH, Shupack JL, Thaler S, Kenny C, Jondreau L. A portable pulsed electromagnetic field (PEMF) device to enhance healing of recalcitrant venous ulcers: a double-blind, placebo-controlled clinical trial. Br J Dermatol 1992 Aug;127(2):147-54.

889. Layton AM, Ibbotson SH, Davies JA, Goodfield MJ. Randomised trial of oral aspirin for chronic venous leg ulcers. Lancet 1994 Jul 16;344(8916):164-5.

890. Huovinen S, Kotilainen P, Jarvinen H, Malanin K, Sarna S, Helander I, Huovinen P. Comparison of ciprofloxacin or trimethoprim therapy for venous leg ulcers: results of a pilot study. J Am Acad Dermatol 1994 Aug;31(2 Pt 1):279-81.

891. Nikolova K. Treatment of post-phlebitic syndrome and venous leg ulcers with flunarizine. Methods Find Exp Clin Pharmacol 1994 Oct;16(8):609-13.

892. Hillström L. Iodosorb compared to standard treatment in chronic venous leg ulcers--a multicenter study. Acta Chir Scand Suppl 1988;544:53-5; discussion 55-6.

893. Cordts PR, Hanrahan LM, Rodriguez AA, Woodson J, LaMorte WW, Menzoian JO. A prospective, randomized trial of Unna's boot versus Duoderm CGF hydroactive dressing plus compression in the management of venous leg ulcers. J Vasc Surg 1992 Mar;15(3):480-6.

894. Barbarino C. Pentoxifylline in the treatment of venous leg ulcers. Curr Med Res Opin 1992;12(9):547-51.

895. Mann RJ. A double blind trial of oral O. B-hydroxyethyl rutosides for stasis leg ulcers. Br J Clin Pract 1981 Feb;35(2):79-81.

896. Todd DJ, Heylings DJ, Allen GE, McMillin WP. Treatment of chronic varicose ulcers with pulsed electromagnetic fields: a controlled pilot study. Ir Med J 1991 Jun;84(2):54-5.

897. Ieran M, Zaffuto S, Bagnacani M, Annovi M, Moratti A, Cadossi R. Effect of low frequency pulsing electromagnetic fields on skin ulcers of venous origin in humans: a double-blind study. J Orthop Res 1990 Mar;8(2):276-82.

898. Falanga V, Eaglstein WH, Bucalo B, Katz MH, Harris B, Carson P. Topical use of human recombinant epidermal growth factor (h-EGF) in venous ulcers. J Dermatol Surg Oncol 1992 Jul;18(7):604-6.

899. Lundeberg T, Nordstrom F, Brodda-Jansen G, Eriksson SV, Kjartansson J, Samuelson UE. Pulsed ultrasound does not improve healing of venous ulcers. Scand J Rehabil Med 1990;22(4):195-7.

900. Callam MJ, Harper DR, Dale JJ, Ruckley CV, Prescott RJ. A controlled trial of weekly ultrasound therapy in chronic leg ulceration. Lancet 1987 Jul 25;2(8552):204-6.

901. Stiller MJ, Pak GH, Shupack JL, Thaler S, Kenny C, Jondreau L. A portable pulsed electromagnetic field (PEMF) device to enhance healing of recalcitrant venous ulcers: a double-blind, placebo-controlled clinical trial. Br J Dermatol 1992 Aug;127(2):147-54.

902. Lundeberg T, Nordstrom F, Brodda-Jansen G, Eriksson SV, Kjartansson J, Samuelson UE. Pulsed ultrasound does not improve healing of venous ulcers. Scand J Rehabil Med 1990;22(4):195-7.

903. Callam MJ, Harper DR, Dale JJ, Ruckley CV, Prescott RJ. A controlled trial of weekly ultrasound therapy in chronic leg ulceration. Lancet 1987 Jul 25;2(8552):204-6.

904. Todd DJ, Heylings DJ, Allen GE, McMillin WP. Treatment of chronic varicose ulcers with pulsed electromagnetic fields: a controlled pilot study. Ir Med J 1991 Jun;84(2):54-5.

905. Ieran M, Zaffuto S, Bagnacani M, Annovi M, Moratti A, Cadossi R. Effect of low frequency pulsing electromagnetic fields on skin ulcers of venous origin in humans: a double-blind study. J Orthop Res 1990 Mar;8(2):276-82.

906. LeVasseur SA, Helme RD. A double-blind clinical trial to compare the efficacy of an active based cream F14001 against a placebo non-active based cream for the treatment of pressure ulcers in a population of elderly subjects. J Adv Nurs 1991 Aug;16(8):952-6.

907. Darkovich SL, Brown-Etris M, Spencer M. Biofilm hydrogel dressing: a clinical evaluation in the treatment of pressure sores. Ostomy Wound Manage 1990 Jul-Aug;29:47-60.

908. Alm A, Hornmark AM, Fall PA, Linder L, Bergstrand B, Ehrnebo M, Madsen SM, Setterberg G. Care of pressure sores: a controlled study of the use of a hydrocolloid dressing compared with wet saline gauze compresses. Acta Derm Venereol Suppl (Stockh) 1989;149:1-10.

909. Neill KM, Conforti C, Kedas A, Burris JF. Pressure sore response to a new hydrocolloid dressing. Wounds 1989 Nov;1(3):173-85.

910. Oleske DM, Smith XP, White P, Pottage J, Donovan MI. A randomized clinical trial of two dressing methods for the treatment of low-grade pressure ulcers. J Enterostomal Ther 1986 May-Jun;13(3):90-8.

911. Sebern MD. Pressure ulcer management in home health care: efficacy and cost effectiveness of moisture vapor permeable dressing. Arch Phys Med Rehabil 1986 Oct;67(10):726-9.

912. Moberg S, Hoffman L, Grennert ML, Holst A. A randomized trial of cadexomer iodine in decubitus ulcers. J Am Geriatr Soc 1983 Aug;31(8):462-5.

913. Salzberg CA, Cooper-Vastola SA, Perez F, Viehbeck MG, Byrne DW. The effects of non-thermal pulsed electromagnetic energy on wound healing of pressure ulcers in spinal cord-injured patients: a randomized, double-blind study. Ostomy Wound Manage 1995 Apr;41(3):42-4, 46, 48 passim.

914. LeVasseur SA, Helme RD. A double-blind clinical trial to compare the efficacy of an active based cream F14001 against a placebo non-active based cream for the treatment of pressure ulcers in a population of elderly subjects. J Adv Nurs 1991 Aug;16(8):952-6.

915. Alm A, Hornmark AM, Fall PA, Linder L, Bergstrand B, Ehrnebo M, Madsen SM, Setterberg G. Care of pressure sores: a controlled study of the use of a hydrocolloid dressing compared with wet saline gauze compresses. Acta Derm Venereol Suppl (Stockh) 1989;149:1-10.

916. Oleske DM, Smith XP, White P, Pottage J, Donovan MI. A randomized clinical trial of two dressing methods for the treatment of low-grade pressure ulcers. J Enterostomal Ther 1986 May-Jun;13(3):90-8.

917. Moberg S, Hoffman L, Grennert ML, Holst A. A randomized trial of cadexomer iodine in decubitus ulcers. J Am Geriatr Soc 1983 Aug;31(8):462-5.

918. Wood JM, Evans PE 3rd, Schallreuter KU, Jacobson WE, Sufit R, Newman J, White C, Jacobson M. A multicenter study on the use of pulsed low-intensity direct current for healing chronic stage II and stage III decubitus ulcers. Arch Dermatol 1993 Aug;129(8):999-1009.

919. Darkovich SL, Brown-Etris M, Spencer M. Biofilm hydrogel dressing: a clinical evaluation in the treatment of pressure sores. Ostomy Wound Manage 1990 Jul-Aug;29:47-60.

920. Neill KM, Conforti C, Kedas A, Burris JF. Pressure sore response to a new hydrocolloid dressing. Wounds 1989 Nov;1(3):173-85.

921. Oleske DM, Smith XP, White P, Pottage J, Donovan MI. A randomized clinical trial of two dressing methods for the treatment of low-grade pressure ulcers. J Enterostomal Ther 1986 May-Jun;13(3):90-8.

922. Sebern MD. Pressure ulcer management in home health care: efficacy and cost effectiveness of moisture vapor permeable dressing. Arch Phys Med Rehabil 1986 Oct;67(10):726-9.

923. Moberg S, Hoffman L, Grennert ML, Holst A. A randomized trial of cadexomer iodine in decubitus ulcers. J Am Geriatr Soc 1983 Aug;31(8):462-5.

924. Gentzkow GD, Miller KH. Electrical stimulation for dermal wound healing. Clin Podiatr Med Surg 1991 Oct;8(4):827-41.

925. Oleske DM, Smith XP, White P, Pottage J, Donovan MI. A randomized clinical trial of two dressing methods for the treatment of low-grade pressure ulcers. J Enterostomal Ther 1986 May-Jun;13(3):90-8.

926. Moberg S, Hoffman L, Grennert ML, Holst A. A randomized trial of cadexomer iodine in decubitus ulcers. J Am Geriatr Soc 1983 Aug;31(8):462-5.

927. Kloth LC, Feedar JA. Acceleration of wound healing with high voltage, monophasic, pulsed current [published erratum appears in Phys Ther 1989 Aug;69(8):702]. Phys Ther 1988 Apr;68(4):503-8.

928. Darkovich SL, Brown-Etris M, Spencer M. Biofilm hydrogel dressing: a clinical evaluation in the treatment of pressure sores. Ostomy Wound Manage 1990 Jul-Aug;29:47-60.

929. Neill KM, Conforti C, Kedas A, Burris JF. Pressure sore response to a new hydrocolloid dressing. Wounds 1989 Nov;1(3):173-85.

930. Oleske DM, Smith XP, White P, Pottage J, Donovan MI. A randomized clinical trial of two dressing methods for the treatment of low-grade pressure ulcers. J Enterostomal Ther 1986 May-Jun;13(3):90-8.

931. Moberg S, Hoffman L, Grennert ML, Holst A. A randomized trial of cadexomer iodine in decubitus ulcers. J Am Geriatr Soc 1983 Aug;31(8):462-5.

932. Unger P, Eddy J, Raimastry S. A controlled study of the effect of high voltage pulse current (HVPC) on wound healing [abstract]. Phys Ther 1991 Jun;71(6 Suppl):S119.

933. Feedar JA, Kloth LC. Acceleration of wound healing with high voltage pulsating direct current [abstract]. Phys Ther 1985 May;65(5):741.

934. Gentzkow GD, Pollack SV, Kloth LC, Stubbs HA. Improved healing of pressure ulcers using Dermapulse, a new electrical stimulation device. Wounds 1991 Sep-Oct;3(5):158-70.

935. Griffin JW, Tooms RE, Mendius RA, Clifft JK, Vander Zwaag R, el-Zeky F. Efficacy of high voltage pulsed current for healing of pressure ulcers in patients with spinal cord injury. Phys Ther 1991 Jun;71(6):433-42; discussion 442-4.

936. Salzberg CA, Cooper-Vastola SA, Perez F, Viehbeck MG, Byrne DW. The effects of non-thermal pulsed electromagnetic energy on wound healing of pressure ulcers in spinal cord-injured patients: a randomized, double-blind study. Ostomy Wound Manage 1995 Apr;41(3):42-4, 46, 48 passim.

937. Mustoe TA, Cutler NR, Allman RM, Goode PS, Deuel TF, Prause JA, Bear M, Serdar CM, Pierce GF. A phase II study to evaluate recombinant platelet-derived growth factor-BB in the treatment of stage 3 and 4 pressure ulcers. Arch Surg 1994 Feb;129(2):213-9.

