DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

Fiscal Year 2005 Budget Request

Witness appearing before the
Senate Subcommittee on Labor-HHS-Education Appropriations

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April 1, 2004

William Beldon, Acting Deputy Assistant Secretary, Budget

Mr. Chairman and Members of the Committee:

I am pleased to present the President's budget request for the National Institute of Biomedical Imaging and Bioengineering (NIBIB) of the National Institutes of Health (NIH). The fiscal year (FY) 2005 budget includes $297,647,000, an increase of $8,817,000 over the FY 2004 enacted level of $288,830,000 over the comparable FY 2004 appropriation.

The NIBIB's mission is to improve human health by leading the development and accelerating the application of biomedical technologies. The Institute is committed to integrating the physical and engineering sciences with the life sciences to advance basic research and health care. Our vision is to profoundly change healthcare by pushing the frontiers of technology to make the possible a reality.

PROGRESS TOWARDS SUCCESS

Established by law in December 2000, the NIBIB has already demonstrated an impressive track record as a conscientious steward of public funds and has achieved significant milestones. In FY 2003 the NIBIB funded approximately 750 awards, including 300 new awards that received outstanding scores in a highly competitive peer review system. Consistent with our mission, approximately one-third of our new awards were for innovative, high-impact, though high-risk, exploratory studies. These studies addressed the feasibility of a novel avenue of investigation and/or breakthroughs in biomedical imaging and bioengineering within a specific area. The Institute has also been effective at reaching segments of the scientific community that traditionally have not been supported by the NIH, especially those from the engineering and quantitative sciences. Between the first and second years of our grant-making authority, proposals to the NIBIB from first-time NIH applicants increased significantly. In FY 2003, approximately 50 percent of respondents to requests for targeted applications identified themselves as first-time NIH applicants.

The Institute has built a solid research infrastructure through the issuance of numerous basic and applied research solicitations in promising areas of scientific investigation. Responses to the Institute's targeted initiatives far exceeded even the most optimistic estimates based on prior NIH experience. Coupling this to the successful outreach to new applicants and to the science community, it is clear that NIBIB is filling an important need with regard to catalyzing interdisciplinary science and supporting engineering research aimed at translating scientific discoveries to practical applications.

The NIBIB continues to foster successful linkages and collaborations with other NIH Institutes and Centers, Federal agencies, academic institutions, and private industry. We regard input from industry as critical for helping to identify research needs that will result in significant healthcare improvements as well as for translating technologies and research results to patient applications. As a first step in establishing collaboration with the biomedical industry, the NIBIB sponsored a workshop on "Biomedical Industry Research and Training Opportunities" in December 2003. Recommendations from this meeting will be considered in the planning and development of future NIBIB programs.

ADVANCING TOMORROW'S TECHNOLOGIES TODAY

Biomedical imaging and bioengineering are interdisciplinary fields requiring collaborations not only among imagers and engineers, but also with biologists, chemists, mathematicians, computer scientists, and clinicians of all specialties. Today, the imaging and engineering sciences are essential for improved understanding of biological systems, detecting and treating disease, and improving human health. Recent advances in these fields have enabled the diagnosis and treatment of various diseases using increasingly less invasive procedures. Benefits associated with minimally invasive imaging applications include quicker and more accurate diagnoses leading to improved patient outcomes at reduced costs. Minimally invasive image-guided interventions now serve as powerful tools in the operating room and can be applied to surgical procedures in urology, oncology, neurosurgery, ophthalmology, orthopedics, and cardiology.

The quest for faster and more effective minimally invasive surgical interventions has resulted in the introduction of computer-assisted robotic technology, whereby the surgeon works with small tools through small incisions. However, current instrumentation prohibits the surgeon from actually feeling the forces exerted when manipulating tissue. This lack of sensory control can be particularly detrimental in surgery, where the forces applied to sutures are critical in creating knots that are strong enough to hold, but do not damage the tissue. To overcome this problem, NIBIB investigators are developing instruments with three-dimensional sensors designed to give the surgeon a feeling comparable to that of performing the task manually. This research has additional applications as well, including expert-assisted surgery in remote locations.

Magnetic resonance imaging (MRI) has been used successfully for over 15 years to generate soft tissue images of the human body. However, a number of diagnostic MRI applications require further improvements in both imaging speed and spatial resolution. For example, accurate abdominal imaging generally requires a complete image obtained during a single "breath-hold" period, which can take up to 30 seconds. Many patients, especially those with respiratory illnesses, cannot tolerate long breath-holds. The NIBIB supports an active research program on optimizing MRI speed and spatial resolution. One new approach under study, called parallel imaging, collects MRI signals from a number of independent coil shaped antennas. The appropriate combination of these signals can provide an order of magnitude improvement in imaging speed or resolution. Enhancements such as this hold promise for greatly enhancing the non-invasive diagnosis and treatment of abdominal and neurological diseases.

