Speakers and Panelists

Chairs:	Stephen M. Pizer, Ph.D.	University of North Carolina at Chapel Hill
	Ron Kikinis, M.D.	Brigham and Women's Hospital
	Kunio Doi, Ph.D.	University of Chicago
Session 1:	**Clinical Imaging Overviews**	
Session Leader:	Michael W. Vannier, M.D.	University of Iowa Hospitals and Clinics
Speakers:	Randall Hawkins, M.D., Ph.D.	University of California at San Francisco
	Ron Kikinis, M.D.	Brigham and Women's Hospital
	Daniel B. Kopans, M.D.	Massachusetts General Hospital
	Anna S. Lev-Toaff, M.D.	Thomas Jefferson University Hospital
	Robert M. Nishikawa, Ph.D.	University of Chicago
	Stephen M. Pizer, Ph.D.	University of North Carolina at Chapel Hill
	Robert A. Schmidt, M.D.	New York University School of Medicine
	Faina Shtern, M.D.	U.S. Public Health Service's Office on Women's Healtl
	Michael W. Vannier, M.D.	University of Iowa Hospitals and Clinics
Session 2:	**Computer-Aided Diagnosis for X-Ray Mammography**	
Session Leader:	Carl J. Vyborny, M.D., Ph.D.	University of Chicago
Speakers:	Kevin W. Bowyer, Ph.D.	University of South Florida
	Heang-Ping Chan, Ph.D.	University of Michigan
	Laurence P. Clarke, Ph.D.	University of South Florida
	Maryellen L. Giger, Ph.D.	University of Chicago
	Jan H.C.L. Hendriks, M.D.	St. Radboud University Hospital
	Nico Karssemeijer, Ph.D.	University of Nijmegen
	Shyh-Liang (Andrew) Lou, Ph.D.	University of California at San Francisco
	Robert M. Nishikawa, Ph.D.	University of Chicago
	James Roehrig, Ph.D.	R2 Technology, Inc.
Session 3:	**3D Image Segmentation**	
Session Leader:	James S. Duncan, Ph.D.	Yale University School of Medicine
Speakers:	Nicholas Ayache, Ph.D.	INRIA
	J. Michael Brady, Ph.D.	University of Oxford
	James S. Duncan, Ph.D.	Yale University School of Medicine
	Guido Gerig, Ph.D.	University of North Carolina at Chapel Hill
	Murray H. Loew, Ph.D.	George Washington University
	Christopher J. Taylor, Ph.D.	University of Manchester
Session 4:	**3D Image Registration and Fusion**	
Session Leader:	J. Michael Fitzpatrick, Ph.D.	Vanderbilt University
Speakers:	Ruzena K. Bajcsy, Ph.D.	University of Pennsylvania
	J. Michael Fitzpatrick, Ph.D.	Vanderbilt University
	Eric Grimson, Ph.D.	Massachusetts Institute of Technology
	David J. Hawkes, Ph.D.	King's College London
	Charles A. Pelizzari	University of Chicago

Session 5:	**3D Image Visualization and User Interfaces**	
Session Leader:	Richard A. Robb, Ph.D.	Mayo Foundation
Speakers:	Ali Bani-Hashemi, Ph.D.	Siemens Corporate Research, Inc.
	Henry Fuchs, Ph.D.	University of North Carolina at Chapel Hill
	William Lorensen, M.S.	General Electric Corporate Research and Development
	Wido Menhardt, Ph.D.	Platforms and Advanced Technologies
	Julian Rosenman, Ph.D., M.D.	University of North Carolina at Chapel Hill
Panelists:	Marc L. Kessler, Ph.D.	University of Michigan Medical School
	Andrew Maidment, Ph.D.	Thomas Jefferson University Hospital
	Hans-Peter Pfister, Ph.D.	Mitsubishi Electric Research Laboratories
	Karel Zuiderveld, Ph.D.	Vital Images, Inc.

Introduction

In March 1996, the U.S. Public Health Service's Office on Women's Health (USPHS OWH) established a Federal Multi-Agency Consortium for Imaging and Other Technologies to Improve Women's Health to support technology transfer from laboratories to patients. The membership of the consortium includes, but is not limited to, the National Cancer Institute, Food and Drug Administration, Health Care Financing Administration, Central Intelligence Agency, Department of Defense, Department of Energy, and National Aeronautics and Space Administration. The activities of this consortium have been critical for sharing expertise, resources, and technologies by multiple government agencies for the advancement of novel breast imaging for early diagnosis of cancer, such as digital mammography, magnetic resonance imaging (MRI), ultrasound, nuclear medicine, and positron emission tomography (PET), as well as related image display, analysis, transmission, storage, and minimally invasive biopsy and treatment.

The consortium sponsored a public conference entitled "Technology Transfer Workshop on Breast Cancer Detection, Diagnosis, and Treatment" convened on May 12, 1997.[1] During this meeting, consortium members developed recommendations for the scientific and technologic projects critical for advancement of novel breast imaging.

Subsequently, USPHS OWH and the National Cancer Institute (NCI) jointly sponsored the establishment of several working groups to define even further the research agenda in the areas of breast imaging examined by the May 1997 conference. These groups focused on specific recommendations for research priorities and technology development and transfer opportunities across multiple areas of breast imaging:

- Nonionizing imaging (e.g., ultrasound, MRI, optical imaging) for the development and testing of novel modalities free of ionizing radiation
- Functional imaging (e.g., PET, MR imaging and spectroscopy, and optical imaging and spectroscopy) for the achievement of comprehensive in vivo cellular and ultimately molecular biologic tissue characterization
- Image processing, computer-aided diagnosis (CAD), and three-dimensional (3D) digital display for enhanced lesion visualization and radiologic image interpretation
- Telemammography, teleradiology, and related information management for facilitated expert consultations
- Digital X-ray mammography, with an emphasis on digital display technologies and workstation design for image interpretation
- Image-guided diagnosis and treatment for potential replacement of open surgery with minimally invasive and/or noninvasive interventions
- Methodological issues for diagnostic and screening trials for imaging technologies, with specific focus on the development of computer models for analysis of patient outcomes and cost-effectiveness.

This report summarizes the results of the Joint USPHS OWH/NCI Working Group on Computer-Aided Diagnosis and 3D Image Analysis and Display. Approximately 55 international scientific leaders, representing clinical practice, academic research, government agencies and laboratories, and medical imaging system manufacturers, attended the meeting held October 8–9, 1998, in Cambridge, Massachusetts. This paper describes the group's findings and recommendations.

Goals of the Joint USPHS OWH/NCI Working Group

1) Review the state of the art of 3D image analysis and display and computer-aided diagnosis, including current and future clinical applications and technical challenges.

2) Outline a research agenda, including short- and long-term priorities in technology development, basic research, and clinical testing.

3) Identify technical limitations and develop problem statement(s) seeking new or emerging technologies.

While breast cancer is a priority of the USPHS OWH and NCI, consideration of technology development and research opportunities was extended to other applications in the detection and diagnosis of cancer in women. The Working Group meeting consisted of the following sessions:

Session 1: The clinical imaging overviews session set a common vocabulary between multidisciplinary participants. The session provided an overview of the current and future clinical applications of CAD and analysis to several imaging modalities (e.g., digital X-ray, MRI, 3D ultrasound, and nuclear medicine/PET).

Acad Radiol 1999; 6(suppl 5): S221–S256

Session 2: The session on computer-aided diagnosis for X-ray mammography presented the strides made in recent years in the automated analysis of digital X-ray mammographic images, illustrating the potential utility of CAD in the future clinical practice.

Session 3: The 3D image segmentation session described an operation fundamental to a variety of 3D image analysis tasks that result in the measurement and visualization of anatomical and physiological information related to women's health issues. Speakers discussed key technical challenges in efficiently and robustly extracting and understanding image structure from 3D images and relating this structure to normal anatomy, pathology, microstructure, and tissue function.

Session 4: The 3D image registration and fusion session presented the current challenges and opportunities in the incorporation of 3D images into computer-aided diagnosis and therapy. The growing need for multiple images and multiple imaging modalities, both for diagnosis and for surgical planning, has led to a concomitant increase in interest in the synthesis of images through registration and fusion.

Session 5: The session on 3D image visualization and user interfaces addressed current roadblocks and the technical requirements for future advancement of visualization technology. These advances eventually will provide new tools and procedures for interactive treatment based upon medical images. Current advanced computer image processing research has facilitated major progress toward fully interactive 3D visualization and realistic simulation. This, in turn, enables the images to be directly displayed and manipulated with intuitive immediacy and with sufficient detail and speed.

Working Session: Working group members met to formulate consensus reports describing the current state of the art and recommendations for future priorities in research and technology development.

Summary Session: The consensus reports were presented during the summary session. The reports addressed (1) the current state of the art and fundamental clinical/technical roadblocks, (2) technical parameters required to meet current and future clinical needs, and (3) future priorities in technology development and related basic and clinical research.

Subsequent to the working group meeting, its leaders developed written summary reports with input from session participants. These summary reports have been integrated into this article with editorial input from the working group chairs and sponsors.

References

1. Asher S, Shtern F, Winfield D, et al. Final report of the technology transfer workshop on breast cancer detection, diagnosis, and treatment. Washington, D.C., USA. May 1-2, 1997. Acad Radiol 1998; 5 (Suppl. 3):S465-501.

Summary of the Working Group Discussions

Imaging offers a high potential to benefit the screening; diagnosis; and therapy planning, delivery, and monitoring for breast, lung, prostate, ovary, and colon tumors. Among the obstacles to greater acceptance and increased use of imaging is the variability of image interpretation among radiologists. The reason for this variability is that standard practice consists of analysis that is often qualitative and two-dimensional (2D).

Two-dimensional computer-based image analysis techniques are already seriously strengthening breast cancer diagnosis. Research results give great encouragement that the use of three-dimensional imaging and quantitative analysis instead of 2D qualitative assessment can provide earlier diagnosis and knowledge of treatment effect. Cancer diagnosis and treatment can be further improved by applying these techniques to new modalities in medical imaging. Despite the potential for 3D imaging, however, current approaches to cancer diagnosis and treatment do not routinely use it because adequate 3D image analysis and display tools are unavailable. The working group therefore recommends further research to allow strides in the development and application of methods for quantitative 3D medical image analysis and display.

The possible areas for development are discussed in detail in the session overviews contained in this report. This summary highlights the recurring themes of these sessions.

Medical image analysis and display have helped achieve a wide range of clinical objectives. In diagnosis, not only detection but also staging of tumors can be aided. Recent successes in computer-aided diagnosis need to be extended to the staging process. It is understood that this will be aided by using images from multiple image modalities, including newer ones showing blood supply to tumors and genetic properties at a very small scale.

Image display and analysis also have significantly aided the planning, delivery, and evaluation of therapeutic treatments. It has been demonstrated that 3D imaging, image analysis, and display are distinctly superior to 2D in surgery and radiotherapy. These findings indicate the need

to extend 3D techniques into diagnosis and to develop more robust 3D techniques that will further aid therapeutic objectives. These objectives are particularly challenging with breast cancer, where the information frequently is at a small scale, complicated patterns form the diagnostic information, and the physical mobility of the breast leads to challenges of registration of multiple images and atlases.

As with human analysis of medical images, computer-based image analysis must be able to distinguish anatomic objects provided by image segmentation and provide information on how physiology is affected by cancer. Good databases of typical images and good atlases of anatomy and physiology are needed. Atlases must take the form of models that efficiently capture in 3D, and sometimes in real time, those aspects of human anatomy and physiology that vary among normals and that vary as cancer is developing. The work of a variety of groups led to the conclusion that segmentation based on such models can be dramatically improved and that research on the most effective form of modeling is needed.

Statistical techniques support the analysis of normal and pathological variations in anatomy and physiology. Similar techniques must be developed for analyzing the spatial changes involved in interhuman variation, in the growth or removal of lesions, or within different imaging situations. Although it is based on the fundamentals, spatial statistics is an immature discipline that requires considerable research. Further advances in statistical science will enable medical image analysis to attain its potential in cancer diagnosis and treatment.

Statistical approaches are also a component in the validation of computer-based image analysis techniques compared to human analysis. Such validation must be a routine component of the research. The validation must show that high detection rates can be achieved when cancer is visualized without a high false-positive rate.