938. Nussbaum EL, Biemann I, Mustard B. Comparison of ultrasound/ultraviolet-C and laser for treatment of pressure ulcers in patients with spinal cord injury. Phys Ther 1994 Sep;74(9):812-23; discussion 824-5.

939. Robson MC, Phillips LG, Lawrence WT, Bishop JB, Youngerman JS, Hayward PG, Broemeling LD, Heggers JP. The safety and effect of topically applied recombinant basic fibroblast growth factor on the healing of chronic pressure sores. Ann Surg 1992 Oct;216(4):401-6; discussion 406-8.

940. Wills EE, Anderson TW, Beattie BL, Scott A. A randomized placebo-controlled trial of ultraviolet light in the treatment of superficial pressure sores. J Am Geriatr Soc 1983 Mar;31(3):131-3.

941. Salzberg CA, Cooper-Vastola SA, Perez F, Viehbeck MG, Byrne DW. The effects of non-thermal pulsed electromagnetic energy on wound healing of pressure ulcers in spinal cord-injured patients: a randomized, double-blind study. Ostomy Wound Manage 1995 Apr;41(3):42-4, 46, 48 passim.

942. Nussbaum EL, Biemann I, Mustard B. Comparison of ultrasound/ultraviolet-C and laser for treatment of pressure ulcers in patients with spinal cord injury. Phys Ther 1994 Sep;74(9):812-23; discussion 824-5.

943. Robson MC, Phillips LG, Lawrence WT, Bishop JB, Youngerman JS, Hayward PG, Broemeling LD, Heggers JP. The safety and effect of topically applied recombinant basic fibroblast growth factor on the healing of chronic pressure sores. Ann Surg 1992 Oct;216(4):401-6; discussion 406-8.

944. Wills EE, Anderson TW, Beattie BL, Scott A. A randomized placebo-controlled trial of ultraviolet light in the treatment of superficial pressure sores. J Am Geriatr Soc 1983 Mar;31(3):131-3.

945. Wood JM, Evans PE 3rd, Schallreuter KU, Jacobson WE, Sufit R, Newman J, White C, Jacobson M. A multicenter study on the use of pulsed low-intensity direct current for healing chronic stage II and stage III decubitus ulcers. Arch Dermatol 1993 Aug;129(8):999-1009.

946. Mustoe TA, Cutler NR, Allman RM, Goode PS, Deuel TF, Prause JA, Bear M, Serdar CM, Pierce GF. A phase II study to evaluate recombinant platelet-derived growth factor-BB in the treatment of stage 3 and 4 pressure ulcers. Arch Surg 1994 Feb;129(2):213-9.

947. Gentzkow GD, Miller KH. Electrical stimulation for dermal wound healing. Clin Podiatr Med Surg 1991 Oct;8(4):827-41.

948. Kloth LC, Feedar JA. Acceleration of wound healing with high voltage, monophasic, pulsed current [published erratum appears in Phys Ther 1989 Aug;69(8):702]. Phys Ther 1988 Apr;68(4):503-8.

949. Mustoe TA, Cutler NR, Allman RM, Goode PS, Deuel TF, Prause JA, Bear M, Serdar CM, Pierce GF. A phase II study to evaluate recombinant platelet-derived growth factor-BB in the treatment of stage 3 and 4 pressure ulcers. Arch Surg 1994 Feb;129(2):213-9.

950. Unger P, Eddy J, Raimastry S. A controlled study of the effect of high voltage pulse current (HVPC) on wound healing [abstract]. Phys Ther 1991 Jun;71(6 Suppl):S119.

951. Feedar JA, Kloth LC. Acceleration of wound healing with high voltage pulsating direct current [abstract]. Phys Ther 1985 May;65(5):741.

952. Gentzkow GD, Pollack SV, Kloth LC, Stubbs HA. Improved healing of pressure ulcers using Dermapulse, a new electrical stimulation device. Wounds 1991 Sep-Oct;3(5):158-70.

953. Griffin JW, Tooms RE, Mendius RA, Clifft JK, Vander Zwaag R, el-Zeky F. Efficacy of high voltage pulsed current for healing of pressure ulcers in patients with spinal cord injury. Phys Ther 1991 Jun;71(6):433-42; discussion 442-4.

954. Salzberg CA, Cooper-Vastola SA, Perez F, Viehbeck MG, Byrne DW. The effects of non-thermal pulsed electromagnetic energy on wound healing of pressure ulcers in spinal cord-injured patients: a randomized, double-blind study. Ostomy Wound Manage 1995 Apr;41(3):42-4, 46, 48 passim.

955. Wood JM, Evans PE 3rd, Schallreuter KU, Jacobson WE, Sufit R, Newman J, White C, Jacobson M. A multicenter study on the use of pulsed low-intensity direct current for healing chronic stage II and stage III decubitus ulcers. Arch Dermatol 1993 Aug;129(8):999-1009.

956. Karba R, Vodovnik L, Presern-Strukelj M, Klesnik M. Promoted healing of chronic wounds due to electrical stimulation. Wounds 1991 Jan-Feb;3(1):16-23.

957. Stefanovska A, Vodovnik L, Benko H, Turk R. Treatment of chronic wounds by means of electric and electromagnetic fields. Part 2. Value of FES parameters for pressure sore treatment. Med Biol Eng Comput 1993 May;31(3):213-20.

958. Begg CB. Publication bias. In: Cooper H, Hedges LV, editors. The handbook of research synthesis. New York: Russell Sage Foundation; 1994. p. 399-409.

959. Petitti DB. Meta-analysis, decision analysis, and cost-effectiveness analysis: methods for quantitative synthesis in medicine. New York: Oxford University Press; 1994. 246 p. (Monographs in epidemiology and biostatistics; vol. 24).

960. Agency for Health Care Policy and Research (AHCPR). Treatment of pressure ulcers. Rockville (MD): U.S. Department of Health and Human Services, Public Health Service, AHCPR; 1994 Dec. 154 p. AHCPR publication no. 95-0652. (Clinical practice guideline; no. 15).

14.1 Citations from ECRI Databases and Publications

ECRI had identified the following references from its internal databases and publications.

17. Agency for Health Care Policy and Research (AHCPR). Treatment of pressure ulcers. Rockville (MD): U.S. Department of Health and Human Services, Public Health Service, AHCPR; 1994 Dec. 154 p. AHCPR publication no. 95-0652. (Clinical practice guideline; no. 15).

18. Weingarten MS. Advances in wound healing. In: Oloff LM. Musculoskeletal disorders of the lower extremities. Philadelphia: Saunders; 1994. p. 52-64.

76. Wound, Ostomy and Continence Nurses Society (WOCN). Standards of care. Patients with dermal wounds: pressure ulcers. Costa Mesa (CA): WOCN; 1992. 40 p.

77. Wound, Ostomy and Continence Nurses Society (WOCN). Standards of care. Patients with dermal wounds: lower extremity ulcers. Costa Mesa (CA): WOCN; 1993. 50 p.

78. University Hospital Consortium (UHC), Technology Advancement Center. Guidelines for the use of pressure relief devices in the treatment and prevention of pressure ulcers. Oak Brook (IL): UHC; 1990. [various pagings].

84. Hotta SS, Holohan TV. Procuren: a platelet-derived wound healing formula. Rockville (MD): U.S. Department of Health and Human Services, Public Health Service, Agency for Health Care Policy and Research (AHCPR); 1992 Jul. 3 p. AHCPR publication no. 92-0065. (Health technology review; no. 2).

94. Wiseman DM, Rovee DT, Alvarez OM. Wound dressings: design and use. In: Cohen IK, Diegelmann RF, Lindblad WJ, editors. Wound healing: biochemical & clinical aspects. Philadelphia: Saunders; 1992. p. 562-80.

95. Edlich RF, Rodeheaver GT, Thacker JG. Surgical devices in wound healing management. In: Cohen IK, Diegelmann RF, Lindblad WJ, editors. Wound healing: biochemical & clinical aspects. Philadelphia: Saunders; 1992. p. 581-600.

98. Agency for Health Care Policy and Research (AHCPR). Pressure ulcers in adults: prediction and prevention. Rockville (MD): U.S. Department of Health and Human Services, Public Health Service, AHCPR; 1992. 63 p. AHCPR publication no. 92-0047. (Clinical practice guideline; no. 3).

102. Sheps SB. Hyperbaric oxygen for osteomyelitis and osteoradionecrosis. Vancouver, British Columbia (Canada): British Columbia Office of Health Technology Assessment, Centre for Health Services & Policy Research; 1992 Oct. 21 p. (British Columbia Office of Health Technology Assessment discussion paper series).

103. National Center for Health Services Research (NCHSR). Public Health Service assessment of ultraviolet light treatment for decubitus ulcers, 1981. Rockville (MD): U.S. Department of Health and Human Services, Public Health Service, Office of the Assistant Secretary for Health, NCHSR; 1981. 8 p. (Health technology assessment series, 1981; no. 3).

104. National Center for Health Services Research (NCHSR). Public Health Service assessment of hydrotherapy (whirlpool) baths for treatment of decubitus ulcers, 1981. Rockville (MD): U.S. Department of Health and Human Services, Public Health Service, Office of the Assistant Secretary for Health, NCHSR; 1981. 5 p. (Health technology assessment series, 1981; no. 2).

110. ECRI. Electrical bone growth stimulation for the spine and lower leg [technology assessment report]. Plymouth Meeting (PA): ECRI; 1993 Oct. 106 p.

124. ECRI. Electrical bone growth stimulation for the spine [technology assessment report]. Plymouth Meeting (PA): ECRI; 1993 Oct. 70 p.

125. ECRI. Electrical bone growth stimulation for the wrist [technology assessment report]. Plymouth Meeting (PA): ECRI; 1994 Apr. 88 p.

126. ECRI. Spinal cord (dorsal column) stimulation for chronic intractable pain [technology assessment report]. Plymouth Meeting (PA): ECRI; 1993 Oct. 87 p.

160. Frantz RA. The effectiveness of transcutaneous electrical nerve stimulation (TENS) on decubitus ulcer healing in adult patients. In: Funk SG, Tornquist EM, Champagne MT, Copp LA, Wiese RA, editors. Key aspects of recovery: improving nutrition, rest, and mobility. New York: Springer; 1990. p. 197-205.

264. ECRI. Stimulators, electroanalgesic, transcutaneous electrical nerve. In: Healthcare product comparison system. Plymouth Meeting (PA): ECRI; 1994 May. 20 p.

271. ECRI. Ultrasound units, physical therapy; ultrasound units/neuromuscular stimulators, physical therapy. In: Healthcare product comparison system. Plymouth Meeting (PA): ECRI; 1994 Oct. 19 p.

506. Frantz RA. The effectiveness of transcutaneous electrical nerve stimulation (TENS) on decubitus ulcer healing in adult patients. In: Funk SG, Tornquist EM, Champagne MT, Copp LA, Wiese RA, editors. Key aspects of recovery: improving nutrition, rest, and mobility. New York: Springer; 1990. p. 197-205.

654. Petitti DB. Meta-analysis, decision analysis, and cost-effectiveness analysis: methods for quantitative synthesis in medicine. New York: Oxford University Press; 1994. Chapter 8, Other statistical issues in meta-analysis; p. 115-30. (Monographs in epidemiology and biostatistices; vol. 24).

662. Rosenthal R. Meta-analytic procedures for social research. Rev. ed. Newbury Park (CA): Sage Publications; 1991. Chapter 4, Comparing and combining research results; p. 59-88. (Applied social research methods series; vol. 6).

667. Rosenthal R. Meta-analytic procedures for social research. Rev. ed. Newbury Park (CA): Sage Publications; 1991. Chapter 5, Combining probabilities; p. 89-109. (Applied social research methods series; vol. 6).

