Track 2: Data Management: Databases and Digital Libraries
Biomedical Imaging Perspective
(Computer-Aided Diagnosis)

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Symposium Focus

- Symposium focuses on approaches that will ultimately deliver the benefits of biomedical information technologies to patients at the time and place where decision are made regarding risk, diagnosis, treatment, and follow up.
- Thus, databases are needed including images, molecular sequences and structure, gene and protein expression, and patient medical records including histories and exam data (such ECGs).

Biomedical *Imaging* Perspective

- Computerized Image Analysis & Computer-Aided Diagnosis: Statement of the Problem relative to human interpretation
- Role of Image Databases & Digital Libraries
- Biomedical Image Databases
- Issues and Needs

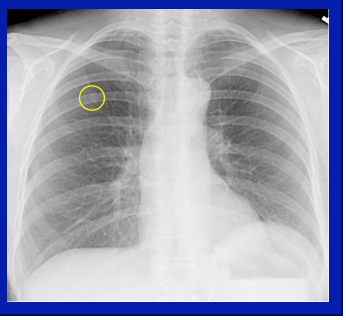
The benefit of a medical imaging examination in terms of its ability to yield an accurate diagnosis depends on:

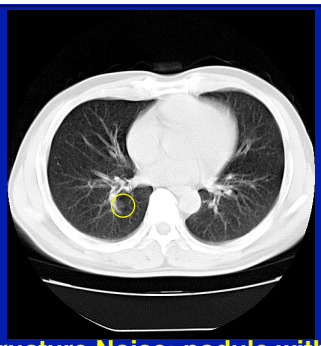
- Quality of the image acquisition and
- Quality of the image interpretation

Image interpretation has been provided by the human

Problems with Human Interpretation: (1) Limitations of Human Eye-Brain System

- Search & perception problems (miss obvious lesions)
- Image noise (which includes confounding normal structures, i.e., structure noise --->



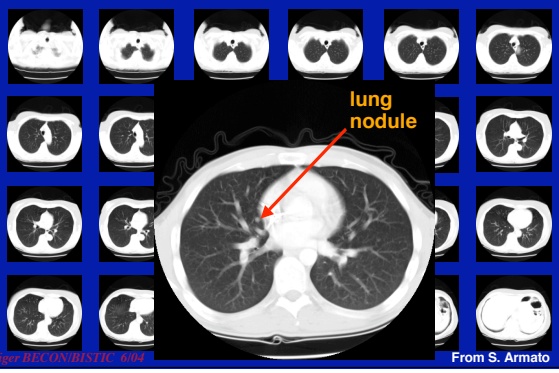


Structure Noise: nodule with a neighboring vessel

Problems with Human Interpretation: (2) Vast amount of data for interpretation

- Especially in cancer screening programs
- Makes lesion detection a burdensome task
- Impacts radiologists' workloads
- Causes oversight errors
- For example, in mammography:
  - Screening of asymtomatic women
  - Currently, the best method for early detection
  - Radiologists, however, do not detect all cancers on mammograms.

Vast Amount of Data: Now Envision 1500 slices

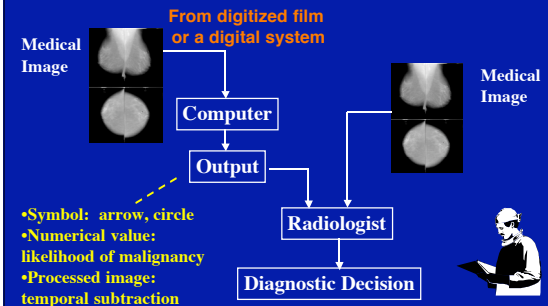


From S. Armato

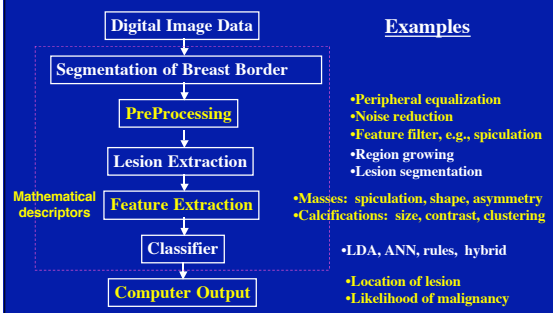
The Solution: CAD

- Incorporation of computer technology into the image interpretation component.
- Computer-aided diagnosis is a diagnosis made by a radiologist who takes into consideration the output from a computer analysis of an image.
- The final decision is made by the human.
- Goal is to reduce search errors, reduce interpretation errors, & reduce variation between and within observers