The images in the databases must come from multiple imaging modalities, because it has been shown that more complete information useful for treatment and diagnosis of cancer comes from several images. Fusing this information requires 3D registration, and this, in turn, requires the nascent methodology of image analysis approaches based on the mechanical behavior of tissue. These techniques are strongly tied to tissue segmentation, since the mechanical behavior varies among image objects. The models used and the databases generated thus must include greater knowledge of the biologic and mechanical behavior of tissues and the statistical variations across a normal patient population.

The images that support cancer diagnosis and treatment cover multiple scales. Integrating microscale images that show blood supply to tumors and genetic changes may offer great benefits in diagnosing cancer early and staging the tumors found. While there has been some interesting research on analysis across scales, the needs in the multiscale area require additional research.

Techniques that attempt to solve a clinical problem with a combination of technical capability developments in interactive 3D display and manipulation, object segmentation, image registration, and pattern recognition are more likely to succeed than solutions that focus on a single area. Research should integrate various areas and combine biomedical knowledge and clinical goals.

The vast datasets of 3D images require significant computing power to achieve the practical level of interaction for fast display and analysis.

Finally, success in developing CAD and 3D imaging techniques is most effective through multidisciplinary collaboration. Radiologists, surgeons, radiotherapists, primary care and specialty physicians, computer scientists, mathematicians, statisticians, medical physicists, biomedical engineers, and perception experts are needed. Interdisciplinary teams must both test technical developments in clinical trials and let the results from clinical trials drive the technical research. Image display and analysis technologies can be used not only in developing clinically applicable cancer treatments but also in the scientific research necessary to advance the fundamental understanding of cancer biology.

Session 1: Clinical Imaging Overviews

Screening

Imaging has potential to improve early detection of many common cancers, including but not limited to that of the breast, lung, prostate, ovary, and colon. Among the obstacles to greater acceptance and increased use of screening imaging is the variability among observers. Experience with screening mammography indicates that the performance of unaided experts has significant room for improvement, and computer-aided diagnosis may achieve this goal.

To realize the full potential for screening using imaging, current methods for CAD, which are principally ad hoc and

two-dimensional, may be extended or developed for three-dimensional data. CAD should be able to reliably distinguish normal variability from potentially malignant lesions to avoid unnecessary alarm and cost in otherwise healthy individuals. The cost of screening is a practical concern, and reduction in the number of false alarms without increasing the number of false negatives is sought.

The value of screening imaging would be enhanced by better discriminating benign conditions and normal variants from malignant lesions. Even more important, in cases where suspicious or frankly abnormal lesions are detected, is prediction of risk based on image features. These features, when combined with molecular biological markers, would discriminate subpopulations with subclinical disease where surveillance for emergence of overt disease is practical and effective.

Tumor Microvasculature

The pattern of microvessels in solid tumors is significantly different from normal parenchyma and can predict the metastagenicity of the primary lesion. If this hypothesis is confirmed, image-based analysis of microvascular patterns would be useful for therapy selection and prognosis. To test this concept, rigorous correlation of dynamic images from several modalities with histological analysis of microvascular patterns may provide tools for quantitative imaging that guide treatment decision making and improve survival.

Prediction of clinical outcome in tumors. Image-based measurements (e.g., of exogenous contrast material in pharmacokinetic maps) may allow prediction of tumor clinical outcome. These measurements also may serve to better select those patients who will fail "routine" therapy. If the outcome of a treatment is known early in the course of disease, alternatives may be selected that would be unnecessary for most patients. Increased overall survival may be obtained by discriminating nonmalignant lesions from recurrent and resistant variants.

Image-Based Endpoints for Clinical Response Assessment

Clinical response is not an endpoint in most cancer therapy trials. Instead, survival statistics or semiquantitative assessments of images are frequently employed as the principal endpoint. Despite the availability and potential for 3D imaging in most cancer treatment trials, 2D analysis is standard practice. The use of 3D instead of 2D assessment could provide earlier knowledge of treatment effect and predict outcomes. Serial 3D quantification of tumor volume and tissue properties for solid tumors would provide measurements that are reliable and reproducible.

Automated Staging of Detected Disease

Novel imaging technologies, such as detecting occult disease through positron emission tomography with fluorodeoxyglucose (FDG), should be improved with "better" agents and less costly instruments. There is need for better within-organ (e.g., breast) staging using magnetic resonance imaging and contrast agents, due to bilaterality, multifocality, and multicentricity of many tumors and especially to distinguish occult and "precancerous" conditions from overt disease.

The use of ancillary nonimage data in staging decisions may be fruitful. Methods to improve lymph node characterization for malignant spread and sentinel node identification would avoid unnecessary morbidity and cost by reducing the extent of surgical procedures while providing more definitive results. Identification of less advanced/aggressive tumors and prediction of tumors' invasiveness and metastagenicity would make imaging technologies a counterpart of histological grade to classify lesions according to their clinical significance and biological potential.

Follow-Up

There is need for better understanding of metabolic changes over time after treatment, in residual or recurrent disease. This would help to characterize treatment effects and relate them to treatment plans, so that this a priori knowledge can be used to improve post-therapy assessments.

Gene Therapy

The optimization of molecular/genetic therapies using image monitoring over time with tracer/reporter gene methods (or their successors) is sought. The use of radioactive tracer imaging methods and sequential examinations to study tumor angiogenesis in vivo appears especially promising.

Clinical Trials for Developing Imaging Methods

To date, almost purely technical criteria have guided imaging method improvement. This can be better accomplished, however, by an effort to employ evaluation methods for discovery (imaging technology and methods development) that are relevant to clinical outcomes (using

preliminary clinical trials, phase 0, 1, etc.). This working group seeks to develop and adopt clinically (or biologically) meaningful criteria to judge the performance of imaging methods that are akin to drug discovery methods. Such methods avoid the proliferation of inadequately evaluated methods and the tendency to overstate their benefits or deficiencies in the absence of clinically/biologically meaningful evidence.

Clinical Decision Support

A commitment to consider the diagnostic process as a whole, rather than individual parts in isolation, enhances the effect of imaging on clinical decision making. The imaging workstation should be considered a clinical decision making aid, and its influence on outcomes should be measured. Technical developments should focus on specific diseases and critical decision points where errors are common. Technological developments should be aligned with demonstrated clinical needs. By concentrating on the usability of tools and their efficiency in practical everyday applications, the total cost of ownership for imaging workstations can be minimized and the investment will provide acceptable returns. The effort should employ formal methods to understand performance of clinical decision making based on images.

Submillimeter Imaging in Vivo

It is possible to detect micrometastatic spread of tumors requiring orders of magnitude increases in signal-to-noise ratios and resolution compared with today's methods by observing that the physics of medical imaging is independent of scale. To achieve histologic morphologic resolution in vivo for deep organs, submillimeter detail is required. This working group seeks to achieve histochemical staining (or its equivalent) in vivo for deep organs and to delineate microvascular patterns, drug-receptor distribution, gene expression, and metabolite concentrations with submillimeter detail, although micron-level detail is preferred.

Research Priorities

Short term

- Apply CAD methods to 3D datasets and measure the gain in performance.
- Test the efficacy of CAD in reducing interobserver variability.
- Investigate methods to monitor gene therapy and angiogenesis using dynamic image sequences.

Intermediate term

- Improve risk prediction for malignancy based on image feature analysis and molecular markers.
- Predict tumor response to treatment based on image feature analysis and molecular markers.
- Automate and simplify the use of image-based endpoints for clinical response assessment.
- Establish a needs-based evaluation of imaging technology that guides future developments and their prioritization.

Long term

- Discriminate benign and malignant lesions based on image features.
- Fully automate the staging of malignancy based on images and electronic patient record analysis.
- Support clinical decision making based on best evidence and current knowledge in an image-based context.
- Perform clinical in vivo imaging with submillimeter spatial resolution, high contrast, and real-time performance to delineate microvascular patterns, drug-receptor distribution, gene expression, and metabolite concentrations.

Session 2: Computer-Aided Diagnosis for X-Ray Mammography

Breast X-ray film radiography reviewed subjectively by a human observer defines mammography in current clinical practice. The human observer, however experienced and skilled in mammography, is susceptible to perceptual limitations resulting in avoidable mistakes. Automated assistance to improve the observer's diagnostic performance is the goal of computer-aided diagnosis, a technology that has potential to significantly reduce mammographic interpretation errors.

Radiologic images, however, as either digital or potentially digital lend themselves quite well to computer analysis. The earliest attempt to evaluate mammographic images by computer was made more than 30 years ago. The concerted effort to apply computer vision and artificial intelligence methods to mammographic diagnosis has necessarily awaited the development of high-speed digital

computers and is now just over 10 year old. In the past decade, a large number of researchers have made great strides in the automated evaluation of mammographic images, showing beyond doubt its potential utility in the future practice of mammography. [1]

Clinical Mammography

The successful identification of early breast cancer on screening mammograms is a difficult task for radiologists. Depending on the patient population being studied, only between three and ten detectable cancers will be present for every thousand cases reviewed. Breast images are nevertheless visually complex and provide a wide array of real or fortuitous findings that either may simulate cancer or that may distract the radiologist from the detection of cancer.

It has been known for some time that radiologists do not detect all signs of breast cancer present on mammographic images. The percentage of cancers visible in retrospect on previous screening mammograms approaches 70% in some studies.[2,3] Radiologists must contend with numerous borderline findings that almost never develop into malignant lesions.[4] For this reason, it is unlikely that all such retrospectively visible cancers are reasonably recoverable in clinical practice. Nevertheless, there is clearly room for improvement in the detection performance of radiologists.

Even when a potentially significant finding is successfully identified by radiologists, it may still be dismissed as normal or benign in nature. Conversely, radiologists may consistently recommend the biopsy of lesions that have little likelihood of malignancy, resulting in a low positive predictive value for mammography.[5] This lessens the cost-effectiveness and patient acceptance of the examination.

Computer-Aided Diagnosis

The limitations of human observers in the interpretation of mammograms provide a natural and compelling application for computer-based diagnostic methods in mammography.[1,6] At its present level of development, computer-generated information is viewed as a potential aid to radiologists in the detection and characterization decisions they confront in routine clinical practice—hence the term computer-aided diagnosis.

Computer analysis of mammographic images requires first that they exist in a digital form. Today, this is generally accomplished by digitization of conventional mammographic films. Further, the ready adaptability of primary digital mammographic images to analysis by computer remains one motivation for the development of the latter technology. Although there can be almost limitless nuance and subtlety in the computer analysis of mammograms, most algorithms rely on three basic strategies to extract useful information:

- An image-processing stage in which features of interest are enhanced
- A feature-extraction stage in which target findings are identified
- An artificial intelligence stage in which these findings are evaluated for their significance using a variety of approaches.[1]

The output of a CAD algorithm can take a variety of forms. Should the algorithm be designed to assist radiologists in detection tasks, a single mark displayed at the site of a possible abnormality might suffice.[3,7] Should the algorithm primarily assist the radiologist in characterization decisions (i.e., ultimately in biopsy decisions), a computer-generated likelihood of malignancy might be given.[8] Alternatively, the system might display other images having features that are similar to the case at hand and with which the radiologist has a familiarity.[9]

State of the Art

The cutting edge of CAD research, of course, evolves constantly, with any summary of such risks becoming outdated quickly. Nevertheless, it is clear that very significant progress has been made by researchers during the past decade, setting the stage for the eventual everyday usage of CAD techniques by radiologists.