730. Rosenthal R. Meta-analytic procedures for social research. Rev. ed. Newbury Park (CA): Sage Publications; 1991. Chapter 2, Defining research results; p. 13-35. (Applied social research methods series; vol. 6).

958. Begg CB. Publication bias. In: Cooper H, Hedges LV, editors. The handbook of research synthesis. New York: Russell Sage Foundation; 1994. p. 399-409.

959. Petitti DB. Meta-analysis, decision analysis, and cost-effectiveness analysis: methods for quantitative synthesis in medicine. New York: Oxford University Press; 1994. 246 p. (Monographs in epidemiology and biostatistics; vol. 24).

14.2 Citations (Bibliographic Format)

For your convenience, this section lists each referenced citation once, in alphabetic order. There are 347 citations.

3M Health Care, St. Paul, MN. 3M TENS Stimulators: treatment flexibility, quality and value for all your TENS patients [promotional material]. St. Paul (MN): 3M Health Care. 1992. 7 p.

Agency for Health Care Policy and Research (AHCPR). Pressure ulcers in adults: prediction and prevention. Rockville (MD): U.S. Department of Health and Human Services, Public Health Service, AHCPR; 1992. 63 p. AHCPR publication no. 92-0047. (Clinical practice guideline; no. 3).

Agency for Health Care Policy and Research (AHCPR). Treatment of pressure ulcers. Rockville (MD): U.S. Department of Health and Human Services, Public Health Service, AHCPR; 1994 Dec. 154 p. AHCPR publication no. 95-0652. (Clinical practice guideline; no. 15).

Ågren MS, Strömberg HE. Topical treatment of pressure ulcers. A randomized comparative trial of Varidase and zinc oxide. Scand J Plast Reconstr Surg 1985;19(1):97-100.

Akai M, Wadano Y, Yabuki T, Oda H, Sirasaki Y, Tateishi T. [Effect of a direct electric current on modification of bone and ligament repair processes--experimental investigation of a rabbit model]. Nippon Seikeigeka Gakkai Zasshi 1991 Apr;65(4):196-206. (Jpn).

Akers TK, Gabrielson AL. The effect of high voltage galvanic stimulation on the rate of healing of decubitus ulcers. Biomed Sci Instrum 1984;20:99-100.

Akman MN, Loubser PG, Fife CE, Donovan WH. Hyperbaric oxygen therapy: implications for spinal cord injury patients with intrathecal baclofen infusion pumps. Case report. Paraplegia 1994 Apr;32(4):281-4.

Alinovi A, Bassissi P, Pini M. Systemic administration of antibiotics in the management of venous ulcers. A randomized clinical trial. J Am Acad Dermatol 1986 Aug;15(2 Pt 1):186-91.

Allman RM, Walker JM, Hart MK, Laprade CA, Noel LB, Smith CR. Air-fluidized beds or conventional therapy for pressure sores. A randomized trial. Ann Intern Med 1987 Nov;107(5):641-8.

Allman RM. Epidemiology of pressure sores in different populations. Decubitus 1989 May;2(2):30-3.

Alm A, Hornmark AM, Fall PA, Linder L, Bergstrand B, Ehrnebo M, Madsen SM, Setterberg G. Care of pressure sores: a controlled study of the use of a hydrocolloid dressing compared with wet saline gauze compresses. Acta Derm Venereol Suppl (Stockh) 1989;149:1-10.

Alon G, Azaria M, Stein H. Diabetic ulcer healing using high voltage TENS [abstract]. Phys Ther 1986 May;66(5):775.

Alvarez OM, Mertz PM, Smerbeck RV, Eaglstein WH. The healing of superficial skin wounds is stimulated by external electrical current. J Invest Dermatol 1983 Aug;81(2):144-8.

American Imex, Irvine, CA. A-TENS AI-86: a conservative and major step in pain management [promotional material]. Irvine (CA): American Imex. 2 p.

American Imex, Irvine, CA. MES iF microcurrent interferential [promotional material]. Irvine (CA): American Imex. 2 p.

American Imex, Irvine, CA. TENS for conservative non-invasive pain management [promotional material]. Irvine (CA): American Imex. 2 p.

American Imex, Irvine, CA. ULTIMA Xs microampere current: clinical microcurrent therapy on a personal scale [promotional material]. Irvine (CA): American Imex. 2 p.

Arnold TE, Stanley JC, Fellows EP, Moncada GA, Allen R, Hutchinson JJ, Swartz WM, Bolton LL, Vickers CF, Kerstein MD. Prospective, multicenter study of managing lower extremity venous ulcers. Ann Vasc Surg 1994 Jul;8(4):356-62.

Aronofsky DH. Reduction of dental postsurgical symptoms using nonthermal pulsed high-peak-power electromagnetic energy. Oral Surg Oral Med Oral Pathol 1971 Nov;32(5):688-96.

Assimacopoulos D. Low intensity negative electric current in the treatment of ulcers of the leg due to chronic venous insufficiency. Preliminary report of three cases. Am J Surg 1968 May;115(5):683-7.

Assimacopoulos D. Wound healing promotion by the use of negative electric current. Am Surg 1968 Jun;34(6):423-31.

AVRA Tronics Corp., Greenvale, NY. Model 770 GALVANATOR: a physical therapy stimulator instrument for pulsed galvanic stimulation of muscles and localized tissues [promotional material]. Greenvale (NY): AVRA Tronics. 2 p.

Backhouse CM, Blair SD, Savage AP, Walton J, McCollum CN. Controlled trial of occlusive dressings in healing chronic venous ulcers. Br J Surg 1987 Jul;74(7):626-7.

Bailey KR. Inter-study differences: how should they influence the interpretation and analysis of results? Stat Med 1987 Apr-May;6(3):351-60.

Barbarino C. Pentoxifylline in the treatment of venous leg ulcers. Curr Med Res Opin 1992;12(9):547-51.

Barclay V, Collier RJ, Jones A. Treatment of various hand injuries by pulsed electromagnetic energy (Diapulse). Physiotherapy 1983 Jun 10;69(6):186-8.

Baroni G, Porro T, Faglia E, Pizzi G, Mastropasqua A, Oriani G, Pedesini G, Favales F. Hyperbaric oxygen in diabetic gangrene treatment. Diabetes Care 1987 Jan-Feb;10(1):81-6.

Barranco SD, Spadaro JA, Berger TJ, Becker RO. In vitro effect of weak direct current on Staphylococcus aureus. Clin Orthop 1974 May;(100):250-5.

Barron JJ, Jacobson WE, Tidd G. Treatment of decubitus ulcers. A new approach. Minn Med 1985 Feb;68(2):103-6.

Begg CB. Publication bias. In: Cooper H, Hedges LV, editors. The handbook of research synthesis. New York: Russell Sage Foundation; 1994. p. 399-409.

Biland L, Hürlimann F, Goor W, Körner WF, Kündig A, Madar G, Widmer LK, Ziegler WJ. Treatment of venous ulcers. A multi-center randomized double-blind study. Vasa 1985;14(4):383-9.

[Biomedical Life Systems, Inc., Vista, CA]. BioMed and Systems TENS series [promotional material]. Scarborough, Ontario (Canada): Canadian Medical Products Ltd. 1 p.

[Biomedical Life Systems, Inc., Vista, CA]. EMS 2000 [promotional material]. Scarborough, Ontario (Canada): Canadian Medical Products Ltd. 1 p.

Biorem Elettromedicali, Agropoli, Italy. TopLine COMPACT 100 electrotherapy low and medium frequency BRT/100 [promotional material]. Agropoli (Italy): Biorem. 2 p.

Biorem Elettromedicali, Agropoli, Italy. TopLine ERGON electrotherapy medium frequency [promotional material]. Agropoli (Italy): Biorem. 2 p.

Biorem Elettromedicali, Agropoli, Italy. TopLine EXPERT electrotherapy low and medium frequency BRT/70 [promotional material]. Agropoli (Italy): Biorem. 2 p.

Biorem Elettromedicali, Agropoli, Italy. TopLine EXPERT Mini electrotherapy low and medium frequency BRT/8 [promotional material]. Agropoli (Italy): Biorem. 2 p.

Biorem Elettromedicali, Agropoli, Italy. TopLine EXPERT Plus low and medium frequency expert system in electrotherapy [promotional material]. Agropoli (Italy): Biorem. 2 p.

Biorem Elettromedicali, Agropoli, Italy. TopLine MAXIMA Magnetic Field B20-1/2 programmable magnetotherapy [promotional material]. Agropoli (Italy): Biorem. 2 p.

Biorem Elettromedicali, Agropoli, Italy. TopLine MICRA magnetotherapy [promotional material]. Agropoli (Italy): Biorem. 2 p.

Bishop JB, Phillips LG, Mustoe TA, VanderZee AJ, Wiersema L, Roach DE, Heggers JP, Hill DP Jr, Taylor EL, Robson MC. A prospective randomized evaluator-blinded trial of two potential wound healing agents for the treatment of venous stasis ulcers. J Vasc Surg 1992 Aug;16(2):251-7.

Blair SD, Wright DD, Backhouse CM, Riddle E, McCollum CN. Sustained compression and healing of chronic venous ulcers [published erratum appears in BMJ 1988 Dec 10;297(6662):1500]. BMJ 1988 Nov 5;297(6657):1159-61.

Bloomex International, Inc., Elmwood Park, NJ. [Bloomex product catalog]. Elmwood Park (NJ): Bloomex. 14 p.

Bourguignon GJ, Bourguignon LY. Electric stimulation of protein and DNA synthesis in human fibroblasts. FASEB J 1987 Nov;1(5):398-402.

Bowszyc J, Bowszyc-Dmochowska M, Kazmierowski M, Ben-Amer HM, Garbowska T, Harding E. Comparison of two dressings in the treatment of venous leg ulcers. J Wound Care 1995 Mar;4(3):106-10.

Brandeis GH, Berlowitz DR, Hossain M, Morris JN. Pressure ulcers: the minimum data set and the resident assessment protocol. Adv Wound Care 1995 Nov-Dec;8(6):18-25.

Brandrup F, Menné T, Ågren MS, Strömberg HE, Holst R, Frisén M. A randomized trial of two occlusive dressings in the treatment of leg ulcers. Acta Derm Venereol 1990;70(3):231-5.

Brown GL, Curtsinger L, Jurkiewicz MJ, Nahai F, Schultz G. Stimulation of healing of chronic wounds by epidermal growth factor. Plast Reconstr Surg 1991 Aug;88(2):189-94; discussion 195-6.

Burgos H, Herd A, Bennett JP. Placental angiogenic and growth factors in the treatment of chronic varicose ulcers: preliminary communication. J R Soc Med 1989 Oct;82(10):598-9.

Callam MJ, Harper DR, Dale JJ, Ruckley CV, Prescott RJ. A controlled trial of weekly ultrasound therapy in chronic leg ulceration. Lancet 1987 Jul 25;2(8552):204-6.

Carey LC, Lepley D Jr. Effect of continuous direct electric current on healing wounds. Surg Forum 1962;13:33-5.

Carin Electromedicarin, S.A., Barcelona, Spain. Carin Electromedicarin, S.A. [product catalog]. Barcelona (Spain): Carin. 20 p.

Carley PJ, Wainapel SF. Electrotherapy for acceleration of wound healing: low intensity direct current. Arch Phys Med Rehabil 1985 Jul;66(7):443-6.

Cefar medical products ab, Lund, Sweden. Sensory electrostimulation [product catalog]. Lund (Sweden): Cefar. 14 p.

Chattanooga Group, Inc., Hixson, TN. Forte ES450 Electrotherapy System: a new world of flexibility and simplicity for today and tomorrow [promotional material]. Hixson (TN): Chattanooga Group. 1994. 2 p.