Computer-Aided Diagnosis



Generic Flowchart for the Computerized Analysis of Breast Images



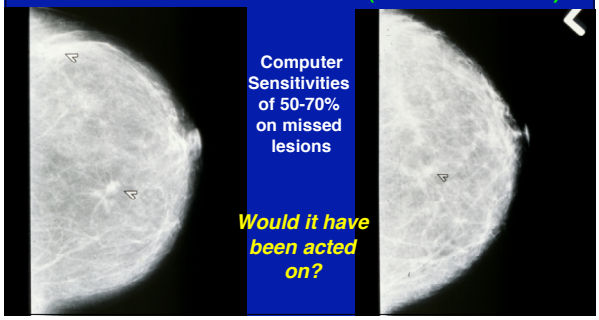
CAD: Some Major Tasks

- Computer-Aided Detection
- Use computer output to direct a radiologists' attention to regions on a medical image that the computer deems to have features associated with cancer. (like a spell checker).
- Computer-Aided Diagnosis
- Use computer output to help characterize and potentially indicate a computer-determined probability of malignancy of a found lesion.
- Computer-Aided Risk Assessment
- Use computer to quantify the risk of acquiring a disease for a population and ultimately individuals.

Current Mammogram

Computer Detection

Prior Mammogram ("missed" lesion)

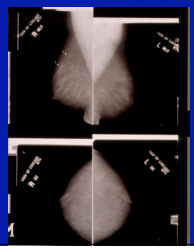


Computer Sensitivities of 50-70% on missed lesions

Would it have been acted on?

University of Chicago 1994 Prototype System for Computer-Aided Detection

Detection of Mass Lesions & Clustered Microcalcifications

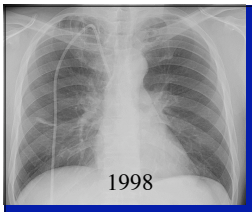


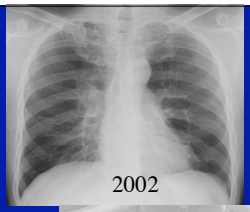
Computerized Nodule Detection in Chest Radiography

Started in mid-80's
Why slow until now?
-- not the only disease
-- now digital

Note - detection of actionable regions

Giger BECON/BISTIC 6/04





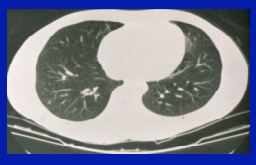
Temporal Analysis of Chest Radiographs for Detection of Interval Change: Now being incorporated in commercial systems.

MacMahon et al.

Giger BECON/BISTIC 6/04

CAD in CT of the Thorax: Detection of Lung Nodules

Growing acceptance of low-dose CT for lung cancer screening

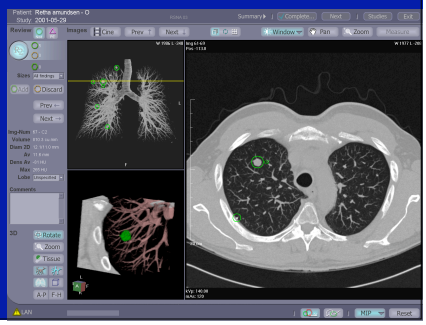


Probably the most active field of CAD research now. Also, need to contend with changing acquisitions.