Computer detection. The radiographic manifestations of early breast cancer fall into two relatively distinct categories: (1) microcalcifications arising from necrotic cells or debris within ductal structures and (2) mass or mass-like findings arising from the differential X-ray attenuation between the tumor (or the reaction it incites) and the adjacent normal parenchyma. Given the very different radiographic characteristics of these findings, researchers have generally approached the detection of these entities by computer separately.[1]

Microcalcifications are ideal targets for computer detection since they are unlike any normal structures within the breast, competing only with structured and quantum noise for attention. Numerous researchers have studied microcalcification detection, often achieving impressive results on laboratory databases.[7,10] More recently, microcalcification detection schemes have been tested on large

series of unselected clinical cases.[3, 11] In these tests, sensitivities for the detection of malignant calcifications of greater than 90% (at one false-positive per image) have been reported.[3] A particularly telling indication of computer algorithm performance is its ability to detect calcifications of significance that were missed by radiologists in routine clinical practice. Research indicates that present algorithms are capable of detecting nearly 50% or more of such cases when all subtleties are included.[3, 12] This figure increases to 100% (again at one false-positive per image) for instances in which the calcifications were fairly obvious in retrospect.[3]

Mass lesions represent a more difficult target for detection by computer than do microcalcifications, principally because of the greater overlap between the characteristics of masses and normal breast tissue. Features such as the spiculated margins of many early breast cancers do not occur in the normal breast, however, and have been used by investigators as the basis for detecting masses having potential significance.[13, 14] Despite the inherent difficulties, investigators have derived methods to detect large proportions of masses on digital mammograms.[15, 16] Not surprisingly, detection in unselected or "missed" cases is generally no better, and often worse, for masses than for micro-calcifications in the same subtlety categories.[3, 11]

Computer characterization. The first successful attempts to use computers to characterize breast lesions as benign or malignant date almost to the time of the first detection experiments. In recent years, researchers have shown that abnormalities on mammograms can be readily characterized by computer. Early work in computerized characterization generally relied on human observers to extract image features, with these features then evaluated by artificial intelligence techniques.[17] More recently, features extracted directly by computer have served as the basis for classification of lesions by such techniques.[18, 19]

Computer characterization schemes have been shown to consistently outperform general radiologists in making benign or malignant distinctions.[17] In particular, computer output has been observed to be more specific than general radiologists, being able to classify a greater proportion of lesions as benign at the very high or perfect sensitivities for identification of malignancy required in clinical practice.[8, 20] Recent data also suggest that fully automated computer classification techniques may have the potential to outperform expert mammographers in distinguishing benign and malignant abnormalities.[18]

Computer assistance to radiologists. In the near term, computer output will be applied as an aid to radiologists in their detection and classification decisions. It has been shown in the laboratory that computer-generated information can improve radiologists' detection of microcalcifications[7] or masses,[13] decreasing the radiologist "miss rate" by as much as 50%. It is of interest that such improvements in radiologist performance may occur, even if the computer is less sensitive than the radiologist in the detection task at hand[7] or if the radiologist does not believe all true positive prompts given by the computer.[13]

It has been established that computers can assist radiologists in their decisions regarding differential diagnoses by suggesting cases having comparable features and known diagnoses.[9] Very recently, it has also been shown that radiologic characterization of microcalcifications can be improved in a highly significant way using computer-generated likelihoods of malignancy, increasing radiologist sensitivity while at the same time improving specificity.[8] Given the success of many investigators in correctly characterizing lesions by computer, similar results can be expected in the near future.

Attention is now turning from the laboratory to the clinic, where the ultimate assessment of the efficacy of CAD will take place. It has been shown that the yield of screening mammography for early malignancies can be increased by 6% to 15% when films are reviewed by two radiologists.[21] It is thus a reasonable first goal for CAD to achieve the efficacy of radiologist "double reading" through machine prompting of a single radiologist. Verification of such benefit when the diagnostic output is based on radiologist-computer collaboration is not a trivial exercise since, unlike double human interpretation, it may not be clear when the presence of the computer has made an actual difference.

The success of CAD systems in detecting missed cancers that are relatively conspicuous in retrospect (and so suggesting that the computer output will likely be "believed" by the radiologist) implies that general implementation of CAD can increase the yield of screening mammography by as much as 20%.[3] Proof of such benefit in practice would require very large clinical trials because of the low incidence of breast cancer in screened populations and the relatively small anticipated increase in yield. Of interest, however, is that routine use of CAD in everyday practice does not seem to increase work-up rates.[3] This obviates a potential drawback to the general use of CAD.

Current Issues in CAD

As is typical in any newly emerging line of scientific investigation, early work raises a number of important issues that are only resolved after further careful study. Below is a short summary of some unsettled issues or unanswered questions in CAD as applied to mammography.

CAD and mammographic image quality. Emphasis in CAD research to date has been in the extraction of useful information from available clinical mammograms. It is not presently known to what degree the radiographic quality of mammographic images determines the likely success of CAD algorithms. Digital mammography offers clear-cut theoretical advantages as the source of images for CAD, principally in the form of improved signal-to-noise characteristics of the images. Whether these advantages will be manifest in practice has not been fully investigated. Images acquired either conventionally or digitally can be expected to show significant variations among individual patients, in part related to patient age and hormonal status. Such is known to affect the success of human observers in making diagnoses on mammograms, but the implications of these variations in CAD is less clear. Further, it may be that CAD analysis may eventually provide image quality information that is useful to practicing radiologists for quality control purposes.

CAD and image science. Most successful CAD algorithms draw from a wide range of approaches and insights developed elsewhere in image science. These algorithms are computationally intense, a significant problem but one that has been partially alleviated by the ongoing rapid improvement in digital computer technology. Many questions nevertheless remain. For example, the performance of classification schemes can be expected to depend on the pixellation of input image data, although results indicate that this may be highly dependent on the type of abnormality to be categorized.[10, 18] The variability of clinical mammographic image quality suggests that new approaches that make image processing techniques adaptive to image quality and patient characteristics may be of considerable value.[16, 22] Further, despite the large variety of computer vision and artificial intelligence strategies employed by researchers in the field, there is no general assurance that these have been optimally applied or that other approaches, presently unappreciated or untried, might not eventually supplant many current strategies.

CAD and findings on clinical mammograms. The limits of mammographic detection of early lesions by either computer or human observers are not presently known. Work suggests that truly borderline findings identified by radiologists, when followed, almost never "grow" into cancer.[4] Such may also be true for borderline findings identified by computer, but this has not been investigated. Additionally, it is known that many false-positive prompts generated by CAD detection schemes have at their bases true image findings (e.g., one or two nearly subliminal microcalcifications and adjacent quantum noise).[23]

The overlap of mammographic features used by human observers in distinguishing benign from malignant lesions almost certainly prevents an entirely accurate differentiation of such. As described, high-quality computer algorithms using features that humans employ do at least as well as humans in making benign and malignant differentiations. Other information, not directly accessible to human observers, is extractable from mammograms by computer analysis for the purpose of making such differentiations.[20] Whether such information has particular diagnostic benefit has not been fully investigated.

Effectiveness of CAD algorithms. CAD systems are presently evaluated primarily in the environments in which they were developed. Future practical development work on such systems may require or assume that they meet or exceed performance levels already known to have been achieved in other ways by different investigators. This necessitates uniform criteria for system evaluation. One potential approach is the use of standardized databases on which algorithms can be tested.[24] The development of such databases, particularly guaranteeing that their content and variability are typical of clinical practice, is a difficult issue. The way such databases will figure in the eventual infrastructure required to support CAD development and testing in an ideal way is also uncertain. For example, it may well be useful that, for testing the relative effectiveness of different algorithms, portions of standardized databases be sequestered from developers.[25]

CAD and the radiologist. The initial investigations of CAD methods have focused additional attention on the interpretation of mammograms by radiologists. It is possible that factors limiting the effectiveness of radiologists in the interpretation of mammograms may also limit their interactions with computer-generated diagnostic information, but essentially no data exist in this regard. The variability of individual radiologists' skill or expertise may also be a factor. Recent work performed in conjunction with CAD research suggests that such variability may be larger and more significant than previously suspected.[3, 26] Also,

whether computers can be programmed to generate accurate diagnostic information that has a low correlation with that readily accessible by radiologists, and so potentially of greater benefit to radiologists, is an unsettled matter.

The optimal approaches for presentation of CAD information to radiologists remains an open issue. Such issues will evolve as digital mammographic systems become more widely used in standard clinical practice. The unanswered question of the best approaches to convey digital mammographic images to the radiologist (i.e., hard copy versus soft copy, etc.) will inevitably become intertwined with CAD information display.

CAD and the practice of radiology. The double reading of screening mammograms has been a long and widespread practice in Europe. Many logistical impediments exist in its routine adaptation to practices not solely devoted to high-volume screening mammography, however. In the United States, for example, double reading of screening mammograms remains by far the exception rather than the rule. On the surface, "double reading" by a radiologist and a computer may present less difficulty in day-to-day practice, but technologist and radiologist work flow issues remain. It is also not known at present what levels of sensitivity and specificity will be required of computer systems to ensure that their use by radiologists will routinely improve the yield of mammography for the early detection of breast cancer.

Finally, the anticipated role of CAD in mammographic practice a decade or two from now, which should in some sense guide research today, is very uncertain. Although no rational radiologist or scientist would suggest that computers will soon supplant radiologists as the primary interpreters of mammograms, this concept can at least be contemplated even at this early stage of development. First, it is now common to learn of functions once performed solely by humans that are now routinely done by computer. Second, the detection and characterization of lesions in conventional or digital mammography is a relatively stationary, albeit fuzzy, target. Further, advances in CAD will be cumulative and, unlike those accrued by human observers, will not have to be painstakingly "taught" to the next generation of computers.

Data now being generated should give pause to those who believe that computer methods will forever remain out of the mainstream of diagnostic radiology or, if generally adapted, will be employed only to assist radiologist observers. Two recent results are of potential interest in this regard. First, it is reported that at least one CAD algorithm has a 50% sensitivity for breast cancer presenting as masses at a false-positive rate of 0.02 per image.[27] The latter value is comparable to a radiologist having a "call-back" rate of 8% which, in turn, is typical of practice in the United States.[3] Also, the 50% sensitivity is greater than at least some practicing radiologists evaluated in CAD-related sensitivity studies.[3, 26] Further, in one large series, only 2% of all breast cancers in the study were present on examinations in which no prompts were issued by the CAD system.[3] Assuming an average likelihood of cancer in any given screening case being about 0.5% (i.e., 5 per 1,000), this would correspond to a likelihood of cancer on cases without computer prompts of about 0.001%, or 1 in 100,000.

Research Priorities

It is possible that present CAD research in mammography represents the leading edge of a revolution that will eventually change how radiology is practiced. In addition to the anticipated public health benefits that such research will have in the improved detection of early breast cancer, much of this research will serve as a template for CAD applications in other areas of radiologic practice. The overall priority for such research therefore is high.

Although it is not possible to envision all issues that may arise in CAD research in the years to come, aspects of such future work can be readily anticipated. Session participants formulated the following research priorities for the short, intermediate, and long term. These priorities follow naturally from the range of issues that exist in mammography CAD, as well as from its anticipated role in future practice.

Research Priorities

Short term

- Develop better algorithms to improve CAD detection performance, including temporal analysis of mammograms and correlation of two views.
- Develop better algorithms to improve CAD characterization performance, including use of nonimage data (e.g., clinical, genetic).
- Integrate detection and classification schemes.
- Apply CAD to full-field digital mammography, including use of CAD to enhance display of digital mammograms.
- Develop standardized databases, standardized evalua-

tion criteria, and better assessments of radiologists performance.

Intermediate term

- Develop better algorithms, including image adaptation, image modeling for normal tissue recognition, and incorporation of physician knowledge.
- Generalize algorithms for different sensors.
- Optimize CAD presentation to radiologists while refining assessments of efficacy.
- Develop methods for CAD-related radiologist training.
- Apply CAD to tomosynthesis, stereo mammography, and digital subtraction mammography.

Long term

- Develop better algorithms, making continued improvements on all fronts with the goal of exceeding performance of radiologists.
- Evaluate CAD for primary screening (detection).
- Evaluate CAD for primary diagnosis (characterization).
- Enable multimodality image and data fusion for CAD.