Chattanooga Group, Inc., Hixson, TN. Intelect 150 High Voltage Stimulator: the portable, affordable high voltage system [promotional material]. Hixson (TN): Chattanooga Group. 1994. 2 p.

Chattanooga Group, Inc., Hixson, TN. Intelect 500 S High Voltage Stimulator: versatility in treatment parameters [promotional material]. Hixson (TN): Chattanooga Group. 1990. 2 p.

Cheng N, Van Hoof H, Bockx E, Hoogmartens MJ, Mulier JC, De Dijcker FJ, Sansen WM, De Loecker W. The effects of electric currents on ATP generation, protein synthesis, and membrane transport of rat skin. Clin Orthop 1982 Nov-Dec;(171):264-72.

Cohen IK, Diegelmann RF, Lindblad WJ, editors. Wound healing: biochemical & clinical aspects. Philadelphia: Saunders; 1992. 630 p.

Colgan MP, Dormandy JA, Jones PW, Schraibman IG, Shanik DG, Young RA. Oxpentifylline treatment of venous ulcers of the leg. BMJ 1990 Apr 14;300(6730):972-5.

Colwell JC, Foreman MD, Trotter JP. A comparison of the efficacy and cost-effectiveness of two methods of managing pressure ulcers. Decubitus 1993 Jul;6(4):28-36.

Comfort Technologies Inc., Pittstown, NJ. Transcutaneous electrical nerve stimulators (T.E.N.S.) for drug-free pain relief [product brochure]. Pittstown (NJ): Comfort Technologies. 2 p.

Consensus paper on venous leg ulcer. The Alexander House Group. J Dermatol Surg Oncol 1992 Jul;18(7):592-602.

Cook AW, Oygar A, Baggenstos P, Pacheco S, Kleriga E. Vascular disease of extremities. Electric stimulation of spinal cord and posterior roots. N Y State J Med 1976 Mar;76(3):366-8.

Cordts PR, Hanrahan LM, Rodriguez AA, Woodson J, LaMorte WW, Menzoian JO. A prospective, randomized trial of Unna's boot versus Duoderm CGF hydroactive dressing plus compression in the management of venous leg ulcers. J Vasc Surg 1992 Mar;15(3):480-6.

danmeter, Odense, Denmark. AUTOMOVE AM 706: electro myographic controlled stimulation for improved rehabilitation after stroke [promotional material]. Odense (Denmark): danmeter. 4 p.

danmeter, Odense, Denmark. Effective pain and muscle stimulator TS 6000 [promotional material]. Odense (Denmark): danmeter. 4 p.

danmeter, Odense, Denmark. elpha 2000 Muscle and Pain Stimulator [promotional material]. Odense (Denmark): danmeter. 4 p.

Darkovich SL, Brown-Etris M, Spencer M. Biofilm hydrogel dressing: a clinical evaluation in the treatment of pressure sores. Ostomy Wound Manage 1990 Jul-Aug;29:47-60.

Davis JC, Landeen JM, Levine RA. Pyoderma gangrenosum: skin grafting after preparation with hyperbaric oxygen. Plast Reconstr Surg 1987 Feb;79(2):200-7.

Davis LB, McCulloch JM, Neal MB. The effectiveness of Unna Boot and semipermeable film vs. Unna Boot alone in the healing of venous ulcers. A pilot report. Ostomy Wound Manage 1992 Jan-Feb;38(1):19-21.

Day A, Dombranski S, Farkas C, Foster C, Godin J, Moody M, Morrison M, Tamer C. Managing sacral pressure ulcers with hydrocolloid dressings: results of a controlled, clinical study. Ostomy Wound Manage 1995 Mar;41(2):52-4, 56, 58 passim.

Dayton PD, Palladino SJ. Electrical stimulation of cutaneous ulcerations. A literature review. J Am Podiatr Med Assoc 1989 Jul;79(7):318-21.

Demets DL. Methods for combining randomized clinical trials: strengths and limitations. Stat Med 1987 Apr-May;6(3):341-50.

Diamond E, Forst MB, Hyman SA, Rand SA. The effect of hyperbaric oxygen on lower extremity ulcerations. J Am Podiatry Assoc 1982 Apr;72(4):180-5.

Diter-Elektronikka Oy, Turku, Finland. Diter electrotherapy & ultrasoundtherapy devices [product catalog]. Turku (Finland): Diter. 18 p.

Douglas WS, Simpson NB. Guidelines for the management of chronic venous leg ulceration. Report of a multidisciplinary workshop. British Association of Dermatologists and the Research Unit of the Royal College of Physicians. Br J Dermatol 1995 Mar;132(3):446-52.

Dunn MG, Doillon CJ, Berg RA, Olson RM, Silver FH. Wound healing using a collagen matrix: effect of DC electrical stimulation. J Biomed Mater Res 1988 Aug;22(A2 Suppl):191-206.

Dynatronics, Salt Lake City, UT. Dynatron 400: interferential therapy [promotional material]. Salt Lake City (UT): Dynatronics. 1992. 2 p.

Dynatronics, Salt Lake City, UT. Dynatron 500PLUS: interferential, microcurrent and muscle stimulation [promotional material]. Salt Lake City (UT): Dynatronics. 1993. 2 p.

Dynatronics, Salt Lake City, UT. Dynatron 800: combination therapy [promotional material]. Salt Lake City (UT): Dynatronics. 1993. 2 p.

Dynatronics, Salt Lake City, UT. The Dynatron 50 Series: a quantum leap in portable electrotherapy and ultrasound technology [promotional material]. Salt Lake City (UT): Dynatronics. 1994. 2 p.

DynaWave Corporation, Geneva, IL. DynaLator: the ultimate combination [promotional material]. Geneva (IL): DynaWave. 2 p.

DynaWave Corporation, Geneva, IL. DynaWave Model 12 [promotional material]. Geneva (IL): DynaWave. 2 p.

Dyson M, Franks C, Suckling J. Stimulation of healing of varicose ulcers by ultrasound. Ultrasonics 1976 Sep;14(5):232-6.

ECRI. Electrical bone growth stimulation for the spine and lower leg [technology assessment report]. Plymouth Meeting (PA): ECRI; 1993 Oct. 106 p.

ECRI. Electrical bone growth stimulation for the spine [technology assessment report]. Plymouth Meeting (PA): ECRI; 1993 Oct. 70 p.

ECRI. Electrical bone growth stimulation for the wrist [technology assessment report]. Plymouth Meeting (PA): ECRI; 1994 Apr. 88 p.

ECRI. Spinal cord (dorsal column) stimulation for chronic intractable pain [technology assessment report]. Plymouth Meeting (PA): ECRI; 1993 Oct. 87 p.

ECRI. Stimulators, electroanalgesic, transcutaneous electrical nerve. In: Healthcare product comparison system. Plymouth Meeting (PA): ECRI; 1994 May. 20 p.

ECRI. Ultrasound units, physical therapy; ultrasound units/neuromuscular stimulators, physical therapy. In: Healthcare product comparison system. Plymouth Meeting (PA): ECRI; 1994 Oct. 19 p.

Edlich RF, Rodeheaver GT, Thacker JG. Surgical devices in wound healing management. In: Cohen IK, Diegelmann RF, Lindblad WJ, editors. Wound healing: biochemical & clinical aspects. Philadelphia: Saunders; 1992. p. 581-600.

[Electrical stimulation for wound healing]. Federal Research in Progress [database online]. Springfield (VA): National Technical Information Service; [cited 1995 Dec 14]. [36 references]. Available from Knight-Ridder Information, Inc., Mountain View, CA.

Electro-Med Health Industries, Inc., (EMHI), North Miami, FL. EGS-100SL includes the micro-current component! [promotional material]. North Miami (FL): EMHI. 1992 Jan. 1 p.

Electro-Med Health Industries, Inc., (EMHI), North Miami, FL. EGS 100-2S High Voltage Pulsed Galvanic Stimulator [promotional material]. North Miami (FL): EMHI. 1986 Apr. 2 p.

Electro-Med Health Industries, Inc., (EMHI), North Miami, FL. Model 300 High Voltage Pulsed Galvanic Stimulator [promotional material]. North Miami (FL): EMHI. 1986 Jan. 2 p.

Electro-Med Health Industries, Inc., (EMHI), North Miami, FL. Introducing the latest in versatility: VeraStim 380 Medium Frequency Neuro-muscular Stimulator [promotional material]. North Miami (FL): EMHI. 1987 Feb. 2 p.

Electro-Medical Supplies (Greenham) Limited (EMS), Wantage, Oxfordshire, England. MEDI-LINK Electro-Therapy System [promotional material]. Wantage, Oxfordshire (England): EMS. 7 p.

Electro-Medical Supplies (Greenham) Limited (EMS), Wantage, Oxfordshire, England. The new EMS 950: cost effective interferential therapy [promotional material]. Wantage, Oxfordshire (England): EMS. 2 p.

[Electropharmacology, Pompano Beach, FL]. sofPulse [package insert]. Pompano Beach (FL): Magnetic Resonance Therapeutics, Inc. 2 p.

[Electro Therapeutics Devices, Inc., Markham, Ontario, Canada]. ACCU-O-MATIC VM2 advanced transcutaneous electro therapy device: puts effective pain management capabilities in your hands [promotional material]. [Markham, Ontario (Canada): Electro Therapeutic Devices]. 1988 Jan. 2 p.

ELMED Incorporated, Addison, IL. ELMED HVG 500 [promotional material]. Addison (IL): ELMED. 2 p.

EMPI, Inc., St. Paul, MN. ComfortPulse: the portable, medium frequency stimulator that reduces the pain of pain relief [promotional material]. St. Paul (MN): EMPI. 1993 Dec. 4 p.

EMPI, Inc., St. Paul, MN. Eclipse+. Raise your patient's comfort level. And yours [promotional material]. St. Paul (MN): EMPI. 1993 Aug. 4 p.

EMPI, Inc., St. Paul, MN. EPIX XL: advancing the limits of TENS technology [promotional material]. St. Paul (MN): EMPI. 1988. 4 p.

EMPI, Inc., St. Paul, MN. For the best in neuromuscular stimulation, you have to have a FOCUS [promotional material]. St. Paul (MN): EMPI. 2 p.

EMPI, Inc., St. Paul, MN. Respond Select Neuromuscular Stimulator [promotional material]. St. Paul (MN): EMPI. 1994 Jan. 4 p.

Eriksson G. Comparison of two occlusive bandages in the treatment of venous leg ulcers. Br J Dermatol 1986 Feb;114(2):227-30.

Eriksson SV, Lundeberg T, Malm M. A placebo controlled trial of ultrasound therapy in chronic leg ulceration. Scand J Rehabil Med 1991;23(4):211-3.

Excel Tech Ltd., Oakville, Ontario, Canada. Excel Ultra III. Accurately control the total energy transferred to your patient with the world's most advanced combination therapy system [promotional material]. Timonium (MD): Alan G. Day Corporation. 3 p.

Fakhri O, Amin MA. The effect of low-voltage electric therapy on the healing of resistant skin burns. J Burn Care Rehabil 1987 Jan-Feb;8(1):15-8.

Falanga V, Eaglstein WH, Bucalo B, Katz MH, Harris B, Carson P. Topical use of human recombinant epidermal growth factor (h-EGF) in venous ulcers. J Dermatol Surg Oncol 1992 Jul;18(7):604-6.

Feedar J, Kloth L, Gentzkow G. Chronic dermal ulcer healing enhanced with monophasic pulsed electrical stimulation [comment]. Phys Ther 1992 Jul;72(7):539.

Feedar JA, Kloth LC, Gentzkow GD. Chronic dermal ulcer healing enhanced with monophasic pulsed electrical stimulation. Phys Ther 1991 Sep;71(9):639-49.