Giger BECON/BISTIC 6/04

Lung Nodule Detection on CT

With 3D image datasets, the displays contain more information

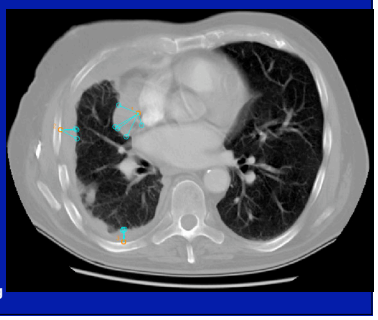


From S. Woods

Giger BECON/BISTIC 6/04

Quantification of Pleural Disease

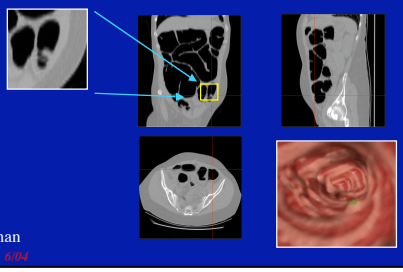
- evaluate the extent of the mesothelioma tumor
- assess tumor progression and response to therapy



Armato, MacMahon, Vogelzang

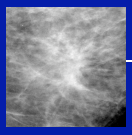
Computerized Analysis in Colonography for Colon Cancer Screening

Computerized polyp detection & methods for image display



Yoshida; Dachman

Computer-Aided Diagnosis

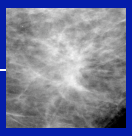


Computer

Output

97%

Radiologist



Suspect lesion

Diagnostic Decision (Biopsy Recommendation)

Note that the computer is analyzing a lesion that has already been found - either by human or computer

Computer performances are high

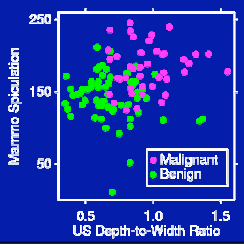
CAD in *Multi-Modality* Imaging of the Breast

Combine computer-extracted features from:

- Mammograms
- Sonograms (2D & 3D)
- MR images of the breast
  - (3D & temporal)
- Clinical information

Goal: Improve characterization of lesions

Note: Could be used with combined mammo/US systems



Intelligent Workstation For Breast CAD

CARS 2000
RSNA 2001
IWDM 2002
RSNA 2002
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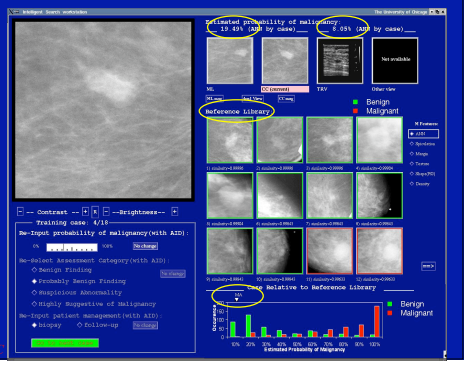
Giger et al.

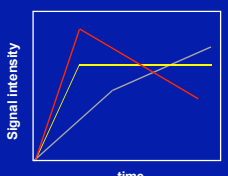
Benign Case



Kinetic information from breast MRI for diagnosis, assessing tumor extent, excised margin analysis, detection of satellite lesions, &/or assessing response to therapy: Image analysis methods exist but need to be integrated into the clinical infrastructure & the into national repositories

- Enhancement Curve types

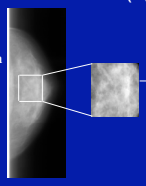
✓Persistent
✓Plateau
✓Washout



Computerized Cancer Risk Assessment

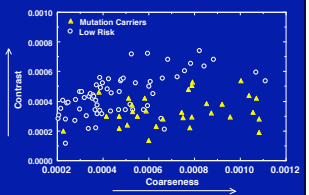
BRCA1/BRCA2 Mutation Carriers vs. Low Risk (Age-Matched Group)

Original "Normal" Mammogram



Computer-extracted texture features characterizing
- percent dense
- texture of parenchyma

→ Numerical value related to risk of breast cancer



Women at high risk for breast cancer tend to have dense breasts with a parenchymal pattern that is coarse and low in contrast.