References

1. Vyborny CJ, Giger ML. Computer vision and artificial intelligence in mammography. AJR 1994; 162:699-709.
2. Harvey JA, Fajardo LL, Innis CA. Previous mammograms in patients with impalpable breast carcinoma: retrospective vs blinded interpretation. AJR 1993; 161:1167-1172.
3. Doi T, Hasegawa A, Hunt B et al. Clinical results with the R2 ImageChecker system. In: Doi K, et al. eds. Proceedings of the First International Workshop on Computer-aided Diagnosis. Amsterdam: Elsevier Science, 1999; (in press).
4. Wolverton DE, Sickles EA. Clinical outcome of doubtful mammographic findings. AJR 1996; 167:1041-1045.
5. Kopans DB. The positive predictive value of mammography. AJR 1992; 158:521-526.
6. Vyborny CJ. Can computers help radiologists read mammograms? Radiology 1994; 191:315-317.
7. Chan HP, Doi K, Vyborny CJ, et al. Improvements in radiologists' detection of clustered microcalcifications on mammograms. The potential of computer-aided diagnosis. Invest Radiol 1990; 25:1102-1110.
8. Jiang Y, Nishikawa RM, Schmidt RA, Metz CE, Giger ML, Doi K. Improving breast cancer diagnosis with computer-aided diagnosis. Acad Radiol 1999; (in press).
9. Swett HA, Giger ML, Doi K. Computer vision and decision support. In: Hendee WR, Wells PNT, eds. The perception of visual information. New York, NY: Springer-Verlag, 1993; 272-315.
10. Qian W, Clarke LP, Song D, Clark RA. Digital mammography: hybrid four-channel wavelet transform for microcalcification segmentation. Acad Radiol 1998; 5:354-365.
11. Nishikawa RM, Giger ML, Wolverton DE, et al. Prospective testing of a clinical mammography workstation for CAD: analysis of the first 10,000 cases. In: Karssemeijer N, et al. eds. Digital mammography '98. Amsterdam: Kluwer, 1999; (in press).
12. Schmidt RA, Nishikawa RM, Osnis RB, Schreibman KL, Giger ML, Doi K. Computerized detection of lesions missed by mammography. In: Doi K, et al. eds. Digital mammography '96. Amsterdam: Elsevier Science, 1997; 105-110.
13. Kegelmeyer WP Jr, Pruneda JM, Bourland PD, Hillis A, Riggs MW, Nipper ML. Computer-aided mammographic screening for spiculated lesions. Radiology 1994; 191:331-337.
14. te Brake GM, Karssemeijer N, Hendriks JH. Automated detection of breast carcinomas not detected in a screening program. Radiology 1998; 207:465-471.
15. Yin FF, Giger ML, Doi K, Metz CE, Vyborny CJ, Schmidt RA. Computerized detection of masses in digital mammograms: analysis of bilateral subtraction images. Med Phys 1991; 18:955-963.
16. Li L, Qian W, Clarke LP, Clark RA. Digital mammography: computer-aided diagnosis method for mass detection with multiorientation and multiresolution wavelet transforms. Acad Radiol 1997; 4:724-731.
17. Wu Y, Giger ML, Doi K, Vyborny CJ, Schmidt RA, Metz CE. Artificial neural networks in mammography: application to decision making in the diagnosis of breast cancer. Radiology 1993; 187:81-87.
18. Huo Z, Giger ML, Vyborny CJ, Wolverton DE, Schmidt RA, Doi K. Automated computerized classification of malignant and benign masses on digital mammograms. Acad Radiol 1998; 5:155-168.
19. Sahiner B, Chan HP, Petrick N, Helvie MA, Goodsitt MM. Computerized characterization of masses on mammograms: the rubber band straightening transform and texture analysis. Med Phys 1998; 25:516-526.
20. Chan HP, Sahiner B, Lam KL, et al. Computerized analysis of mammographic microcalcifications in morphological and texture feature spaces. Med Phys 1998; 25:2007-2019.
21. Thurfell KA, Lerneval AA, Taube AH. Benefit of independent double reading in a population-based mammography screening program. Radiology 1994; 191:241-244.
22. Qian W, Li L, Mao F, Clarke LP. Digital mammography: adaptive directional wavelet transform in mass segmentation and detection. Medical Physics 1999; (in press).
23. Nishikawa RM, Vyborny CJ, Giger ML, Doi K. Analysis of false-positive microcalcification clusters identified by a mammographic computer-aided detection scheme. Proceedings SPIE 1994; 2167:773-777.

24. Bowyer K, Kopans D, Kegelmeyer WP, et al. The digital database for screening mammography. In: Doi K, et al. eds. Digital mammography '96. Amsterdam: Elsevier Science, 1997; 431-434.
25. West J, Fitzpatrick JM., Wang MY, et al. Comparison and evaluation of retrospective intermodality brain image registration techniques. J Comput Assist Tomogr 1997; 21:554-566.
26. Schmidt RA, Newstead GM, Linver MN, et al. Mammographic screening sensitivity of general radiologists: effect of double reading. Radiology 1998; 209(P):392.
27. Karssemeijer N, te Brake GM. Combining single view features and asymmetry for detection of mass lesions In: Karssemeijer N, et al. eds. Digital mammography '98. Amsterdam: Kluwer, 1999; (in press).

Session 3: 3D Image Segmentation

Three-dimensional image segmentation, or object (e.g., tumor) delineation, is an operation fundamental to a variety of 3D image analysis tasks that result in the measurement and visualization of anatomical and physiological information related to critical diseases in general and to women's health issues specifically. The primary goal is to extract and understand gross image structure from 3D images of a patient efficiently and robustly in order to relate it to normal anatomy, pathology, microstructure, and function/behavior.

Segmentation is the separation of organs, vessels, lesions, and other anatomically identifiable substructures in diagnostic images. Organ or tumor size and volume determination, normal structure delineation, measurement of aneurysm morphology, and extraction of surfaces for virtual endoscopy are examples of tasks where segmentation is important.

Segmentation is laborious, variable, and difficult since it is almost universally done by manual outlining, sometimes assisted by semiautomatic tools, and rarely automatic tools. Automatic separation of diagnostic imaging scenes into the anatomic components is very desirable but not often achieved due to serious limitations in segmentation methods.

It is disconcerting to find that a computer imaging system cannot separate gray and white matter in brain MRI scans, a tumor from surrounding edema, ducts from parenchyma in postcontrast liver CT scans, or the true and false lumens in an aneurysm. Automatic segmentation is a goal that cannot be achieved reliably and efficiently with current methods, despite its importance. For example, 3D conformal radiotherapy planning requires delineation of the target (i.e., tumor) as well as critical and normal structures. Automatic segmentation is an essential ingredient of this planning process, and many research groups are developing new methods that eliminate the human operator in this process. So far, success has been elusive, and no general solution for automatic segmentation is available.

Use of Pattern and Texture

Approaches related to recognizing patterns in image data represent some of the earliest and perhaps most basic work in medical image analysis in general, and image segmentation in particular. The idea of extracting dense sets of image-derived features and sending the information to pattern classification schemes is fundamental and remains an approach of interest in many application areas, including mammographic analysis. In recent years, researchers have extracted more meaningful features at higher levels of abstraction (e.g., curvilinear structures as opposed to simply distributed distinct edges) that have helped provide more useful classifications. Furthermore, the ongoing work in texture analysis has provided helpful information for potentially recognizing meaningful patterns in a variety of areas, including a host of cancer-related scenarios.

Finding optimal subsets of key features for different problems, however, remains an elusive goal. This is in large part due to the lack of having test databases with known "ground truth" as well as a lack of clear understanding about ideas of image quality related to particular image analysis tasks. With regards to the latter scenario, only a small community of researchers continues to look at this problem. In general, the development of validation databases and evaluation methodology is critical here.

Use of Prior Information

It has been long been felt that the use of prior information in one form or another is particularly useful in solving image segmentation problems. Object priors can come in many forms and may be both local and global in nature. The discussion focused primarily on the use of global shape priors and how these might be extended.

An important problem area in this work is the need to design principled strategies for forming these priors as well as applying them. Some work has been carried out in terms of developing anatomical atlases for use in finding priors, but to date much of the work has been performed in a more structure-by-structure manner. With respect to applying priors to different segmentation tasks, there have been a number of groups working on using shape-based

priors.[1] A key extension to the use of prior information would be to form more complete models that would include signal intensity information as well. Work has been ongoing in this direction at the University of Manchester in an effort to develop a strategy that could be termed "full appearance modeling." Perhaps the incorporation of object shape with other surrounding information, such as image intensity, surrounding texture, or adjacent vascularity would be useful in uncovering both more difficult normal and abnormal (e.g., tumor) structures.

Use of Multiparametric Image Analysis

In many image analysis problems, multiple sets of images are acquired that are potentially of use for diagnosis and/or treatment. Within these domains, there is often a wealth of information available from a variety of images that can be incorporated into image segmentation approaches. This range of image data—from various imaging modalities acquired at about the same time (e.g., magnetic resonance imaging, ultrasound, single-photon computed tomography, positron emission tomography), the same imaging modality at virtually the same time (e.g., MR-based T1, T2, and proton density images), or the same or different modalities acquired over several time points (e.g., longitudinal studies of the same patient's disease progression)—may provide important complementary information that could be treated as a priori constraints for segmenting structure from any one image within the entire group. The integration of this information, however, is confounded by (1) the different spatial and temporal resolution of the acquisitions, (2) the difference in the fundamental information contained in each voxel of different image types, and (3) the fact that patient positioning may cause different soft tissue and organ deformations for different acquisitions.

Attempts have been made to develop unifying platforms for integrating this information. Underlying structural geometry is the key basis for integrating heterogeneous sources of information across imaging modalities. Geometry has been used to

- Superimpose deformable models of information in one image onto image-derived information from a different image for extracting the liver during surgery and for planning cancer therapy[2]
- Track developments of tumors and microcalcifications over time
- Integrate information about the same structure across various imaging modalities
- Compare image-derived geometry to that found from histological studies.

Some approaches have attempted to form unified image segmentation reasoning strategies that could integrate complementary information related to signal intensity with deformable boundary-related features from the same or different modalities.[3] Open problems in this area remain how to distinguish between morphometrical and morphological variation, how to initialize the geometry-based deformable model strategies, and how to move beyond geometry into different modeling approaches (including biomechanics).

Staging and Temporal Analysis of Datasets

Noninvasive 3D MRI allows serial screening of patients and detection of temporal changes by computer-assisted processing. Analyzing the time domain is a powerful feature: it directly focuses the clinical question of detecting changes due to disease evolution and/or efficacy of therapeutical procedures like drug treatment or radiotherapy. A typical example is temporal lesion analysis in multiple sclerosis patients followed up over 1 year with 12 to 24 MR scans.[4] It is demonstrated that a time-series analysis of registered series of 3D datasets results in a segmentation of active lesions and a characterization of the temporal and spatial characteristics of the lesion pattern.

Another application, which focuses on modeling organ movements in proton beam treatment of prostate cancer patients, demonstrates that a reliable and reproducible model-based 3D segmentation of organs in a large series of computed tomography (CT) datasets will help to build a normative database of the variability of organs. Knowledge about organ variation and motion is required for future high-precision focused treatments of small tumors, for retrospective quality assessment, and for prospectively updating current treatment plans.

Bringing Physics and Clinical Pathology to the Segmentation Problem

Segmentation of medical images is a difficult problem, often requiring analysis of complex information and requiring reliability beyond the norm with respect to typical computer vision problems. The basic difficulties lie in the facts that the shapes of interest contained in the images are complex, changes of interest are often subtle, and there is typically only weak control of the image formation process.

Because of this, it is important to develop models to guide the segmentation process, including models of image

formation, anatomy, pathological processes, and "normality." In addition, image normalization must be provided in order to compare information across image datasets within a test group. Several models of image formation and pathological structure have been developed that used mammographic analysis as a problem area. An X-ray image formation model that accounts for the thickness of interesting (nonfat) breast tissue between each pixel in the image and the X-ray source is a key example of accounting for acquisition vagaries and providing a mapping to a normalized framework for measurement.[5,6] This representation, termed H_{int}, was used to eliminate confusing background information (e.g., mammographic glare) in order to reduce false-negatives and was then used as a basis to better model microcalcifications as features in order to reduce false-positives in mammographic analysis.

Physics-based models such as these, as well as ideas for modeling the breast tissue itself (e.g., mechanics-based finite element strategies), are critical for relating new 3D image information from MR and ultrasound to mammograms in order to better understand and analyze breast cancer.

State of the Art

While the segmentation of image structure from 3D images is a fundamental image analysis task, it cannot be performed without considering the fact that it interacts strongly with a variety of other image analysis tasks, especially image registration, computer-aided diagnosis, and visualization. In this light, it is recommended that image segmentation should not be thought of as an end in itself but as one important task within an image analysis system.