Feedar JA, Kloth LC. Acceleration of wound healing with high voltage pulsating direct current [abstract]. Phys Ther 1985 May;65(5):741.

Fenn JE. Effect of pulsed electromagnetic energy (Diapulse) on experimental hematomas. Can Med Assoc J 1969 Feb 1; 100(5):251-4.

Finsen V, Persen L, Lovlien M, Veslegaard EK, Simensen M, Gasvann AK, Benum P. Transcutaneous electrical nerve stimulation after major amputation. J Bone Joint Surg Br 1988 Jan;70(1):109-12.

Fischer BH. Topical hyperbaric oxygen treatment of pressure sores and skin ulcers. Lancet 1969 Aug 23;2(617):405-9.

Fischer BH. Treatment of ulcers on the legs with hyperbaric oxygen. J Dermatol Surg 1975 Oct;1(3):55-8.

Fitzgerald GK, Newsome D. Treatment of a large infected thoracic spine wound using high voltage pulsed monophasic current. Phys Ther 1993 Jun;73(6):355-60.

Fleiss JL, Gross AJ. Meta-analysis in epidemiology, with special reference to studies of the association between exposure to environmental tobacco smoke and lung cancer: a critique. J Clin Epidemiol 1991;44(2):127-39.

Foulds IS, Barker AT. Human skin battery potentials and their possible role in wound healing. Br J Dermatol 1983 Nov;109(5):515-22.

Frantz RA, Gardner S, Harvey P, Specht J. Adoption of research-based practice for treatment of pressure ulcers in long-term care. Decubitus 1992 Jan;5(1):44-5, 48-54.

Frantz RA, Gardner S. Elderly skin care: principles of chronic wound care. J Gerontol Nurs 1994 Sep;20(9):35-44.

Frantz RA. The effectiveness of transcutaneous electrical nerve stimulation (TENS) on decubitus ulcer healing in adult patients. In: Funk SG, Tornquist EM, Champagne MT, Copp LA, Wiese RA, editors. Key aspects of recovery: improving nutrition, rest, and mobility. New York: Springer; 1990. p. 197-205.

Gault WR, Gatens PF Jr. Use of low intensity direct current in management of ischemic skin ulcers. Phys Ther 1976 Mar;56(3):265-9.

General Physiotherapy, Inc., St. Louis, MO. Porta-Puls II Muscle Stimulator: product bulletin [promotional material]. St. Louis (MO): General Physiotherapy. 2 p.

Gentzkow GD, Miller KH. Electrical stimulation for dermal wound healing. Clin Podiatr Med Surg 1991 Oct;8(4):827-41.

Gentzkow GD, Pollack SV, Kloth LC, Stubbs HA. Improved healing of pressure ulcers using Dermapulse, a new electrical stimulation device. Wounds 1991 Sep-Oct;3(5):158-70.

Gimmon Z, Wexler MR, Rachmilewitz EA. Juvenile leg ulceration in beta-thalassemia major and intermedia. Plast Reconstr Surg 1982 Feb;69(2):320-5.

Gogia PP, Marquez RR, Minerbo GM. Effects of high voltage galvanic stimulation on wound healing. Ostomy Wound Manage 1992 Jan-Feb;38(1):29-35.

Gogia PP, Marquez RR. Effects of helium-neon laser on wound healing. Ostomy Wound Manage 1992 Jul-Aug;38(6):33, 36, 38-41.

Goldin JH, Broadbent NR, Nancarrow JD, Marshall T. The effects of Diapulse on the healing of wounds: a double-blind randomised controlled trial in man. Br J Plast Surg 1981 Jul;34(3):267-70.

Gorse GJ, Messner RL. Improved pressure sore healing with hydrocolloid dressings. Arch Dermatol 1987 Jun;123(6):766-71.

Graber JN, Lifson A. The use of spinal cord stimulation for severe limb-threatening ischemia: a preliminary report. Ann Vasc Surg 1987 Dec;1(5):578-81.

Greaves MW, Ive FA. Double-blind trial of zinc sulphate in the treatment of chronic venous leg ulceration. Br J Dermatol 1972 Dec;87(6):632-4.

Greguric S, Budimcic D, Soldo-Belic A, Tudoric M, Baricevic B, Cajkovac V, Dobric I. Hydrocolloid dressing versus a conventional dressing using magnesium sulphate paste in the management of venous leg ulcers. Acta Derm Venereol 1994;2(2):65-71.

Griffin JW, Tooms RE, Mendius RA, Clifft JK, Vander Zwaag R, el-Zeky F. Efficacy of high voltage pulsed current for healing of pressure ulcers in patients with spinal cord injury. Phys Ther 1991 Jun;71(6):433-42; discussion 442-4.

Hallbook T, Lanner E. Serum-zinc and healing of venous leg ulcers. Lancet 1972 Oct 14;2(781):780-2.

Hammarlund C, Sundberg T. Hyperbaric oxygen reduced size of chronic leg ulcers: a randomized double-blind study. Plast Reconstr Surg 1994 Apr;93(4):829-33; discussion 834.

Handfield-Jones SE, Grattan CE, Simpson RA, Kennedy CT. Comparison of a hydrocolloid dressing and paraffin gauze in the treatment of venous ulcers. Br J Dermatol 1988 Mar;118(3):425-7.

Hedenius P, Odeblad E, Wahlstrom L. Some preliminary investigations on the therapeutic effect of pulsed short waves in intermittent claudication. Curr Ther Res Clin Exp 1966 Jul;8(7):317-21.

Hedges LV, Olkin I. Statistical methods for meta-analysis. Boston: Academic Press; 1985. 369 p.

Heng MC. Hyperbaric oxygen therapy for a foot ulcer in a patient with polyarteritis nodosa. Australas J Dermatol 1983 Dec;24(3):105-8.

Heng MC. Hyperbaric oxygen therapy for pyoderma gangrenosum. Aust N Z J Med 1984 Oct;14(5):618-21.

Henley International, Inc., Sugar Land, TX. Team*mate TRI-STIM: 3 modalities in one [promotional material]. Sugar Land (TX): Henley. 1994. 2 p.

Hillström L. Iodosorb compared to standard treatment in chronic venous leg ulcers--a multicenter study. Acta Chir Scand Suppl 1988;544:53-5; discussion 55-6.

Hoffmann G. Improvement of wound healing in chronic ulcers by hyperbaric oxygenation and by waterfiltered ultrared A induced localized hyperthermia. Adv Exp Med Biol 1994;345:181-8.

Holloway GA Jr, Johansen KH, Barnes RW, Pierce GE. Multicenter trial of cadexomer iodine to treat venous stasis ulcer. West J Med 1989 Jul;151(1):35-8.

Hondé C, Derks C, Tudor D. Local treatment of pressure sores in the elderly: amino acid copolymer membrane versus hydrocolloid dressing. J Am Geriatr Soc 1994 Nov;42(11):1180-3.

Hotta SS, Holohan TV. Procuren: a platelet-derived wound healing formula. Rockville (MD): U.S. Department of Health and Human Services, Public Health Service, Agency for Health Care Policy and Research (AHCPR); 1992 Jul. 3 p. AHCPR publication no. 92-0065. (Health technology review; no. 2).

Huovinen S, Kotilainen P, Jarvinen H, Malanin K, Sarna S, Helander I, Huovinen P. Comparison of ciprofloxacin or trimethoprim therapy for venous leg ulcers: results of a pilot study. J Am Acad Dermatol 1994 Aug;31(2 Pt 1):279-81.

Ieran M, Zaffuto S, Bagnacani M, Annovi M, Moratti A, Cadossi R. Effect of low frequency pulsing electromagnetic fields on skin ulcers of venous origin in humans: a double-blind study. J Orthop Res 1990 Mar;8(2):276-82.

ITO Co., Ltd., Tokyo, Japan. Dual-Channel TENS Model 120Z [promotional material]. Tokyo (Japan): ITO. 1 p.

ITO Co., Ltd., Tokyo, Japan. Microprocessor-controlled TENS 240Z: embodying an entirely new concept [promotional material]. Tokyo (Japan): ITO. 4 p.

ITO Co., Ltd., Tokyo, Japan. Stimulators, electroanalgesic, transcutaneous electrical nerve [table]. Tokyo (Japan): ITO. 1 p.

Itoh M, Montemayor JS Jr, Matsumoto E, Eason A, Lee MH, Folk FS. Accelerated wound healing of pressure ulcers by pulsed high peak power electromagnetic energy (Diapulse). Decubitus 1991 Feb;4(1):24-5, 29-34.

J A Preston Corp. [Preston product catalog]. Jackson (MI): Preston; Ultramax III H.V.P.G.S.; p. 164.

JACE Systems, Inc., Moorestown, NJ. Introducing JACE-STIM [promotional material]. Moorestown (NJ): JACE. 1992 May. 2 p.

Jayakumar K, Rajagopalan T, Sambasivan M, Bai S. Effect of pulsed electromagnetic field (PEMF) in cerebral oedema. Neurol India 1986;34:241-7.

Jeran M, Zaffuto S, Moratti A, Bagnacani M, Cadossi R. PEMF stimulation of skin ulcers of venous origin in humans: preliminary report of a double blind study. J Bioelectr 1987;6(2):181-8.

Jivegård L, Augustinsson LE, Carlsson CA, Holm J. Long-term results by epidural spinal electrical stimulation (ESES) in patients with inoperable severe lower limb ischaemia. Eur J Vasc Surg 1987 Oct;1(5):345-9.

Jivegård LE, Augustinsson LE, Holm J, Risberg B, Ortenwall P. Effects of spinal cord stimulation (SCS) in patients with inoperable severe lower limb ischaemia: a prospective randomised controlled study. Eur J Vasc Endovasc Surg 1995 May;9(4):421-5.

Kaada B, Emru M. Promoted healing of leprous ulcers by transcutaneous nerve stimulation. Acupunct Electrother Res 1988;13(4):165-76.

Kaada B. Promoted healing of chronic ulceration by transcutaneous nerve stimulation (TNS). Vasa 1983;12(3):262-9.

Kaplan EG, Weinstock RE. Clinical evaluation of Diapulse as adjunctive therapy following foot surgery. J Am Podiatry Assoc 1968 May;58(5):218-21.

Karba R, Vodovnik L, Presern-Strukelj M, Klesnik M. Promoted healing of chronic wounds due to electrical stimulation. Wounds 1991 Jan-Feb;3(1):16-23.

Katelaris PM, Fletcher JP, Little JM, McEntyre RJ, Jeffcoate KW. Electrical stimulation in the treatment of chronic venous ulceration. Aust N Z J Surg 1987 Sep;57(9):605-7.

Kesner, C.R. (DynaWave Corporation, Geneva, IL). Personal communication [letter]. 1996 Mar 16. 2 p.

Kikta MJ, Schuler JJ, Meyer JP, Durham JR, Eldrup-Jorgensen J, Schwarcz TH, Flanigan DP. A prospective, randomized trial of Unna's boots versus hydroactive dressing in the treatment of venous stasis ulcers. J Vasc Surg 1988 Mar;7(3):478-86.

Kincaid CB, Lavoie KH. Inhibition of bacterial growth in vitro following stimulation with high voltage, monophasic, pulsed current. Phys Ther 1989 Aug;69(8):651-5.

Kiwerski J, Chrostowska T. [Clinical use of pulsating electromagnetic energy in the treatment of spinal cord injuries]. Chir Narzadow Ruchu Ortop Pol 1980;45(3):273-7. (Pol).

Kjartansson J, Lundeberg T, Samuelson UE, Dalsgaard CJ. Transcutaneous electrical nerve stimulation (TENS) increases survival of ischaemic musculocutaneous flaps. Acta Physiol Scand 1988 Sep;134(1):95-9.