Functional magnetic resonance imaging (fMRI) is a relatively new technique that builds on the basic properties of MRI to measure quick and tiny blood flow related metabolic changes that take place in the active brain. Thus, fMRI studies are capable of providing not only an anatomical view of the brain, but a minute-to-minute recording of actual brain activity. This technology is now being used by NIBIB researchers to precisely map functional areas of the normal, diseased, and injured brain and to assess risks associated with surgery or other invasive treatments. Functional MRI can help physicians determine exactly which parts of the brain are responsible for specific crucial functions such as thought, speech, movement, and sensation. This information allows physicians to better plan surgeries and radiation therapies and to guide interventional strategies for a variety of brain disorders.

Molecular imaging provides a way to monitor cellular activities in normal and diseased states. The development of novel imaging technologies, combined with new or enhanced probes that bind to and "highlight" defined cellular targets, will allow this technique to be more broadly applied to biomolecules that are known indicators of a diseased state. For example, NIBIB researchers have developed nanometer sized fluorescent crystals, called quantum dots, that glow and can act as markers for specific cells when bound to certain targeting agents such as cancer cell antibodies. These agents can more precisely pinpoint the location of the sentinel lymph node in breast cancer patients. The sentinel node (SN) is the first node in the body to come into contact with cancer cells as they leave the breast and begin to spread to the rest of the body. Testing for metastatic cancer cells in the SN allows for accurate staging using information from a single lymph node, rather than 10 to 15 axillary nodes, and allows patients to avoid many of the complications and side effects associated with a traditional axillary lymph node dissection.

Advances in bioinformatics have been identified as having great potential for positively impacting medical science and health care. NIBIB researchers are developing and evaluating several innovative technologies designed to help solve the information management problems faced by today's doctors. Concepts enveloped in this system include a medical record architecture designed for portability; a mechanism for linking laboratory findings with medical problems; and a real-time, context-sensitive visualization of the medical record. Taken together, these concepts form a comprehensive system for facilitating evidence-based medicine in a real-world setting.

NEW BIOMATERIALS FOR TISSUE ENGINEERING

Tissue engineering holds the promise to repair and/or replace damaged organs using biologic materials. For success in this area, a number of scientific and bioengineering challenges must first be met. For example, we must learn to produce, manipulate, and deliver collections of cells not only as building blocks for tissues and organ systems, but as models for studying drug development. Toward this goal, NIBIB researchers have successfully transformed adult rat engineered tissue cells into cells that form cartilage and bone. The two cell types were integrated into separate layers, encapsulated in a gel-like biocompatible material, and shaped into the ball structure of a human jaw joint. Although more work is needed before this tissue-engineered joint can be used in humans, it holds great potential for treating patients with temporomandibular disorders, osteoarthritis, and rheumatoid arthritis. These procedures could also be further refined and adapted for developing artificial knee and hip joints.

Coronary stents are small devices that serve as a scaffold to prop open the inside of an artery and provide vessel support. They are commonly made of stainless steel or nylon mesh and therefore remain as a permanent implant in a blood vessel. Although stents have revolutionized the treatment of coronary artery disease, limitations include an inflammatory reaction and the development of stent closure due to blood clots forming within the device, a process termed restenosis. To address this problem, NIBIB researchers have recently developed a mechanically strong, hemocompatible, and X-ray visible polymer as a noninflammatory fully-degradable coronary stent. While designed as a stent, work continues to refine the device to serve additionally as a drug-delivery vehicle. This may also have application as a drug-delivery mechanism for other diseases, such as cancer.

SENSORS FOR MEDICINE

Biosensors are nanoscale or microscale devices that detect, monitor, and transmit information about a physiological change, or indicate the presence of various chemicals, gases, or biological materials. Laboratory diagnostics used in hematology, clinical chemistry, pathology, and microbiology already employ sensor technologies to perform simultaneous measurements for many substances in urine, blood, saliva, sweat, and interstitial fluids. The Institute has an active research program in sensor technologies and continues to expand this important area. For example, NIBIB researchers are engineering recombinant antibody fragments (recAbs) that will increase the sensitivity and specificity of a type of biosensor called a piezoimmunosensor. Piezoimmunosensors have been proposed for almost 20 years;

however, there has been no procedure for providing a sensing layer that is uniform, chemically stable during the measurement process, and contains high numbers of binding sites. By creating tightly packed monolayers of recAbs that will bind to the surface of the sensing unit, researchers are solving this problem while also preventing non-specific interactions with molecules, and thus improving specificity.

Other researchers are focusing on the design and fabrication of miniaturized implantable responsive drug delivery devices that integrate a smart drug delivery system with a biosensor. These drug delivery systems are aimed at providing individualized therapies that monitor the patient's body chemistry and control drug flow as needed.