The current state of the art in 3D medical image segmentation is that most efforts in the literature have focused on trying to segment a single object that can presumably be isolated and extracted from the image. While there certainly have been some efforts to go after multiple objects at once, these ideas are only now starting to emerge. One approach that is receiving much attention in the neuroimaging field is the use of atlas-based strategies, where atlases of labeled objects are matched to the underlying structure in a test image, implicitly segmenting the structure (an obvious interaction between segmentation and registration). Another critical observation about the state of the art in 3D image segmentation is the lack of a common means of comparing results from different image segmentation algorithms. There has been precious little work in this area in terms of forming common image databases. Furthermore, there have been no efforts specifically aimed at developing an evaluation methodology that would facilitate such comparisons, such as has been done in the image registration community for rigid mappings.[7]

Within the approaches that have been developed to date, various strategies have been used to attack the 3D segmentation problem. These basically break down into three categories: (1) fully data-driven approaches, (2) the use of models of some form to guide the segmentation (e.g., statistical, regularization, biomechanical), and (3) attempts to unify the first two strategies. Furthermore, the use of concepts from scale space theory has often permeated some of the efforts within each of these categories. The most promising results to date have been reported in the second category and relate to the use of deformable model-based approaches for the segmentation of primarily normal anatomy. In these approaches, the model basically captures information about both local and global shape properties of the boundaries of isolated objects, or in some cases about multiple objects.[1,3] More recent, albeit preliminary, efforts beginning to emerge include intensity/appearance, biomechanical, symbolic/syntactic and atlas-related relationships into the basic deformable model framework. It is important to note again, however, that the successes of these strategies are primarily on normal anatomical structures and that developing robust deformable models for dealing with abnormal structure is in its relative infancy. Nonetheless, some efforts are emerging that try to capture, for instance, the essence of the boundaries of spiculated masses. Perhaps more integrated into the current literature is the early use of probabilistic models of normality, assuming that abnormality can be seen as unusual deviations from the normal state while also assuming that the segmentation of either normal or abnormal structure can still be guided by the normal prior information.

Current techniques are only somewhat robust to the vagaries of the image acquisition processes. While segmentation approaches are being developed for use with 3D MRI, CT imaging, ultrasound imaging, and nuclear medicine imaging, all current approaches work best on images acquired using controlled protocols where similar image quality is maintained across all acquisitions. While there is some tolerance of image variability due to a variety of sources (including noise and blur in the acquisition process, patient variability, patient motion, etc.), fully automated 3D segmentation algorithms are not widely robust

to these sorts of problems. On a positive note, however, published work on segmentation algorithms in the field today increasingly shows the algorithms being tested on larger and larger (simulated and actual) experimental test sets.

Recommendations

Because segmentation is an integral part of a system and not an isolated task, it is strongly recommended that future work in this area not be driven along the lines of asking investigators to develop a "bag of tricks" or a toolkit-type platform, which is often the focus of commercial software development. Image analysis investigators should view image segmentation techniques in the context of the entire system with which they will be employed. This implies that segmentation must be considered in an integrated manner with other image analysis system tasks, such as those related to image formation, registration, visualization, and classification. Although a toolkit strategy is not recommended, developing an image interpretation server may be feasible in certain design scenarios. One must still carefully consider where the boundaries are drawn between various subtasks.

The research community needs to move toward the development of an appropriate, integrative framework for image interpretation. Within this, there is a further need for thinking about and developing appropriate unified reasoning strategies (mathematical, logical, statistical, or otherwise) that can bring information from several imaging modalities together. Key to this unified strategy is the development of approaches that can integrate data-driven and model-driven ideas. Another key part of this strategy is that, where model-based ideas are used, investigators need to move beyond the idea of using primarily geometric models. Instead they should be more deliberate about incorporating dynamical/temporal, biomechanical, physiological, biologic, pathological, and topological models into their designs and strategies. Incorporating prior information and constraints related to both normal and abnormal patient variability must be considered, perhaps using atlases. In addition, all of these approaches should consider the impact of looking at different spatial and temporal scales within and across image modalities. Finally, research to develop exemplar systems with provocative goals, such as to design a system to explain a mammogram automatically may nucleate the design process for developing unified systems. Work should be performed to integrate image interpretation with decision support modules to create systems that could provide image-based system support. Such strategies would combine image interpretation with artificial intelligence reasoning or perhaps strategies that can reason and make decisions under uncertainty. In the long term, these approaches could be used to integrate image interpretation with radiological reporting to develop complete health care information/recording systems capable of handling text-based, audio, and video information (including the handling of medical terminology).

Two other issues are paramount within the framework of developing appropriate strategies to meet the needs in medical image interpretation: (1) integrating image-based information with concepts of integrative biology and pathology and (2) developing validation methodologies. With respect to the first issue, information might be gleaned from any particular diagnostic medical image that is complementary to other types of information about a patient, including the range of information available from a variety of imaging-based tests. Image analysis must be considered in this context. Such a strategy would provide opportunities for performing image interpretation to develop in vivo markers for improved basic understanding of disease biology and for therapy planning. In addition, it could be used to aid in determining quantitative endpoints for pharmacological interventions as well as to determine tumor size, extent, and vascularity. Implicit in the notion of integrative study of biology and pathology is that there are major challenges related to understanding the relationship between images taken at different spatial scales, using different imaging sources, and at different time points during the course of a disease. The new image analysis challenges include figuring out how to combine synergistically all of this image-based information.

The need to develop validation methodologies presents a critical challenge to the image analysis research community. Currently, the development of image segmentation strategies is proceeding without significant efforts aimed at validation. This trend should be reversed by encouraging research aimed at developing evaluation methodologies, including ways to compare algorithms as well as to create a statistical database of normal and abnormal cases that can be used for testing and training. It is further suggested that testing needs to be considered in the context of the entire system but that work on segmentation evaluation should consider related work in the area of image registration.[7]

Research Priorities

Short term

- Develop validation databases and evaluation methodology for image interpretation tasks.
- Consider international collaborative mechanisms in image interpretation research, especially regarding validation.
- Initiate cross-disciplinary workshops that bring together image analysis researchers and biologists/pathologists.

Intermediate

- Develop unified strategies and architectures for image interpretation that would cross-fertilize different model-driven and data-driven approaches.

Long term

- Integrate image interpretation systems with decision support systems in order to develop semiautomated radiological reporting systems.
- Develop approaches to quantitative analysis of diagnostic images in the context of integrative biology and pathology.

References

1. Cootes TF, Hill A, Taylor CJ. Medical image interpretation using active shape models: recent advances. 14th International Conference on Information Processing in Medical Imaging 1994; 371-372.
2. Ayache N, Cinquin P, Cohen I, Cohen L, Leitner F, Monga O. Segmentation of complex 3D medical objects: a challenge and a requirement for computer assisted surgery planning and performing. In: Taylor R, Lavallée S, Burdea G, Moesges R, eds. Computer integrated surgery. Cambridge, MA: MIT Press, 1995; 59-74.
3. Chakraborty A, Duncan J. Game theoretic integration for image segmentation. IEEE Transactions on Pattern Analysis and Machine Intelligence 1999; (in press).
4. Gerig G, Welti D, Guttman C, Colchester A, Szekely G. Exploring the discrimination power of the time domain for segmentation and characterization of lesions in serial MR data. In: Proceedings of the 1st International Conference on Medical Image Computing and Computer Assisted Intervention, 1998; 469-480.
5. Highnam R, Brady M. Mammographic image analysis. Kluwer Series on Medical Imaging 1999; (in press).
6. Hayton PM, Brady M, Tarassenko L, Moore N. Analysis of dynamic MR breast images using a model of contrast enhancement. Med Image Anal 1997; 1:207-224.
7. Maurer CR Jr, Fitzpatrick JM, Wang MY, Galloway R Jr, Maciunas RJ, Allen GS. Registration of head volume images using implantable fiducial markers. IEEE Trans Med Imaging 1997; 16:447-462.

Session 4: 3D Image Registration and Fusion

Registration is the alignment of different images. A registration process enables pairwise superimposition of images obtained (1) with different modalities such as PET and MRI—multimodality, (2) at different times—multitemporal, (3) using different acquisition parameters on a single modality—multispectral, (4) from different individuals or groups, or (5) from an electronic atlas.

Alignment is important for image subtraction, to combine anatomically detailed (e.g., MRI scans) with functional (e.g., PET scans) information, to determine interval change and assess therapy, for fractionated radiotherapy treatment verification, and to transfer information in an anatomic context across the temporal, spatial, and spectral domains within and between individuals. Examples of image registration include comparison of FDG PET scans or bone scans with CT scans to evaluate suspected tumor sites, extraction of the vascular tree in selective angiography, pre- and postradiotherapy tumor measurement, and many others.

Image subtraction requires alignment of pre- and postcontrast images, for example. In film-based image subtraction, paired images are aligned visually using rigid registration since each member of the pair maintains its original size and shape. A rubber sheet transformation allows one member of the pair to stretch or compress locally to superimpose more precisely with its counterpart. Methods have been developed to improve the quality of alignment and eliminate systematic errors.

Image registration is defined here as the determination of a point-by-point geometrical mapping from one view to another such that anatomically corresponding points are mapped together. Image fusion is defined as the integration of information from two or more images after they have been registered. A prominent application of fusion is the visual presentation of registered images to the diagnostician or therapist in a way that makes significant similarities and differences readily apparent. This application of fusion is properly a problem of visualization (see Session 5).

Classifying Problems and Methods

Registration problems may be categorized according to the number of dimensions of the images involved: 2D-2D, 2D-3D, and 3D-3D. Two-dimensional images are typically projection images, such those produced by standard X-ray mammography or by planar scintigraphy, which gives quantitative measures of projected gamma radiation produced by injection of radiopharmaceuticals. This section concentrates on 3D images, including X-ray computed tomography, magnetic resonance imaging, single-photon computed tomography, positron-emission tomography, MR spectroscopy, functional MRI, and 3D ultrasound.

Image pairs. Registration problems may also be categorized by whether images are being aligned with other images (image-to-image) or with the physical anatomy of the patient (image-to-physical), whether the registration is between views of the same patient (intrapatient) or different patients (interpatient), and for image-to-image registration according to whether only one imaging modality involved (intramodality) or two (intermodality). In focusing on computer-aided methods, this section is confined to digital images. The term "voxel" is used to refer to the 3D rectangular element of intensity in a digital image.

Anatomy. The problems of medical image registration may in fact best be categorized according to the anatomy being imaged. An important distinction should be drawn as to whether the anatomy can be treated as rigid (e.g., head, vertebra) or as nonrigid (e.g., breast, lungs, abdomen, contents of the pelvis). Despite the prevalence of nonrigid motion in the human anatomy, rigid methods have played a preeminent role in registration. Because of the relative simplicity of the rigid mappings, which can be completely described by six parameters (shifts along the x, y, and z axes and rotations about them), there has been far more progress in the registration of rigid anatomy, particularly the head, than of nonrigid anatomy. Furthermore, when the anatomy is nonrigid, many approaches to registration rely on a first phase in which rigidity is assumed, followed by further phases in which nonrigid mappings are composed with the rigid one. Because of the relatively highly developed state of rigid registration and because of the highly nonrigid nature of the breast, lung, and abdominal and pelvic organs, nonrigid registration problems have become of critical importance in computer-aided solutions to problems associated with the female body.

Registration cues. The methods of registration, as opposed to the problems of registration, can be further categorized according to the cues used to find a mapping that brings the two views into registration. The cues may be distinct geometrical features or, for image-to-image registration, intensity patterns among the voxels themselves. A standard geometrical feature is the anatomical point. Other features include lines (typically curved) and surfaces (also curved). Registration methods may be based on one type of feature or may use two types. All methods based on features require a feature-detection step, which may in fact be the most difficult part of the process. The next step is the determination of a mapping that brings the corresponding features (intrapatient registration) or homologous features (interpatient registration) into alignment. Points that lie between the features are then mapped by interpolation. Feature-based registration can be applied to both image-to-image registration and image-to-physical registration problems. Voxel-based cues typically involve the distribution of intensity values. In this case, mappings are chosen that maximize some measure of similarity between the intensity patterns in the two images (e.g., mean absolute difference, normalized correlation, mutual information).