Kjartansson J, Lundeberg T. Effects of electrical nerve stimulation (ENS) in ischemic tissue. Scand J Plast Reconstr Surg Hand Surg 1990;24(2):129-34.

Kloth LC, Feedar JA. Acceleration of wound healing with high voltage, monophasic, pulsed current [published erratum appears in Phys Ther 1989 Aug;69(8):702]. Phys Ther 1988 Apr;68(4):503-8.

Kloth LC. Physical modalities in wound management: UVC, therapeutic heating and electrical stimulation. Ostomy Wound Manage 1995 Jun;41(5):18-20, 22-4, 26-7.

Knighton DR, Ciresi K, Fiegel VD, Schumerth S, Butler E, Cerra F. Stimulation of repair in chronic, nonhealing, cutaneous ulcers using platelet-derived wound healing formula. Surg Gynecol Obstet 1990 Jan;170(1):56-60.

Knighton DR, Ciresi KF, Fiegel VD, Austin LL, Butler EL. Classification and treatment of chronic nonhealing wounds. Successful treatment with autologous platelet-derived wound healing factors (PDWHF). Ann Surg 1986 Sep;204(3):322-9; discussion 329-30.

Knighton DR, Loss L. Design and implementation of clinical studies in chronic nonhealing wounds. Prog Clin Biol Res 1991;365:67-76.

Konikoff JJ. Electrical promotion of soft tissue repairs. Ann Biomed Eng 1976 Mar;4(1):1-5.

Korenstein R, Somjen D, Fischler H, Binderman I. Capacitative pulsed electric stimulation of bone cells. Induction of cyclic-AMP changes and DNA synthesis. Biochim Biophys Acta 1984 Apr 16;803(4):302-7.

Kraft MR, Lawson L, Pohlmann B, Reid-Lokos C, Barder L. A comparison of Epi-Lock and saline dressings in the treatment of pressure ulcers. Decubitus 1993 Nov;6(6):42-4, 46, 48.

Krupski WC, Reilly LM, Perez S, Moss KM, Crombleholme PA, Rapp JH. A prospective randomized trial of autologous platelet-derived wound healing factors for treatment of chronic nonhealing wounds: a preliminary report. J Vasc Surg 1991 Oct;14(4):526-32; discussion 532-6.

Laudanska H, Gustavson B. In-patient treatment of chronic varicose venous ulcers. A randomized trial of cadexomer iodine versus standard dressings. J Int Med Res 1988 Nov-Dec;16(6):428-35.

Layton AM, Ibbotson SH, Davies JA, Goodfield MJ. Randomised trial of oral aspirin for chronic venous leg ulcers. Lancet 1994 Jul 16;344(8916):164-5.

LeVasseur SA, Helme RD. A double-blind clinical trial to compare the efficacy of an active based cream F14001 against a placebo non-active based cream for the treatment of pressure ulcers in a population of elderly subjects. J Adv Nurs 1991 Aug;16(8):952-6.

Lundeberg T, Kjartansson J, Samuelsson U. Effect of electrical nerve stimulation on healing of ischaemic skin flaps. Lancet 1988 Sep 24;2(8613):712-4.

Lundeberg T, Malm M. Low-power HeNe laser treatment of venous leg ulcers. Ann Plast Surg 1991 Dec;27(6):537-9.

Lundeberg T, Nordstrom F, Brodda-Jansen G, Eriksson SV, Kjartansson J, Samuelson UE. Pulsed ultrasound does not improve healing of venous ulcers. Scand J Rehabil Med 1990;22(4):195-7.

Lundeberg TC, Eriksson SV, Malm M. Electrical nerve stimulation improves healing of diabetic ulcers. Ann Plast Surg 1992 Oct;29(4):328-31.

Malm M, Lundeberg T. Effect of low power gallium arsenide laser on healing of venous ulcers. Scand J Plast Reconstr Surg Hand Surg 1991;25(3):249-51.

Mann RJ. A double blind trial of oral O. B-hydroxyethyl rutosides for stasis leg ulcers. Br J Clin Pract 1981 Feb;35(2):79-81.

Margolis DJ, Cohen JH. Management of chronic venous leg ulcers: a literature-guided approach. Clin Dermatol 1994 Jan-Mar;12(1):19-26.

Masureik C, Eriksson C. Preliminary clinical evaluation of the effect of small electrical currents on the healing of jaw fractures. Clin Orthop 1977 May;(124):84-91.

Mawson AR, Siddiqui FH, Connolly BJ, Sharp CJ, Stewart GW, Summer WR, Biundo JJ Jr. Effect of high voltage pulsed galvanic stimulation on sacral transcutaneous oxygen tension levels in the spinal cord injured. Paraplegia 1993 May;31(5):311-9.

McCulloch JM, Marler KC, Neal MB, Phifer TJ. Intermittent pneumatic compression improves venous ulcer healing. Adv Wound Care 1994 Jul;7(4):22-4, 26.

McDiarmid T, Burns PN, Lewith GT, Machin D. Ultrasound and the treatment of pressure sores. Physiotherapy 1985 Feb;71(2):66-70.

Medical Devices, Inc., St. Paul, MN. FasTENS 30 [promotional material]. St. Paul (MN): Medical Devices. 1987. 1 p.

Medical Devices, Inc., St. Paul, MN. FasTENS [promotional material]. St. Paul (MN): Medical Devices. 1987. 1 p.

Medical Devices, Inc., St. Paul, MN. GV II High Voltage Pulsed Galvanic Stimulator...electromedical technology from Medical Devices, Inc. [promotional material]. St. Paul (MN): Medical Devices. 1990. 2 p.

Medical Devices, Inc., St. Paul, MN. IF II Interferential Stimulator...electromedical technology from Medical Devices, Inc. [promotional material]. St. Paul (MN): Medical Devices. 1989. 2 p.

Medical Devices, Inc., St. Paul, MN. Matrix I Programmed TENS [promotional material]. St. Paul (MN): Medical Devices. 1990. 8 p.

Medical Devices, Inc., St. Paul, MN. MC II Microcurrent Stimulator...electromedical technology from Medical Devices, Inc. [promotional material]. St. Paul (MN): Medical Devices. 1990. 2 p.

Medical Devices, Inc., St. Paul, MN. MediMOD [promotional material]. St. Paul (MN): Medical Devices. 1989. 2 p.

Medical Devices, Inc., St. Paul, MN. MENTOR 159 [promotional material]. St. Paul (MN): Medical Devices. 1988. 1 p.

Medical Devices, Inc., St. Paul, MN. MENTOR 259 [promotional material]. St. Paul (MN): Medical Devices. 1988. 1 p.

Medical Devices, Inc., St. Paul, MN. ULTRAPAC II SX PLUS [promotional material]. St. Paul (MN): Medical Devices. 1987. 1 p.

Medical Devices, Inc., St. Paul, MN. ULTRAPAC II SX [promotional material]. St. Paul (MN): Medical Devices. 1986. 1 p.

Meglio M, Cioni B, Dal Lago A, De Santis M, Pola P, Serricchio M. Pain control and improvement of peripheral blood flow following epidural spinal cord stimulation: case report. J Neurosurg 1981 Jun;54(6):821-3.

Mettler Electronics Corp., Anaheim, CA. Sonicator Plus: get it together [promotional material]. Anaheim (CA): Mettler Electronics. 1993 Oct. 2 p.

Mettler Electronics Corp., Anaheim, CA. Sys*Stim 206: the very affordable, portable stimulator [promotional material]. Anaheim (CA): Mettler Electronics. 1994 May. 2 p.

Mettler Electronics Corp., Anaheim, CA. Sys*Stim 206A: our proven performer now brings more flexibility and control to the table [promotional material]. Anaheim (CA): Mettler Electronics. 1994 Mar. 2 p.

Mettler Electronics Corp., Anaheim, CA. Sys*Stim 207A: the stimulator famous for its extra muscle now packs a one-two punch [promotional material]. Anaheim (CA): Mettler Electronics. 1994 Mar. 2 p.

Mettler Electronics Corp., Anaheim, CA. Sys*Stim 220: it's never been easier to get the beat... with full-featured interferential therapy from Mettler [promotional material]. Anaheim (CA): Mettler Electronics. 1994 Mar. 2 p.

Moberg S, Hoffman L, Grennert ML, Holst A. A randomized trial of cadexomer iodine in decubitus ulcers. J Am Geriatr Soc 1983 Aug;31(8):462-5.

Mulder GD. Treatment of open-skin wounds with electric stimulation. Arch Phys Med Rehabil 1991 May;72(6):375-7.

Murray JC, Farndale RW. Modulation of collagen production in cultured fibroblasts by a low-frequency, pulsed magnetic field. Biochim Biophys Acta 1985 Jan 28;838(1):98-105.

Mustoe TA, Cutler NR, Allman RM, Goode PS, Deuel TF, Prause JA, Bear M, Serdar CM, Pierce GF. A phase II study to evaluate recombinant platelet-derived growth factor-BB in the treatment of stage 3 and 4 pressure ulcers. Arch Surg 1994 Feb;129(2):213-9.

N H Eastwood & Son Ltd., Hertfordshire, England. Mini-Tens: range of transcutaneous electrical nerve stimulators [promotional material]. Hertfordshire (England): N H Eastwood & Son. 4 p.

National Center for Health Services Research (NCHSR). Public Health Service assessment of hydrotherapy (whirlpool) baths for treatment of decubitus ulcers, 1981. Rockville (MD): U.S. Department of Health and Human Services, Public Health Service, Office of the Assistant Secretary for Health, NCHSR; 1981. 5 p. (Health technology assessment series, 1981; no. 2).

National Center for Health Services Research (NCHSR). Public Health Service assessment of ultraviolet light treatment for decubitus ulcers, 1981. Rockville (MD): U.S. Department of Health and Human Services, Public Health Service, Office of the Assistant Secretary for Health, NCHSR; 1981. 8 p. (Health technology assessment series, 1981; no. 3).

Neill KM, Conforti C, Kedas A, Burris JF. Pressure sore response to a new hydrocolloid dressing. Wounds 1989 Nov;1(3):173-85.

Nikolova K. Treatment of post-phlebitic syndrome and venous leg ulcers with flunarizine. Methods Find Exp Clin Pharmacol 1994 Oct;16(8):609-13.

Nussbaum EL, Biemann I, Mustard B. Comparison of ultrasound/ultraviolet-C and laser for treatment of pressure ulcers in patients with spinal cord injury. Phys Ther 1994 Sep;74(9):812-23; discussion 824-5.

Ohlsson P, Larsson K, Lindholm C, Moller M. A cost-effectiveness study of leg ulcer treatment in primary care. Comparison of saline-gauze and hydrocolloid treatment in a prospective, randomized study. Scand J Prim Health Care 1994 Dec;12(4):295-9.

Olejniczak S, Zielinski A. Low hyperbaric therapy in management of leg ulcers. Mich Med 1975 Nov;74(32):707-12.

Oleske DM, Smith XP, White P, Pottage J, Donovan MI. A randomized clinical trial of two dressing methods for the treatment of low-grade pressure ulcers. J Enterostomal Ther 1986 May-Jun;13(3):90-8.

OMS Medical Supplies. OMS Medical Supplies 1992-93 catalog; p. 36-9.

OMS Medical Supplies. OMS new products supplement and price list for 1992-93 catalog; 1995 Jan. p. 14.

Ormiston MC, Seymour MT, Venn GE, Cohen RI, Fox JA. Controlled trial of Iodosorb in chronic venous ulcers. Br Med J (Clin Res Ed) 1985 Aug 3;291(6491):308-10.

Orwin RG. A fail-safe N for effect size in meta-analysis. J Educ Stat 1983 Summer;8(2):157-9.