NIH ROADMAP

To transform the Nation's medical research capabilities and to speed the movement of research discoveries from the bench to the bedside and into medical practice, the NIH has laid out a series of far-reaching initiatives known collectively as the NIH Roadmap for Medical Research. The NIH Roadmap focuses on the most compelling opportunities in three main areas: new pathways to discovery, research teams of the future, and re-engineering the clinical research enterprise.

The NIBIB mission also strongly supports the NIH Roadmap initiative, since the Roadmap goal is to facilitate the development of innovative, novel and multidisciplinary science and technology that has the potential to further advances in health care. For example, the NIBIB is participating in an initiative that will facilitate the formation of collaborative research teams capable of generating novel probes for molecular and cellular imaging. The overall goal is to establish programs to create complete tool sets for the detection of single molecule events in living cells and to generate new strategies for dramatically increasing the imaging resolution of dynamic cellular processes.

Other areas of immediate interest to and supported by the NIBIB include the development of nanomedicine technologies, new tools for the study of proteomics and metabolic pathways, data and techniques for computational biology, and advances in bioinformatics. The NIBIB also strongly supports the NIH Roadmap theme on research teams of the future through sponsoring multidisciplinary research and interdisciplinary training.

MULTIDISCIPLINARY RESEARCH TEAMS

The value of collaboration among disciplines and organizations has long been recognized as important for developing novel approaches to problems in biology and medicine, and for effectively translating research results to patient applications. We are pleased to report that there have already been some successful "NIBIB partnerships" between biomedical engineers and imaging scientists that have had significant impacts on healthcare. For example, an ongoing Bioengineering Research Partnership team is using fMRI to integrate information on the suspected location of brain seizures with information about surrounding brain function in order to improve surgical outcome and reduce or eliminate seizures. In one early phase study, surgery employing fMRI strategies was used to almost eliminate seizures in a patient who had been suffering from as many as 100 seizures daily.

In conclusion, the NIBIB is dedicated to promoting the development of emerging technologies and interdisciplinary collaborations that drive healthcare advances. I would be pleased to respond to any questions that the Committee may have.

Department of Health and Human Services
National Institutes of Health
National Institute of Biomedical Imaging and Bioengineering

Roderic I. Pettigrew, Ph.D., M.D.

Roderic I. Pettigrew, Ph.D., M.D., is the first Director of the National Institute of Biomedical Imaging and Bioengineering at the NIH. Prior to his appointment at the NIH, he was Professor of Radiology, Medicine (Cardiology) at Emory University and Bioengineering at the Georgia Institute of Technology and Director of the Emory Center for MR Research, Emory University School of Medicine, Atlanta, Georgia.

Dr. Pettigrew is known for his pioneering work at Emory University involving four-dimensional imaging of the heart using magnetic resonance (MRI). Dr. Pettigrew graduated cum laude from Morehouse College with a B.S. in physics, where he was a Merrill Scholar; has an M.S. in nuclear science and engineering from Rensselaer Polytechnic Institute; and a Ph.D. in applied radiation physics from the Massachusetts Institute of Technology, where he was a Whitaker Harvard-MIT Health Sciences Scholar. Subsequently, he received an M.D. from the University of Miami School of Medicine in an accelerated two-year program, did an internship and residency in internal medicine at Emory University and completed a residency in nuclear medicine at the University of California, San Diego. Dr. Pettigrew then spent a year as a clinical research scientist with Picker International, the first manufacturer of MRI equipment. In 1985, he joined Emory as a Robert Wood Johnson Foundation Fellow with an interest in non-invasive cardiac imaging.

Dr. Pettigrew's awards include membership in Phi Beta Kappa, the Bennie Award (Benjamin E. Mays) for Achievement, and being named the Most Distinguished Alumnus of the University of Miami. In 1989, when the Radiological Society of North America celebrated its 75th Diamond anniversary scientific meeting, it selected Dr. Pettigrew to give the keynote Eugene P. Pendergrass New Horizons Lecture. He has also served as chairman of the Diagnostic Radiology Study Section, Center for Scientific Review, NIH.

Department of Health and Human Services

Office of Budget

William R. Beldon

Mr. Beldon is currently serving as Acting Deputy Assistant Secretary for Budget, HHS. He has been a Division Director in the Budget Office for 16 years, most recently as Director of the Division of Discretionary Programs. Mr. Beldon started in federal service as an auditor in the Health, Education and Welfare Financial Management Intern program. Over the course of 30 years in the Budget Office, Mr. Beldon has held Program Analyst, Branch Chief and Division Director positions. Mr. Beldon received a Bachelor's Degree in History and Political Science from Marshall University and attended the University of Pittsburgh where he studied Public Administration. He resides in Fort Washington, Maryland.