Rigidity. The difficulty of these registration methods is strongly affected by whether the registration problem involves rigid or nonrigid anatomy. For the rigid case, the class of feasible mappings is known (shift plus rotation). If three or more points can be recognized in one view and three corresponding or homologous points can be found in a second view, the rigid mapping is completely determined (provided the points do not lie on the same straight line). Furthermore, deterministic algorithms are available to find the optimal rigid mapping once point correspondences are established. Such algorithms can also take as input unordered sets of points whose correspondences are determined as part of the registration process itself. Nonrigid mappings can be based on sets of points. Both rigid and nonrigid mappings can be determined from sets of lines; sets of surfaces; or combinations of points, lines, and surfaces, with or without known correspondences. In contrast to rigid mappings, however, nonrigid mappings typically require many more features as input. The choice of nonrigid mapping function is part of the problem, and only heuristic search algorithms are available to find the optimal function.[1]

Automation. Registration methods often involve some user interaction. It may be required that landmarks be identified, that unimportant or confusing regions be excluded, that a rough initial alignment be provided, or that

optimization parameters be chosen. Such interaction has two major disadvantages: (1) it occupies user time and (2) it makes the quality of the registration subject to the expertise of the user. The former increases the expense of the process, and the latter decreases the consistency. Automation is thus a highly desirable feature of registration methods and, in some cases, may be worthy of a slight loss in accuracy. Automation also makes large-scale retrospective studies feasible and facilitates screening. The latter application may be incorporated as background process in picture archiving and communication systems (PACS). While automation reduces the active human time involved in the registration process and may even eliminate it, the overall time required for registration may be much less when interaction is employed. The human, drawing on some a priori knowledge, may be able to guide the algorithm via a good initial starting pose or by emphasizing some parts of the image and eliminating others from consideration. The extra time required by a totally automatic algorithm may be long enough to represent a clinical bottleneck. Thus, once automated, a process can still be improved if the automatic algorithm can be accelerated.

When automatic algorithms fail, they rarely report that they have failed. Thus, once an automatic algorithm has completed its registration task, visual inspection may be required to verify the quality of the registration. This step was recognized as being crucial in a recent evaluation of registration methods in which unexpected errors of several centimeters appeared among registrations that were typically accurate to 2 or 3 millimeters. Algorithms that "know" when they have failed would represent an important step forward in the automation of image registration.

Prospective vs. retrospective. A final dichotomy should be recognized in registration methods: prospective versus retrospective methods. A prospective method is any method in which a special physical apparatus is attached to the anatomy before imaging to facilitate registration. Retrospective methods are simply methods that are not prospective. The earliest prospective methods were based on the stereotactic frame, in which a rigid frame of known shape is attached to the anatomy, typically via bone-implanted mounts. Recently, prospective methods have been developed that are based on individually mounted markers, both bone-implanted and skin-attached. The latter methods are sometimes called "frameless" methods. Both frame-based and frameless methods always involve feature-based registration, are restricted to rigid mappings, are typically applied to the head, and are used only to guide surgery or therapeutic radiation. Retrospective methods are used when such preparation is considered to be too invasive or when the decision to employ registration is made only after the images are acquired. The hallmark of the prospective methods is their accuracy. Such methods have been used as "gold standards" for measuring the accuracy of retrospective methods.[2]

Reviews of registration literature. An expanded and heavily annotated categorization along with an extensive bibliography of recently (since 1993) published registration methods can be found in a 1998 review article by Maintz and Viergever.[3] An earlier (before 1993) bibliography can be found in the 1993 review by Maurer and Fitzpatrick.[4] These bibliographies include over 500 articles, almost all of which were published within the past 8 years, indicating a growing recognition of the importance of registration in medical imaging.

Relation to Segmentation

Image segmentation, which is defined here as the partitioning of an image into meaningful parts, is a classic field of image processing, both in medical and nonmedical applications, and is considerably older then the field of registration (see Session 3). Registration is strongly related to segmentation: segmentation can be used in the registration process and registration can be used in the segmentation process. This two-way street can be exploited to produce an iterative process in which registration and segmentation alternate. An excellent example of such an approach is the 3D-2D registration method developed at Yale for matching a 3D CT scan to megavoltage radiation therapy portal radiographs. In this method, each iteration of the registration algorithm supports a refined segmentation of features (bones in the radiograph), which then are used in the next iteration of registration.[5]

Segmentation is a necessary first step in feature-based registration methods, in which features must be found before a mapping can be determined. As pointed out above, this step may be the most difficult, and hence the least reliable, part of a feature-based registration algorithm. The fundamental advantage of the prospective methods with respect to precision of image registration is the accuracy with which the added apparatus can be segmented.

In the inverse relationship, registration is of potential use in segmentation when two or more images of the same anatomy are available. For example, when two images of different modalities of the same patient are available tissue segmentation, the two images may be brought into

alignment in a registration step. Subsequently, pattern analysis methods may be applied to a feature space whose dimensions are the intensities of corresponding voxels in the registered images. Clusters in that space correspond to tissues of the same type. As a second example, an image of some given modality may be carefully segmented manually for one patient so that it can serve as an atlas. Subsequently, other patients' images can be segmented automatically by registering them (nonrigidly) to the atlas. In either case, registration helps to solve the segmentation problem, but it also becomes a potential source of error for the segmentation process.

A further application of segmentation to registration lies in the validation of registration methods. Techniques for validation often rely on measurement of mapping error for corresponding features that are not used in the registration process. A segmentation error in either or both registered images produces features that do not correspond in the two images. Thus, even perfect registrations are assessed errors, and imperfect ones are charged with errors that are, in the mean, too large.

Clinical Application Area: Breast

Registration has applications in breast imaging as a means to evaluate temporal changes for comparison between the left and right breasts and for measurement of contrast uptake. The major challenge in registration of breast images is their nonrigidity. Nonrigidity is a particularly difficult problem for 2D X-ray projection imaging, which is the current default in mammography. Comparison of serial mammograms for change detection is a particularly difficult 2D-2D registration problem, both due to the nonrigid nature of the breast and to the lack of ability to reproduce the geometry of acquisitions separated in time by 1 or more years. The confusion of overlying and underlying tissue and their relative in-plane motion between images may confound registration to the extent that it is useless for projection imaging. MR mammography on the other hand, while it is currently not commercially viable because of its higher cost, is far more amenable to registration because of its 3D images. Accurate, robust, and clinically usable solutions to the problem of nonrigid 3D-3D registration will be critical to the optimal use of MR in mammography. With the anticipated introduction of MRI as a mammographic modality, 2D-3D registration of MRI with X-ray mammography will become critical to correlate features observed in the two modalities. Adequate treatment of this registration problem may require use of a biomechanical model of the breast, as discussed above. There is a great deal of work to be done before nonrigid registration techniques achieve the level of robustness and automation needed for use as part of screening procedures. Research directed toward this end should be pursued with high priority.

Ultrasound also produces 2D images. An important distinction from X-ray mammography, however, is that an ultrasound image is not a projection image. Tracking the ultrasound probe as it is scanned over the breast makes it possible to place an ultrasound image in three-dimensional space or even to construct a volume from sequentially acquired planar images. Such images may be used to guide biopsies. Ultrasound is cheap, can be acquired in real time, is robust to surgical procedures, and as a low power imaging technique is harmless. Its chief disadvantage is its low signal-to-noise ratio. Registration of preoperative MR to 3D intraoperative ultrasound may make it possible to combine the high signal-to-noise ratio of MR with the real-time capability of ultrasound.

Other modalities are of importance in breast imaging as well, including nuclear medicine images and magnetic resonance spectroscopy. In every case, however, registration is confounded by the problem of nonrigid motion. As pointed out above, the form of the nonrigid mapping is critical for any registration method. The availability of accurate biomechanical models of the breast will be crucial in choosing the mapping.

Clinical Application Area: Pelvic Organs

The pelvic region contains some rigid anatomy in the pelvis itself and in the vertebrae, but nonrigid anatomy predominates. Some organs undergo radical changes in shape, such as the bladder and the colon. Advantage may be taken of the rigid pelvis for initial rigid-registration steps, but the challenge here, as with the breast, is nonrigid registration. A further complication is that there are multiple organs, each of which is nonrigid, with nonrigid connections among organs. As with the breast, biomechanical modeling will be important to accurate registration. As an example of a treatment that could be improved by the development of appropriate registration techniques, radiation therapy of the cervix and uterus would benefit greatly from the ability to fuse ultrasound with CT, as well as from further development of 3D-2D registration methods for localizing radiographically visualized implanted radioactive sources in the 3D context of CT-defined anatomical structures.

Clinical Application Area: Liver

Like the breast and the pelvic organs, the liver is a decidedly nonrigid object and is therefore likely to be a more challenging problem for registration than the rigid anatomy. The liver is, however, considerably more homogeneous than other nonrigid anatomy. Its biomechanical model will be simplified. It may be treated as a prototype for all elastically deformable organs. Research on registration problems for the liver would serve as a bridge from the methods developed for rigid anatomy, such as the head, to methods for nonrigid anatomy with more complex models. Registration problems would include ultrasound-to-MR for image-guided interventions. Ultrasound would need to be registered in real time with MR images acquired in the planning phase. MR-to-MR registration would be appropriate for postoperative evaluation and for long-term monitoring of tumor growth or other changes.

Short-Term Research Needs

In the short term, researchers need improved access to methods for validating registration algorithms. Validation requires databases of registered images and validation tools that are easily accessible to registration researchers worldwide. A recently developed database of clinical images (Vanderbilt) is accessible via the Internet for the rigid registration of CT, MR, and PET images of the head.[3] Such databases should be encouraged but should be expanded to include nonrigid anatomy. Full information must be available detailing the acquisition protocols and scanner characteristics. Ideally, images would be clinically acquired patient images with ground-truth registration mappings available. A time series of X-ray mammograms with some indication of ground truth would be valuable. The difficulty is determining the true mapping. Alternate strategies include computer generation of a simulated image of one modality from a clinically acquired image of another modality (e.g., PET generated from MR). Because the second image is generated from the first, the mapping is known exactly. For nonrigid registration, however, the generation step includes the choice of the nonrigid mapping function as part of the problem. Although databases of phantom images may provide an important companion to clinical databases for calibration purposes, they are of only limited value.

Development of improved patient-image registration methods will contribute to the further advancement of image-guided therapeutic procedures, such as endoscopic surgery, image-guided biopsy, and radiotherapy. To date, patient-image registration procedures are idiosyncratic, having been developed as components of integrated systems using particular localization hardware and computer platforms. The high cost of accurate localizer systems with sufficiently large working volume to be useful in many applications has slowed development of generally applicable systems and limited the use of image guidance to a few research institutions. Research leading to the development of low-cost 3D patient-image registration methods with sufficient accuracy and working volume would be very helpful in extending the potential benefit of image guidance into the community.

Researchers in registration, segmentation, or any field that makes use of registration methods also would benefit from the provision of a database of information on registration methods. Such a database would allow researchers to determine quickly the state of the art and find the software for specific registration problems. The database should be organized so that it can be queried by target organ, registration method (rigid vs. nonrigid, surface-based, model-based, etc.), modalities (CT-MR, PET-MR, ultrasound-MR, etc.), claimed performance (visually accurate to 3 millimeters, better than another method, improves diagnosis, etc.), and possibly other categorizations.

Although methods for the registration of rigid anatomy are far advanced over those for nonrigid anatomy, the automation of rigid-body registration techniques still needs improvement. Such improvements will allow for wider applications of registration because of the increased potential for screening, retrospective studies, and improved clinical throughput. Furthermore, algorithms that determine whether or not they have failed would reduce the effort required for visual inspection.

Many registration methods perform reasonably well with good-quality data. In a clinical setting, data may not always have been acquired in an optimal fashion, or they may come from an inherently noisy or low-contrast modality such as ultrasound or high-energy X-ray radiography. Ultrasound in particular is a modality, that appears to have application in nearly every anatomic site and is highly suited to real-time visualization of internal anatomy for guidance of therapy. Investigation into registration techniques that are robust with respect to low image quality is important.

Practical problems with regard to funding need to be considered. Three problems that should be dealt with are (1) the *sine qua non* status of hypothesis testing, (2) the reluctance to fund planned computer upgrades, and (3) the

difficulty of international cooperation. The first problem hampers non–hypothesis-driven attempts to produce standard databases for the benefit of research that is hypothesis driven. The second problem hampers research that depends on bringing promising methods to the clinic. The difficulty is that state-of-the-art computing platforms are developing so rapidly that they become obsolete in about 3 years. The problem might be addressed by acceptance of a rate of 30% per year depreciation for computing platforms. The third problem hampers attempts to combine the expertise and efforts of researchers who happen to reside in different countries (e.g., in the United States and Europe). New collaborative mechanisms might explore means to reduce the administrative differential between intranational and international cooperation.