Pennington GM, Danley DL, Sumko MH, Bucknell A, Nelson JH. Pulsed, non-thermal, high-frequency electromagnetic energy (DIAPULSE) in the treatment of grade I and grade II ankle sprains. Mil Med 1993 Feb;158(2):101-4.

Petitti DB. Meta-analysis, decision analysis, and cost-effectiveness analysis: methods for quantitative synthesis in medicine. New York: Oxford University Press; 1994. Chapter 8, Other statistical issues in meta-analysis; p. 115-30. (Monographs in epidemiology and biostatistices; vol. 24).

Petitti DB. Meta-analysis, decision analysis, and cost-effectiveness analysis: methods for quantitative synthesis in medicine. New York: Oxford University Press; 1994. 246 p. (Monographs in epidemiology and biostatistics; vol. 24).

Phillips A, Davidson M, Greaves MW. Venous leg ulceration: evaluation of zinc treatment, serum zinc and rate of healing. Clin Exp Dermatol 1977 Dec;2(4):395-9.

Piérard GE, Piérard-Franchimont C. Planimetry of the healing rate of leg ulcers. Eur J Dermatol 1995 Apr-May;5(3):257-62.

Pierce GF, Tarpley JE, Allman RM, Goode PS, Serdar CM, Morris B, Mustoe TA, Vande Berg J. Tissue repair processes in healing chronic pressure ulcers treated with recombinant platelet-derived growth factor BB. Am J Pathol 1994 Dec;145(6):1399-410.

Politis MJ, Zanakis MF, Miller JE. Enhanced survival of full-thickness skin grafts following the application of DC electrical fields. Plast Reconstr Surg 1989 Aug;84(2):267-72.

Poskitt KR, James AH, Lloyd-Davies ER, Walton J, McCollum C. Pinch skin grafting or porcine dermis in venous ulcers: a randomised clinical trial. Br Med J (Clin Res Ed) 1987 Mar 14;294(6573):674-6.

Pressure ulcers prevalence, cost and risk assessment: consensus development conference statement--The National Pressure Ulcer Advisory Panel. Decubitus 1989 May;2(2):24-8.

PTI, Topeka, KS. PTI Omnisound Combination Therapy 2500C System [promotional material]. Topeka (KS): PTI. 1993 Jul. 6 p.

PTI, Topeka, KS. PTI Omnistim 500 Portable/Clinical Multi-Modality Electrotherapy and Rehabilitation System [promotional material]. Topeka (KS): PTI. 1993 Mar. 4 p.

Queral LA, Criado FJ, Lilly MP, Rudolphi D. The role of sclerotherapy as an adjunct to Unna's boot for treating venous ulcers: a prospective study. J Vasc Surg 1990 Apr;11(4):572-5.

R.J. Lindquist Co., Los Angeles, CA. Introducing Model 370: with high voltage galvanic [promotional material]. Los Angeles (CA): Lindquist. 2 p.

R.J. Lindquist Co., Los Angeles, CA. Introducing the CHRONOWAVE: low voltage generator [promotional material]. Los Angeles (CA): Lindquist. 2 p.

R.J. Lindquist Co., Los Angeles, CA. MINISOUND Model 600 Ultrasound [promotional material]. Los Angeles (CA): Lindquist. 2 p.

Raji AR, Bowden RE. Effects of high-peak pulsed electromagnetic field on the degeneration and regeneration of the common peroneal nerve in rats. J Bone Joint Surg Br 1983 Aug;65(4):478-92.

Rasmussen LH, Avnstorp C, Karlsmark T, Peters K, Horslev-Petersen K. Dose-response study of human growth hormone in venous ulcers: influence on healing and synthesis of collagen types I and III. Phlebology 1994;9(3):92-8.

Rasmussen LH, Karlsmark T, Avnstorp C, Peters K, Jorgensen M, Jensen LT. Topical human growth hormone treatment of chronic leg ulcers. Phlebology 1991;6(1):23-30.

Reger SI, Hyodo A, Reyes ET, Browne EZ. Treatment of pressure ulcers by electrical stimulation. Rehabil Res Dev Prog Rep 1992;29:467-8.

Resch CS, Kerner E, Robson MC, Heggers JP, Scherer M, Boertman JA, Schileru R. Pressure sore volume measurement. A technique to document and record wound healing. J Am Geriatr Soc 1988 May;36(5):444-6.

Rhodes C. The adjunctive utilization of Diapulse therapy (pulsed high peak power electromagnetic energy) in accelerating tissue healing in oral surgery. The Quarterly, NDA 1981 Jul;39(4):166-75 contd.

Rhodes C. The adjunctive utilization of Diapulse therapy (pulsed high peak power electromagnetic energy) in accelerating tissue healing in oral surgery. The Quarterly, NDA 1981 Oct;40(1):4-11 concl.

Rich-Mar Corporation, [Inola, OK]. Rich-Mar III and III-G: economical and portable low volt stimulators [promotional material]. [Inola (OK)]: Rich-Mar. 2 p.

Rich-Mar Corporation, [Inola, OK]. Rich-Mar Theratouch 3.3: a new twist in electrotherapy [promotional material]. [Inola (OK)]: Rich-Mar. 1994. 2 p.

Rich-Mar Corporation, [Inola, OK]. Rich-Mar Theratouch 4.7: a stimulator that actually improves with age [promotional material]. [Inola (OK)]: Rich-Mar. 1994. 2 p.

Richard JL, Parer-Richard C, Daures JP, Clouet S, Vannereau D, Bringer J, Rodier M, Jacob C, Comte-Bardonnet M. Effect of topical basic fibroblast growth factor on the healing of chronic diabetic neuropathic ulcer of the foot. A pilot, randomized, double-blind, placebo-controlled study. Diabetes Care 1995 Jan;18(1):64-9.

Richardson RR, Cerullo LJ, Meyer PR. Autonomic hyper-reflexia modulated by percutaneous epidural neurostimulation: a preliminary report. Neurosurgery 1979 Jun;4(6):517-20.

Richmond MN, Galbraith KA, Rogerson JT. Hyperbaric oxygen for a thalassaemic leg ulcer. J R Army Med Corps 1987 Feb;133(1):23-5.

Robson MC, Phillips LG, Lawrence WT, Bishop JB, Youngerman JS, Hayward PG, Broemeling LD, Heggers JP. The safety and effect of topically applied recombinant basic fibroblast growth factor on the healing of chronic pressure sores. Ann Surg 1992 Oct;216(4):401-6; discussion 406-8.

Robson MC, Phillips LG, Thomason A, Altrock BW, Pence PC, Heggers JP, Johnston AF, McHugh TP, Anthony MS, Robson LE, et al. Recombinant human platelet-derived growth factor-BB for the treatment of chronic pressure ulcers. Ann Plast Surg 1992 Sep;29(3):193-201.

Robson MC, Phillips LG, Thomason A, Robson LE, Pierce GF. Platelet-derived growth factor BB for the treatment of chronic pressure ulcers. Lancet 1992 Jan 4;339(8784):23-5.

Rodeheaver G, Baharestani MM, Brabec ME, Byrd HJ, Salzberg CA, Scherer P, Vogelpohl TS. Wound healing and wound management: focus on debridement. An interdisciplinary round table, September 18, 1992, Jackson Hole, WY. Adv Wound Care 1994 Jan;7(1):22-4, 26-9, 32-6; quiz 37-9.

Roe BH, Griffiths JM, Kenrick M, Cullum NA, Hutton JL. Nursing treatment of patients with chronic leg ulcers in the community. J Clin Nurs 1994 May;3(3):159-68.

Roelens P. Double-blind placebo-controlled study with topical 2% ketanserin ointment in the treatment of venous ulcers. Dermatologica 1989;178(2):98-102.

Romanko KP. Pressure ulcers. Clin Podiatr Med Surg 1991 Oct;8(4):857-67.

Rosenthal AM, Schurman A. Hyperbaric treatment of pressure sores. Arch Phys Med Rehabil 1971 Sep;52(9):413-5, 433.

Rosenthal R. Meta-analytic procedures for social research. Rev. ed. Newbury Park (CA): Sage Publications; 1991. Chapter 5, Combining probabilities; p. 89-109. (Applied social research methods series; vol. 6).

Rosenthal R. Meta-analytic procedures for social research. Rev. ed. Newbury Park (CA): Sage Publications; 1991. Chapter 2, Defining research results; p. 13-35. (Applied social research methods series; vol. 6).

Rosenthal R. Meta-analytic procedures for social research. Rev. ed. Newbury Park (CA): Sage Publications; 1991. Chapter 4, Comparing and combining research results; p. 59-88. (Applied social research methods series; vol. 6).

Ross CR, Segal D. High voltage galvanic stimulation: an aid to post-operative healing. Curr Podiatry 1981;30(5):19-25.

Ross, Jesse, D.Sci. (Diapulse Corporation of America, Great Neck, NY). Personal communication [letter]. 1996 Mar 15. 16 p.

Rubin JR, Alexander J, Plecha EJ, Marman C. Unna's boot vs polyurethane foam dressings for the treatment of venous ulceration. A randomized prospective study. Arch Surg 1990 Apr;125(4):489-90.

Rudofsky G. Intravenous prostaglandin E1 in the treatment of venous ulcers--a double-blind, placebo-controlled trial. Vasa Suppl 1989;28:39-43.

Sacks H, Chalmers TC, Smith H Jr. Randomized versus historical controls for clinical trials. Am J Med 1982 Feb;72(2):233-40.

Sale & Service, S.L., Electromedicina, Spain. TENS 3002 Pro - multifunción: transcutaneous electrical nerve stimulator (dual channel) [promotional material]. Spain: Sale & Service. 2 p.

Salzberg CA, Cooper-Vastola SA, Perez F, Viehbeck MG, Byrne DW. The effects of non-thermal pulsed electromagnetic energy on wound healing of pressure ulcers in spinal cord-injured patients: a randomized, double-blind study. Ostomy Wound Manage 1995 Apr;41(3):42-4, 46, 48 passim.

Sambasivan M. Pulsed electromagnetic field in management of head injuries. Neurol India 1993;41 Suppl:56-9.

Savage K, Siebert E, Swann D. The effect of platelet-derived growth factor on cell division and glycosaminoglycan synthesis by human skin and scar fibroblasts. J Invest Dermatol 1987 Jul;89(1):93-9.

Sebern MD. Pressure ulcer management in home health care: efficacy and cost effectiveness of moisture vapor permeable dressing. Arch Phys Med Rehabil 1986 Oct;67(10):726-9.

Sheps SB. Hyperbaric oxygen for osteomyelitis and osteoradionecrosis. Vancouver, British Columbia (Canada): British Columbia Office of Health Technology Assessment, Centre for Health Services & Policy Research; 1992 Oct. 21 p. (British Columbia Office of Health Technology Assessment discussion paper series).

Smith BA. The dressing makes the difference. Trial of two modern dressings on venous ulcers. Prof Nurse 1994 Feb;9(5):348, 350-2.

Smith DM. Pressure ulcers in the nursing home. Ann Intern Med 1995 Sep 15;123(6):433-42.

Smith PC, Sarin S, Hasty J, Scurr JH. Sequential gradient pneumatic compression enhances venous ulcer healing: a randomized trial. Surgery 1990 Nov;108(5):871-5.

Sourifman HA, Thomas MP, Epstein DL. Hyperbaric oxygenation and ulcer treatment: a case report. J Am Podiatry Assoc 1981 Jul;71(7):381-5.

Sporn MB, Roberts AB, Wakefield LM, Assoian RK. Transforming growth factor-beta: biological function and chemical structure. Science 1986 Aug 1;233(4763):532-4.

ST - Electromedicina, S.A., Barcelona, Spain. Sarria ST-110: electrotherapy unit [promotional material]. Barcelona (Spain): ST. 2 p.