Huo, et al., 1998, 2002

Role of Images in Treatment

- Pre-interventional images as well as images for guiding therapy
- Example: insertion of stent-grafts for aneurysms
- Example: treatment planning in radiation therapy

In addition to medical image analysis …

- The given example applications require development of mathematical descriptors and recognition of patterns of normals and malignancies. Basically data mining the image data to locate and diagnose disease, assess risk, etc.
- Similar techniques are also used in the data mining of molecular sequences and structure, gene and protein expression, and patient medical records including histories and exam data (such ECGs).
- Development and validation of such techniques require large databases.

Biomedical *Imaging* Perspective (Computer-Aided Diagnosis) Outline

- Computerized Image Analysis & Computer-Aided Diagnosis
- Role of Image Databases & Digital Libraries
- Biomedical Image Databases
- Issues and Needs

Hospitals & Clinics Becoming "Digital"

- Images and data requiring local and remote interpretations -- authenticity issues
- Data security and privacy issues
- Images and information should be available for research
- Medical images and information will ultimately move with the patient
- Examples of sizes
  - Digital mammogram: 30-40 mB of just image data
  - CT exam: 1500 slices

Role of Image Databases & Digital Libraries

- Beyond the "digital health care environment" which can deliver to both patient databases and research databases
- Development & validation of computerized image analysis methods
- Training of users, e.g., radiologists, in both conventional human vision tasks and humans-using-computer-vision-output tasks (e.g., CAD)
- Epidemiology studies, e.g., risk assessment
- FDA approval studies

Example (1): Evaluation of CAD Systems

- Performance of the computer detection method alone in terms of sensitivity and false-positive marks per image.
- Investigation of the effect that a CAD system has on radiologists' performance when it is used as an aid is the ultimate test, its additive value.

Potential Contribution of Computer-aided Detection to the Sensitivity of Screening Mammography

Burhenne LJ, Wood SA, D'Orsi CJ, Feig SA, Kopans DB, O'Shaughnessy KF, Sickles EA, Tabar L, Vyborny CJ and Castellino RA (*Radiology* 2000; 215 : 554-562)

- 13 institutions contributed all consecutive, biopsy proven cancers detected by screening mammography (2 years)

CAD sensitivity (1,083 consecutive breast cancers**)

microcalcifications	98.3%*	(399/406)
masses	85.7%*	(580/677)
all cases	90.4%*	(979/1083)

FP CAD marks (347 normal exams) 0.5* marks / image

* updated in Castellino et al, *Radiology* 2000;217 (P), 400

** May be more cancers than seen in the lifetime of a typical radiologist

Computer aided detection (CAD) in screening mammography:

Sensitivity of commercial systems in detecting architectural distortions

Baker et al, AJR 2003; 181, 1083-1088

Malignant Architectural Distortions

sensitivity	System X	System Y	p value
case (n = 27)	48%	19%	p = 0.027
image (n = 51)	31%	10%	p = 0.01
FP marks/image	0.70	1.27	p = <0.0001

Example (2): Evaluation of CAD Systems

- Performance of the method alone in terms of sensitivity and false-positive marks per image.
- Investigation of the effect that a CAD system has on radiologists' performance when it is used as an aid is the ultimate test, its additive value.
  - Observer studies that measure performance of radiologists interpreting alone and also interpreting with the use of computer assistance.
  - Prospective clinical studies

Computer aided detection in screening mammography:

prospective study of 12,860 patients in a community breast center

Freer TW and Ulissey MJ - *Radiology* 2001; 220: 781-786

12,860 consecutive screening mammograms (12 months) prospectively interpreted sequentially as follows:

- initial interpretation without CAD prompting
- immediate re-evaluation of CAD prompted areas
- tracked cases where CAD changed from "-" to "+"
- tracked all biopsies performed, cancer detection rates etc

Cancer detection rate -- increased 19.5% (from 3.2 to 3.8 cancers/1,000 screens)

Recall rate -- increased by 18.5% (from 6.5% to 7.7%)

Need many cases to demonstrate the reality of CAD detection in screening environment!!!