Intermediate-Term Research Needs

A problem that is deemed too difficult to be solved in the short term is the development of realistic biomechanical models. These models are important for the improvement of nonrigid registration methods. It should also be recognized that the determination of an accurate biomechanical model is equally crucial to the development of validation methods. Research into methods for validation should recognize this problem. Thus, improvements of these models will lead to improvements of both registration methods and validation methods. The models should be based on direct measurement of physical parameters of living tissue. The primary needs for models are breast, pelvic organs, and liver, with liver being the organ likely to yield the first results.

Until biomechanical models can be developed, statistical models based on phenomenological observations can be substituted. Such models need to be based on large studies with careful statistical controls and involving many subjects.

Although properly classified as visualization, improved image fusion techniques are key to the realization of the potential gain from any improved registration methods. This is particularly true in situations where registered information needs to be fused and used in real time, such as in image-guided surgery. Adequate testing of image registration and fusion in such challenging settings will require access to high-speed computation and state-of-the-art networking and display technologies. Even outside real-time applications, registration and fusion methods will demand very high-speed data processing, communication, and display in order to become practically useful clinical tools. Research into image compression and communication, already important for teleradiology applications for example, will become important to getting registration and fusion methods into widespread use.

Long-Term Research Needs

Because of the great variety of human tissues and organs and the challenge of measuring stresses and strains for any given organ, it can safely be predicted that significant improvements to biomechanical modeling will be needed far into the future of image registration research. These problems may require new methods for gathering physical information, incorporating both macroscopic and microscopic measurements (e.g., MR microscopy). Microscopic, cellular-level images may need to be registered with conventional macroscopic images. New imaging modalities, or at least new modifications of familiar modalities, may be developed. Such new modalities will probably require the development of new registration techniques.

As new imaging techniques are developed to which registration needs to be applied, the database of registered images described earlier will need to be updated to accommodate the state of the art in imaging. Data volumes generated by microscopic imaging techniques will be huge. Researchers will need continuing access to state-of-the-art networking and computation capabilities to deal with such data.

Research Priorities

Short term

- Establish easily accessible databases of registered images and registration methods available via the Internet.
- Develop lower-cost image-to-patient registration systems.
- Improve automation of the registration of rigid anatomy:
  - Greater automation
  - Faster methods
  - Methods that recognize their failure to register
  - Methods that work on low-quality images.
- Establish realistic funding patterns for computer upgrades.
- Improve support for international collaboration.

Intermediate term

- Develop biomechanical models for nonrigid anatomy, including the liver, breast, and pelvic organs.
- Develop statistical models for nonrigid anatomy.
- Develop higher-speed systems for registration and fusion.

Long term

- Continue development of biomechanical models for nonrigid anatomy.
- Develop registration methods for microscopic-to-macroscopic images.
- Create databases of registered microscopic-macroscopic modalities.

References

1. Muthupillai R, Lomas DJ, Rossman PJ, Greenleaf JF, Manduca A, Ehman RL. Magnetic resonance elastography by direct visualization of propagating acoustic strain waves. Science 1995; 269:1854-1857.
2. West J, Fitzpatrick JM., Wang MY, et al. Comparison and evaluation of retrospective intermodality brain image registration techniques. J Comput Assist Tomogr 1997; 21:554-566.
3. Maintz JBA, Viergever MA. A survey of medical image registration. Medical Image Analysis 1998; 2:1-36.
4. Maurer CR Jr, Fitzpatrick JM. A review of medical image registration. In: Maciunas RJ, ed. Interactive image-guided neurosurgery. Park Ridge, IL: American Association of Neurological Surgeons, 1993; 17-44.
5. Bansal R, Staib L, Chen Z, et al. A novel approach for the registration of 2D portal and 3D CT images for treatment setup verification in radiotherapy. In: Wells WM, Colchester ACF, Delp S, eds. Medical image computing and computer-assisted intervention. Berlin: Springer-Verlag, 1998; 1075-1086.

Session 5: 3D Image Visualization and User Interfaces

Three-dimensional image visualization in medicine may be defined as the transformation, presentation, and interaction with multidimensional medical and/or biological image datasets. CT, MRI, PET, SPECT, and sometimes ultrasound provide 3D or 4D images. Our ability to acquire detailed image volumes rapidly is increasing dramatically, but the methods used to display and understand these data are better suited to traditional lower capacity and slower imaging systems.

Image acquisition in 3D MRI and spiral/helical CT scanning now permits acquisition of data volumes in minutes that are impractical to reproduce on film in slice-by-slice format for off-line subjective review. There is a critical and immediate need for better means of softcopy display and review systems to address the widening discrepancy between our ability to gather image data and use it for diagnosis and therapy. The emerging trend to produce volume data in real time with MRI, CT, ultrasound, and X-ray fluoroscopy exceed the capacity of current clinical display systems.

The need for better display systems arises from the demand for minimally invasive image-guided therapies where pre-op images may be combined with a real-time source. Endovascular and interventional procedures require immediate reference to image data gathered before and during the therapy. Biopsy of deep lesions and drainage of cysts or abscesses are guided by real time X-ray, CT, or MRI fluoroscopy that require a display system that provides immediate information on the target and percutaneous probe locations.

Increased image volume acquisition speed provides an opportunity to reduce the time needed to diagnose, stage, treat, and evaluate anatomic abnormalities. The management and display of current with previously obtained image data in the context of an individual patient's clinical needs has central importance in modern radiologic practice. The integration of disparate clinical information sources in the context of a patient's images for decision support is an important long-term goal that will realize the potential for controlling costs and improving outcomes.

In discussing this subject, it is instructive at the outset to provide some related definitions.

Definitions

Real-time imaging. In computer display applications, this implies a frame refresh/update rate sufficiently high to avoid perception of "jerkiness" or stutter (that is, a smooth display), generally accepted to be 15 to 30 frames/second. This means that the display system must compute and display each complete new view in approximately 75 milliseconds or less. In data collection, video rates generally are considered real time (i.e., 30 frames/second).

Interactive imaging. This refers to sufficiently high response time and repetition rate of the system, which senses a user action of some type (e.g., mouse movement, key press, wand motion) and computes a corresponding result (e.g., updating the view on the screen) so that the

user will perceive (near) instantaneous response to the action. This generally requires a response/repetition rate of 10 to 20 frames/second. Interactivity, however, is application or procedure dependent; that is, higher response rates are needed for highly dynamic situations (e.g., catheter positioning) and lower rates for more static activity (e.g., tumor approach).

3D imaging. This refers primarily to acquiring digital samples of objects distributed throughout three space dimensions (i.e., x, y, z), usually but not necessarily with isotropic spacing. The term is often generalized to include processing, display, and analysis of 3D image datasets as well. A 3D image or 3D imaging process can sometimes, but not always, be synthesized by approximating successive 2D steps. Ideally, however, the image is acquired directly in 3D and/or the imaging process is applied congruently in 3D.

Multimodal imaging. This generally refers to the use of different imaging systems (e.g., computed tomography, magnetic resonance imaging, positron emission tomography) to acquire images of the same object (e.g., a patient brain), providing complementary and more detailed information about the object than can be obtained from any single, unimodal image type. More typically, the term may be used to describe a spatial-temporal "fusion" of images of the same object obtained from different imaging systems, determined by spatially and/or temporally registering the images with sophisticated mathematical algorithms so that their individual samples align in space and/or time.

3D visualization. This generally refers to display of 3D objects so as to represent effectively the 3D nature of the objects. Examples of such displays include shaded graphics in 2D display devices (sometimes referred to as 2½D), stereoscopic-type displays requiring special glasses, autostereoscopic and/or holographic 3D displays requiring no physical aids, and "immersive" displays that project the viewer into the scene (e.g., virtual reality environments). But the term visualization as used in computer imaging also implies the capability to manipulate and analyze the displayed information.

The Potential for 3D Visualization

The traditional disciplines of biological and medical science are significantly grounded in the observation and visualization of living structures and in the measurement of various properties of these structures (e.g., their functions). These observations and measurements are often recorded as images. Ever since the invention of the microscope and the discovery of X rays, physicians, surgeons, and life scientists have been using images to diagnose and treat disease and to better understand basic physiology and biology. The value of biomedical images depends largely upon the context from which they are obtained and the scientific or medical interest and goals that motivate their production and use. In biological science, visualizations are used to study the relationship of anatomic structure to biologic function. In clinical practice, visualizations are used to detect and treat disease and trauma that disturb or threaten normal life processes. Traditionally, these visualizations have either been direct, via surgery or biopsy, or indirect, requiring extensive mental reconstruction. The revolutionary new 3D and 4D medical imaging modalities, along with powerful computational capabilities that provide efficient reconstruction and rendering of multidimensional medical and histologic volume image data, now obviate the need for physical dissection or abstract assembly of anatomy and provide powerful new opportunities for medical diagnosis and treatment.

The significant potential for 3D visualization in medicine remains largely unexploited, and practical tools are undeveloped. Many life-threatening diseases and/or quality-of-life afflictions still require physical interventions into the body to reduce or remove disease or to alleviate harmful or painful conditions. But minimally invasive or noninvasive interventions are now within reach that effectively increase physician performance in arresting or curing disease or in reducing risk, pain, complications, reoccurrence, and health care costs. What is yet required is focused reduction to practice of recent and continuing advances in visualization technology to provide new tools and procedures that physicians "must have" to treat their patients. A respected surgeon once said to his scientific colleague, "If I can see it, I can fix it." This simple statement at first glance engenders confidence. However, most current medical interventional procedures to cure or arrest disease, such as surgery, biopsy, and catheterization, still require blind approaches. That is, the physician cannot directly see the target and/or determine the most effective and harmless pathway to the target during the procedure. If visualizations are available, they are often limited to 2D images, slow, and/or off-line. Interventional procedures often depend on gross approximations and estimates of target position and orientation based on preoperative and/or indirect recordings (e.g., X rays, electrocardiogram, etc.).

Interactive visualization and advanced display technologies open new realms into the practice of medicine by permitting the images obtained from modern medical imaging systems to be directly displayed and manipulated with intuitive immediacy and with sufficient detail and speed to evoke sensorial experience similar to that of real experience. Such interactive 3D environments allow physicians to "enter" the visualizations to take up any view point, see dynamic functional processes as well as detailed anatomy, make accurate on-line measurements, and manipulate and control interventional processes. The value of such visualization technology in medicine will derive more from the enhancement of real experience than from the simulation of reality.

Visualizable objects in medicine extend across a vast range of scale, from individual molecules and cells to the varieties of tissue and interstitial interfaces to complete organs, organ systems, and body parts. Visualizations can include functional attributes of these systems, such as biophysical, biomechanical, and physiological properties. Medical applications include accurate anatomy and function mapping, enhanced diagnosis, and accurate treatment planning and rehearsal. The greatest potential for revolutionary innovation in the practice of medicine, however, lies in direct, fully immersive multisensory fusion of real and virtual information data streams into an on-line, real-time visualization during an actual clinical procedure. Such capabilities are not yet available to the general practitioner; however, current advanced computer image processing research has recently facilitated major progress toward fully interactive 3D visualization and realistic simulation. With these advances in hand, there are several important clinical applications possible to be delivered soon that will have a significant impact on medicine, including the detection and treatment of cancer.

Relevant Technologies

3D interfaces for radiation oncology. Important progress has been made in fusing multidimensional image data for effective treatment plans in radiation therapy of cancer. On-line updating and refinement of treatment plans during the treatment procedure also has advanced. The power of multimodal imaging and high-performance computing provides possibilities for more accurate treatment planning and plan adjustments during therapy than ever. The inclusion of 3D user interfaces for effective visualization of plans and interactive manipulation of plan parameters has set the pace for 3D interfaces, but greater improvements are still needed.

Augmented reality technology. The state of the art in immersive interactive displays is promising for some clinical applications, such as 3D image-guided breast biopsies. It is not sufficient, however, for routine, highly accurate, precise, sensitive, and specific applications in clinical situations. Further technological advancement in miniature sensor elements and graphic display chips will begin to approach these requirements in the near future.

Visualization platforms. There has been a rapid emergence of personal computer (PC)-level architectures. This has blurred the boundary between powerful workstations and PC systems. A variety of useful toolkit software packages have emerged that are now poised for rapid prototyping of custom visualization applications for use in clinical diagnosis and treatment. Standardization of languages in medical imaging application programs will hasten the practical use of powerful visualization and display capabilities in health care practice.