ST - Electromedicina, S.A., Barcelona, Spain. Sarria ST-120: electrotherapy unit [promotional material]. Barcelona (Spain): ST. 2 p.

Staodyn, Inc., Longmont, CO. Advanced TENS products [promotional material]. Longmont (CO): Staodyn. 1990. 6 p.

Staodyn, Inc., Longmont, CO. Dermapulse for accelerated healing [promotional material]. Longmont (CO): Staodyn. 1994. 4 p.

Staodyn, Inc., Longmont, CO. EMS+2 Neuromuscular Stimulator. EMS+2 puts you in control [promotional material]. Longmont (CO): Staodyn. 2 p.

Staodyn, Inc., Longmont, CO. Introducing TUWAVE the 2 in one modality [promotional material]. Longmont (CO): Staodyn. 1992. 4 p.

Staodyn, Inc., Longmont, CO. Maxima II TENS: a powerful multi-mode unit that's easy to use [promotional material]. Longmont (CO): Staodyn. 2 p.

Staodyn, Inc., Longmont, CO. Maxima III TENS: strength duration modulation combined with intelligence [promotional material]. Longmont (CO): Staodyn. 1990. 2 p.

Staodyn, Inc., Longmont, CO. Maxima III: reflex sympathetic dystrophy syndrome. TENS clinical guidelines. Longmont (CO): Staodyn. 1990. 4 p.

Staodyn, Inc., Longmont, CO. NUWAVE: the unconventional pain management modality [promotional material]. Longmont (CO): Staodyn. 1992. 2 p.

Steed DL, Goslen JB, Holloway GA, Malone JM, Bunt TJ, Webster MW. Randomized prospective double-blind trial in healing chronic diabetic foot ulcers. CT-102 activated platelet supernatant, topical versus placebo. Diabetes Care 1992 Nov;15(11):1598-604.

Steed DL. Clinical evaluation of recombinant human platelet-derived growth factor for the treatment of lower extremity diabetic ulcers. Diabetic Ulcer Study Group. J Vasc Surg 1995 Jan;21(1):71-8; discussion 79-81.

Stefanovska A, Vodovnik L, Benko H, Turk R. Treatment of chronic wounds by means of electric and electromagnetic fields. Part 2. Value of FES parameters for pressure sore treatment. Med Biol Eng Comput 1993 May;31(3):213-20.

Stiller MJ, Pak GH, Shupack JL, Thaler S, Kenny C, Jondreau L. A portable pulsed electromagnetic field (PEMF) device to enhance healing of recalcitrant venous ulcers: a double-blind, placebo-controlled clinical trial. Br J Dermatol 1992 Aug;127(2):147-54.

Stillwell GK. Therapeutic heat and cold. In: Krusen FH, editor. Handbook of physical medicine and rehabilitation. 2nd ed. Philadelphia: Saunders; 1971. p. 259-72.

Szuminsky NJ, Albers AC, Unger P, Eddy JG. Effect of narrow, pulsed high voltages on bacterial viability. Phys Ther 1994 Jul;74(7):660-7.

T.H. Charters, Inc., Beaverton, OR. ElectroBLOC [promotional material]. Beaverton (OR): T.H. Charters. 2 p.

T.H. Charters, Inc., Beaverton, OR. EXER-STIM 2 Dual Channel Muscle Stimulator [promotional material]. Beaverton (OR): T.H. Charters. 2 p.

T.H. Charters, Inc., Beaverton, OR. EXER-STIM Single Channel Muscle Stimulator [promotional material]. Beaverton (OR): T.H. Charters. 2 p.

T.H. Charters, Inc., Beaverton, OR. MINI-1 TENS [promotional material]. Beaverton (OR): T.H. Charters. 1 p.

T.H. Charters, Inc., Beaverton, OR. Myopulse Stimulator relieves muscle fatigue spasm [promotional material]. Beaverton (OR): T.H. Charters. 2 p.

T.H. Charters, Inc., Beaverton, OR. NeuroPulser 2+ TENS [promotional material]. Beaverton (OR): T.H. Charters. 1991. 2 p.

Taylor TV, Rimmer S, Day B, Butcher J, Dymock IW. Ascorbic acid supplementation in the treatment of pressure-sores. Lancet 1974 Sep 7;2(7880):544-6.

Teepe RG, Roseeuw DI, Hermans J, Koebrugge EJ, Altena T, de Coninck A, Ponec M, Vermeer BJ. Randomized trial comparing cryopreserved cultured epidermal allografts with hydrocolloid dressings in healing chronic venous ulcers. J Am Acad Dermatol 1993 Dec;29(6):982-8.

ter Riet G, Kessels AG, Knipschild P. Randomised clinical trial of ultrasound treatment for pressure ulcers [published erratum appears in BMJ 1995 May 20;310(6990):1300]. BMJ 1995 Apr 22;310(6986):1040-1.

Thurman BF, Christian EL. Response of a serious circulatory lesion to electrical stimulation. Phys Ther 1971 Oct;51(10):1107-10.

Titan Electronics Ltd., Tiberias, Israel. Compact-TENS: a compact system for pain relief [promotional material]. Tiberias (Israel): Titan. 3 p.

Titan Electronics Ltd., Tiberias, Israel. Wave away menstrual pain with TiCi-EL [promotional material]. Tiberias (Israel): Titan. 15 p.

Todd DJ, Heylings DJ, Allen GE, McMillin WP. Treatment of chronic varicose ulcers with pulsed electromagnetic fields: a controlled pilot study. Ir Med J 1991 Jun;84(2):54-5.

Tung S, Khaski A, Milano E, Kay C. The application of Diapulse in the treatment of decubitus ulcers: case reports. Contemp Surg 1995 Jul;47(1):27-32.

Ultraschall Dr. Born GmbH, Frankfurt, Germany. Ultraschall press release. Two in one therapy unit: ultrasonic and stimulus current [promotional material]. Frankfurt (Germany): Ultraschall. 1993 Nov. 3 p.

Unger P, Eddy J, Raimastry S. A controlled study of the effect of high voltage pulse current (HVPC) on wound healing [abstract]. Phys Ther 1991 Jun;71(6 Suppl):S119.

Unger PG. A randomized clinical trial of the effect of HVPC on wound healing [abstract]. Phys Ther 1991 Jun;71(6 Suppl):S118.

Universal Technology Systems, Inc., (UTS), Jacksonville, FL. Therapy through new technology: introducing the PGS-3000 Portable Pulsed Galvanic Stimulator [promotional material]. Jacksonville (FL): UTS. 2 p.

University Hospital Consortium (UHC), Technology Advancement Center. Guidelines for the use of pressure relief devices in the treatment and prevention of pressure ulcers. Oak Brook (IL): UHC; 1990. [various pagings].

Upson AV. Topical hyperbaric oxygenation in the treatment of recalcitrant open wounds. A clinical report. Phys Ther 1986 Sep;66(9):1408-12.

Valtonen V, Karppinen L, Kariniemi AL. A comparative study of ciprofloxacin and conventional therapy in the treatment of patients with chronic lower leg ulcers infected with Pseudomonas aeruginosa or other gram-negative rods. Scand J Infect Dis Suppl 1989;60:79-83.

Vassa N, Twardowski ZJ, Campbell J. Hyperbaric oxygen therapy in calciphylaxis-induced skin necrosis in a peritoneal dialysis patient. Am J Kidney Dis 1994 Jun;23(6):878-81.

Verimed, Fort Lauderdale, FL. Introducing the Veristim II: the ultimate hand held, combination surface EMG - neuro muscular electrical stimulator [promotional material]. Fort Lauderdale (FL): Verimed. 2 p.

Verimed, Fort Lauderdale, FL. Phyaction 780 series has it all...and then some! [promotional material]. Fort Lauderdale (FL): Verimed. 2 p.

Vodovnik L, Karba R. Treatment of chronic wounds by means of electric and electromagnetic fields. Part 1. Literature review. Med Biol Eng Comput 1992 May;30(3):257-66.

Wasserteil V, Bruce S, Sessoms SL, Guntupalli KK. Pyoderma gangrenosum treated with hyperbaric oxygen therapy. Int J Dermatol 1992 Aug;31(8):594-6.

Wattel F, Mathieu D, Coget JM, Billard V. Hyperbaric oxygen therapy in chronic vascular wound management. Angiology 1990 Jan;41(1):59-65.

Weingarten MS. Advances in wound healing. In: Oloff LM. Musculoskeletal disorders of the lower extremities. Philadelphia: Saunders; 1994. p. 52-64.

Weingarten MS. Review: obstacles to wound healing. Wounds 1993 Sep-Oct;5(5):238-44.

Weiss DS, Eaglstein WH, Falanga V. Exogenous electric current can reduce the formation of hypertrophic scars. J Dermatol Surg Oncol 1989 Dec;15(12):1272-5.

Weiss DS, Kirsner R, Eaglstein WH. Electrical stimulation and wound healing. Arch Dermatol 1990 Feb;126(2):222-5.

Werner-Schlenzka H, Kuhlmann RK. Treatment of venous leg ulcers with topical iloprost: a placebo controlled study. Vasa 1994;23(2):145-50.

Westerhof W, Bos JD. Trigeminal trophic syndrome: a successful treatment with transcutaneous electrical stimulation. Br J Dermatol 1983 May;108(5):601-4.

Wills EE, Anderson TW, Beattie BL, Scott A. A randomized placebo-controlled trial of ultraviolet light in the treatment of superficial pressure sores. J Am Geriatr Soc 1983 Mar;31(3):131-3.

Wilson DH, Jagadeesh P. Experimental regeneration in peripheral nerves and the spinal cord in laboratory animals exposed to a pulsed electromagnetic field. Paraplegia 1976 May;14(1):12-20.

Wilson DH. Comparison of short wave diathermy and pulsed electromagnetic energy in treatment of soft tissue injuries. Physiotherapy 1974 Oct;60(10):309-10.

Wilson DH. Treatment of soft-tissue injuries by pulsed electrical energy. Br Med J 1972 Apr 29;2(808):269-70.

Wiseman DM, Rovee DT, Alvarez OM. Wound dressings: design and use. In: Cohen IK, Diegelmann RF, Lindblad WJ, editors. Wound healing: biochemical & clinical aspects. Philadelphia: Saunders; 1992. p. 562-80.

Wolcott LE, Wheeler PC, Hardwicke HM, Rowley BA. Accelerated healing of skin ulcer by electrotherapy: preliminary clinical results. South Med J 1969 Jul;62(7):795-801.

Wood JM, Evans PE 3rd, Schallreuter KU, Jacobson WE, Sufit R, Newman J, White C, Jacobson M. A multicenter study on the use of pulsed low-intensity direct current for healing chronic stage II and stage III decubitus ulcers. Arch Dermatol 1993 Aug;129(8):999-1009.

Wound, Ostomy and Continence Nurses Society (WOCN). Standards of care. Patients with dermal wounds: lower extremity ulcers. Costa Mesa (CA): WOCN; 1993. 50 p.

Wound, Ostomy and Continence Nurses Society (WOCN). Standards of care. Patients with dermal wounds: pressure ulcers. Costa Mesa (CA): WOCN; 1992. 40 p.

Xakellis GC, Chrischilles EA. Hydrocolloid versus saline-gauze dressings in treating pressure ulcers: a cost-effectiveness analysis. Arch Phys Med Rehabil 1992 May;73(5):463-9.

Yen-Patton GP, Patton WF, Beer DM, Jacobson BS. Endothelial cell response to pulsed electromagnetic fields: stimulation of growth rate and angiogenesis in vitro. J Cell Physiol 1988 Jan;134(1):37-46.

Young W. Pulsed electromagnetic fields alter calcium in spinal cord injury. Presented at: The 75th Meeting of the Society of Neurological Surgeons; 1984 Apr 25-28; New York; [1984]. 2 p.