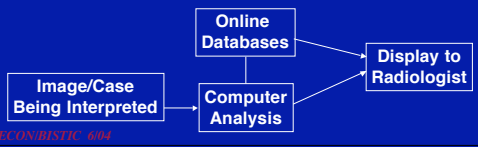
Also, important to TRAIN the users.

Mammographic Computer-Aided Detection Systems in Clinical Practice

- Approximately 1,200 units (including FFDM)
- In 2003, it was estimated that 8,000,000 screening mammograms were read with CAD assistance (United States)
- Represents approximately 20 – 25 % of all screening mammograms done yearly in the United States
- Large accumulation of digital images, which could be used to further improve the methods!!!

Example (3): CAD & Use of *Known Databases and Indices of Similarity*

- **Online** databases with known truth on the disease state
- **Online** searches of the databases based on lesion characteristics or estimated probabilities of malignancy



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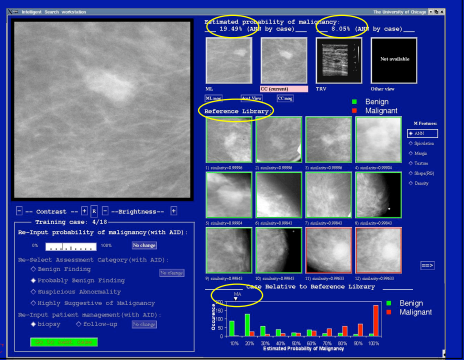


Biomedical *Imaging* Perspective (Computer-Aided Diagnosis) Outline

- Computerized Image Analysis & Computer-Aided Diagnosis
- Role of Image Databases & Digital Libraries
- Biomedical Image Databases
  - Examples mainly from medical imaging, more will be incorporated during the breakout
  - Much effort exists, but needs to be coordinated for maximum benefits!!
- Issues and Needs

Mammography Databases

- MIAS Database -- UK Mammographic Image Analysis Society interested in the understanding of mammograms.
  - 320 digitized films with radiologist's truth-markings
  - 57 copies are in use in 11 countries
- USF Database -- U.S. Army funded to facilitate research in the development of CAD
  - 2500 studies with truth on location & lesion type

Mammography Databases (cont.)

- NDMA -- National Digital Mammography Archive (Penn, Chicago, North Carolina, Toronto, IBM)
  - Addressed digital mammography, telemammography, CAD, and security issues
  - ultimately 28 terabytes per day in traffic (with encryption)
  - Funding period has ended; What's next?
- eDiamond -- A Grid-enabled federated database of annotated mammograms (Michael Brady…)
  - For teaching and supporting diagnosis
  - For training classification computer algorithms
  - For data mining applications
  - Will learn from and work with the NDMA

LIDC: NCI-supported Lung Imaging Database Consortium

- Mission is to share lung images, especially low-dose helical CT scans of adults screened for lung cancer, and related technical and clinical data for development and testing of computer-aided screening and diagnosis technology.
- Much of the time has been in establishing standard formats and processes for managing the data.
- Ultimately to be a web-accessible international research resource for the development, training, and evaluation of CAD for lung cancer detection and diagnosis using helical CT.

Databases from ACRIN

- ACRIN (American College of Radiology Imaging Network)
- Performs imaging clinical trials
- "By-products" are images
  - DMIST trial on screening mammography with FFDM
  - Colon polyps
  - Lung nodules CT screening trial
  - I SPY Trial
- However, require funding for infrastructure to further use the collected images as a database

Other Databases

- The CT based Structural and Functional Atlas of the normal human lung
- The Atlas of digital bronchoscopy
  - to provide images from endoscopic color and texture analysis in normal and disease states
- The Large Image Microscope Array
  - to provide 3D macro/microscopic images of whole organs to provide truth for CT imaging

From McLennan

caBIG from NCI

- Goal: Informatics tools that optimize the value of cancer imaging data
- Establish publicly available image archives, linked to outcome and other clinical data
- Great plan

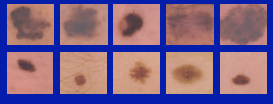
EFMI
Reference Image Database Concept

- EFMI: European Federation for Medical Informatics
- Working group on medical image processing (acknowledge slide contribution from Wittenberg, Horsch/ www.efmi-wg-mip.net)
- Medical Images (ranging in size from 1000 to 8500 images)
- Genetics (nucleotid and protein sequences, gene mutations, cellular processes, etc.)

From Wittenberg and Horsch

Example (from MIE Munich)

- Dermatology
- Skin Surface Microscopy
- Melanocytic Lesions
- 150 naevi + 150 melanomas
- Used by 3 R&D groups, so far, ~20 publications



From Wittenberg and Horsch

EFMI: Reference Image Database Concept
Short term goals (less than 5 years)

- Filling the database
  - Bottom up 2004: 5, 2009: 25
    - collection of datasets + results
    - assessment of relevance & quality → acceptance / refusion
    - preparation for general use / fusion of small datasets to big ones
  - Top down
    - definition of most relevant tasks (2005) Cancer
    - preparation of 3-5 datasets (incl. annotations!) (2009) Modality?

From Wittenberg and Horsch

EFMI: Reference Image Database Concept
Short term goals (less than 5 years) -- cont.

- Define and Establish Standardized Annotation Tools and Data Structures
- Outcome
  - Citation index, collection of published results, query statistics
- Funding (sought from the European Union)

From Wittenberg and Horsch

EFMI: Reference Image Database Concept
Long term goals (10 years)

- European Center for Medical Reference Databases
  - Operates the reference database professionally as a service
  - Continuously defines new tasks and challenges
  - Imaging, biosignals, genomics, molecular imaging, drugs, etc
- Top down branch widely established / used
  - RID datasets are standard in the R&D community
  - Database is accredited for certification of new medical applications (e.g. for FDA approvals)
  - Better and faster development of new applications (shorter turn-around cycles)
  - Continuing update of datasets according to upcoming modalities / tasks

From Wittenberg and Horsch

Biomedical *Imaging* Perspective
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Outline

- Computerized Image Analysis & Computer-Aided Diagnosis
- Role of Image Databases & Digital Libraries
- Biomedical Image Databases
- Summary: Issues and Needs

Database Concerns

- Each group uses own databases and does not share easily (modify culture)
- Current databases are often too small for training, feature selection, optimization, evaluation
- Different annotation
- Different levels of truth
- Sometimes questionable reliability

Database Requirements

- Standardized collection as a repository (similar to a tumor bank)
- Note image databases can be much larger than clinical information databases. (one mammogram: 30-40 mB)
- Authenticity of data and associated truth ---------->>
  - Require "certified" contributors
- Informatics tools for user-friendly front-end loading by contributor and downloading by others -- not just a data archival storage but also extraction tools
- Make submitting to the repository a requirement for funded investigators
- Allow for open datasets as well as those protected for validation (and FDA approval studies)
- Implement similar to open source and grid
- Nationally fund as a national resource

Hypothetical Computer Output

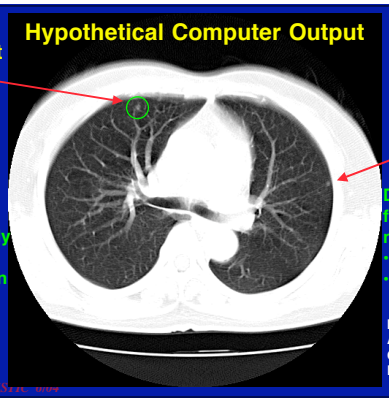

Image from Armato, Li, Giger, Sone, MacMahon, Doi

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Additional Concerns

- Who owns the data?
- Who has access?
- Who maintains the data?
- Who provides the continued funding

Ending Notes

- Appears that in the U.S., there are many databases being collected via funding mechanisms -- just archival usage
- However, there are very limited funds for the infrastructure (perhaps some with NDMA project) -- to achieve other usages
- Need perhaps more government and industrial participation as in Europe with their federated databases. (caBIG is a great start)

Thank You