Multimodal visualization of 3D images. Fusion of scanned images from multiple scanning sources by using parametric information models and other nonimage data will bring very powerful visualization paradigms into use for enhanced diagnosis and treatment of cancer. The rapidly evolving capabilities of super graphics computing at PC levels for doing real-time interactive volume rendering and display show great promise for achieving immediacy of display and practical implementation of 3D image visualization technology.

Migrating research into successful products. The migration of basic science research into successful medical and clinical products begins by delineating clear goals and technical specifications. This must be followed by careful research and scientific validation, culminating in publication of the research results that can be reproduced, refined, and reduced to practice as highly specific products. These products must then be delivered for integration into total system solutions.

Achieving Future Goals

All of these technologies point toward similar future goals for development of visualization technology and implementation in user-friendly interfaces. They can be reduced to two: (1) improvements in speed, quality, and dimensionality of the display and (2) improved access to the data represented in the display through interactive, intuitive manipulation and measurement of the data. In-

cluded in these objectives is determining quantitative information about the properties of anatomic tissues and system functions that relate to and are affected by disease. To achieve these goals, improved and advanced 3D visualization technology is sorely needed and will have significant impact on the care and management of patients with cancer.

Image-guided procedures. These techniques provide more effective planning and execution of interventional medical procedures. These visualization techniques will need to be in 3D, real time, and interactive.

Correlation of multiple datasets. The information provided by various modern medical imaging systems is largely complementary. When appropriately correlated, the data can present the diagnostician and treatment practitioner with a synergistic, integrated view of the anatomy and pathology being investigated. The ability to visualize these datasets simultaneously in a synergistic manner would be a vital contribution to exploiting the rich information that they mutually contain.

Data reduction. The power of human vision and comprehension can greatly simplify the process of localizing and assessing the nature of disease if proper visualizations can be presented to the powerful "human computer." The challenging requirements for automated electronic storage, processing, and quantitative analysis of image datasets need to be overcome by improved visualization. The datasets are becoming larger, and the ability to navigate effectively through them is increasingly difficult. Accurate patient-specific models derived from these large-volume images may provide the real-time performance required.

Orientation, localization, and navigation. The blessing and bane of large medical image datasets are that they provide considerable information in a 3D context, but the magnitude and complexity of that information sometimes confounds effective navigation to accomplish well-defined and sometimes simple goals. One such goal is to find if disease is present and, if it is, to treat and eradicate it effectively. Obtaining that goal may be accomplished by providing three parameters that answer three simple questions: orientation—where are you, localization—where is the target, and navigation—how do you get from where you are to the target? Improved visualization techniques will play an important role in effective navigation and localization of anatomic and pathological targets, both in diagnosis and treatment of cancer.

Augmentation of 2D. In several situations, both traditional and emerging 2D display technologies will continue to be useful in medical diagnosis and treatment. These can be significantly aided, however, by complementary 3D representations (including displays) of the data and of the environment from which the data were obtained. Three-dimensional displays provide information that the two-dimensional displays do not have. But 2D displays can be presented in real time and inexpensively, making them attractive for routine applications. The 3D display technologies may be limited strictly to complementing, not replacing, the 2D technologies. This might also be achieved at lower cost.

Communication and education. Three-dimensional displays have significant potential for effectively teaching anatomy and illustrating the locus and nature of disease. They are useful for practicing and rehearsing procedures in an electronic or virtual environment that may increase skills at lower costs than traditional training techniques. Three-dimensional information is often more intuitive and complete than two-dimensional information, with the latter often requiring some mental reconstruction and extrapolation. Using 3D information to communicate ideas and procedures between collaborators, between colleagues, and between physician and patient has significant promise.

Current 3D Visualization Capabilities

Figures 1–6 illustrate the state of the art in 3D visualization.[1-16] Applications to women's cancer are especially emphasized.

Figure 1 shows 3D segmentation and volume rendering of a head from registered, multimodality data (CT and MRI). Composite rendering can be used to visualize single objects, like the skull (upper left), or to visualize multiple objects simultaneously, like the skull and sinuses (upper right), or multiple tissue types, like the skull and brain (lower left). If spatial resolution is sufficient, endoscopic view points can be rendered to observe, for example, the frontal sinuses from within the skull (lower right).

Intraoperative image fusion and visualization (Figure 2) provide on-line localization and navigation capabilities. For example, during the operation the neurosurgeon can use augmented reality technology to visualize the brain registered and fused with the preoperative 3D scans. These are displayed to provide a type of "X-ray vision" to reveal brain tumors before and during surgical approach. Such visualizations may be accompanied by real-time 3D deformation of the high-resolution preoperative models to accommodate or correct brain shift during the surgical procedure.

Figure 3 displays 3D segmentation and rendering of breast tissues. Registered, multimodal (MRI, CT, and anatomy) image data automatically classified skin, mammary vessels, and two different densities of mammary gland tissues. Such visualization techniques may facilitate precise localization of calcified lesions.

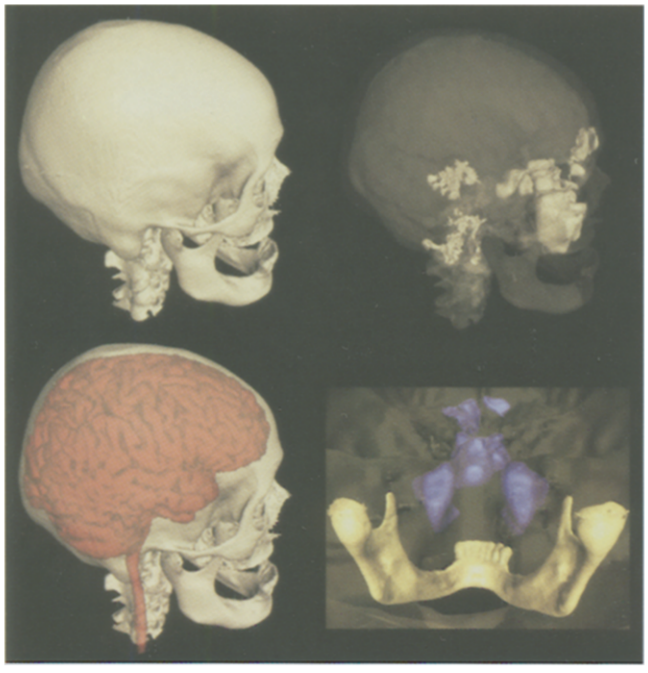

Figure 1. 3D segmentation and volume rendering from registered CT and MRI data.

Figure 4 shows 3D visualization of segmented lungs and computed endoscopic view within the trachea using texture volume rendering. Volume scanning and virtual endoscopy may provide a viable screening tool for airway cancer.

Figure 5 shows 3D modeling of pelvic contents from registered multimodal image data (CT and MRI). Accurate graphic modeling of patient-specific anatomy reduces data size and complexity, facilitating interactive exploration of anatomy for detection of tumors and for planning surgical or radiation treatment.

Figure 6 presents a virtual endoscopic view in the colon of a cancer patient obtained from spiral CT scan. A large polyp is found in sigmoid. The polyp can be automatically segmented and measured, including size and percent vascularity. Vascularity may be a predictive marker for metastatic potential of the polyp.

Image-guided procedures. The state of the art in intraprocedural image guidance is represented by three projects. The first is real-time MRI surgical guidance, where large MRI systems are available in operating rooms to scan the patient during the procedure and immediately following interventions. With such imaging it is possible to update critical information on-line to the surgeon or

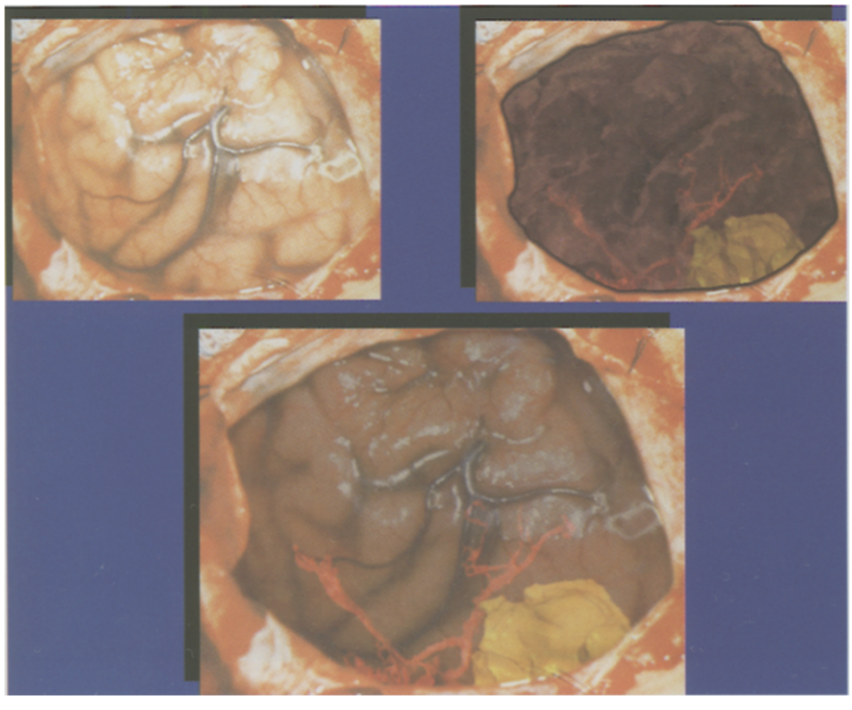

Figure 2. Augmented reality technology with registered and fused preoperative 3D scans.

physician. Another example is 3D radiation treatment planning, where the treatment plan can be modified and updated with images obtained on-line during treatment to accommodate changes, either designed or unexpected, more effectively and accurately. The third example is image-guided breast biopsy using ultrasound and augmented reality techniques, where accurate orientation, localization, and navigation to suspicious sites in the breast is aided by a real-time, image-guided immersive display system.

The state of the art in preoperative image guidance, where high-resolution multimodality scans are often obtained before the procedure, involves appropriately registering, fusing, and presenting images to the surgeon or the physician for viewing of anatomic region(s) of interest and analyzing morphologic and pathologic relationships. Preoperative determination of the approach to the target, along with determination of safe margins around the target (e.g., in resection of a cancerous tumor) can generally be accomplished by such techniques within 24 hours of the procedure.

Correlation of multiple datasets. The availability of multimodality image datasets have stimulated development of a variety of methods to use these datasets in combination in the hopes of realizing more effective diagnostic and treatment procedures.[1-16] The presentation of com-

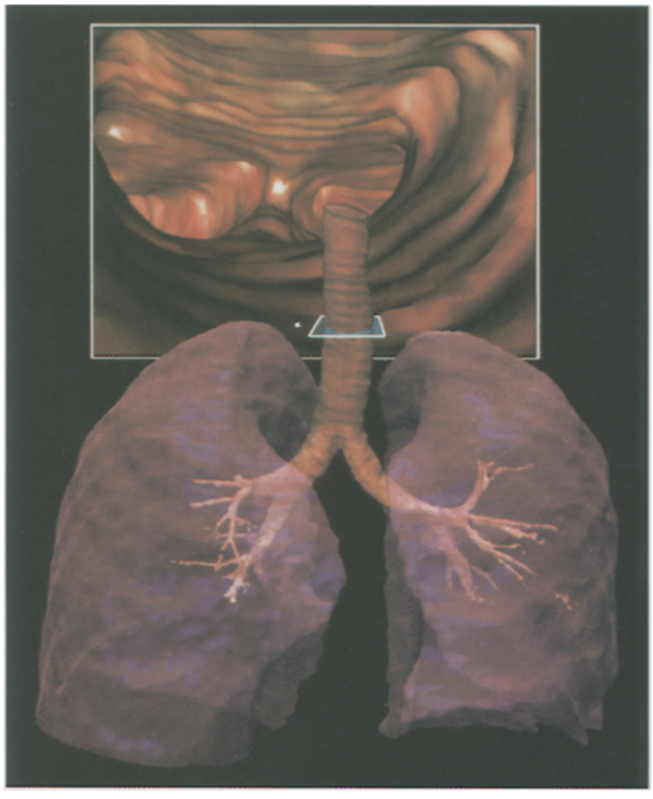

Figure 4. 3D visualization using texture volume rendering.

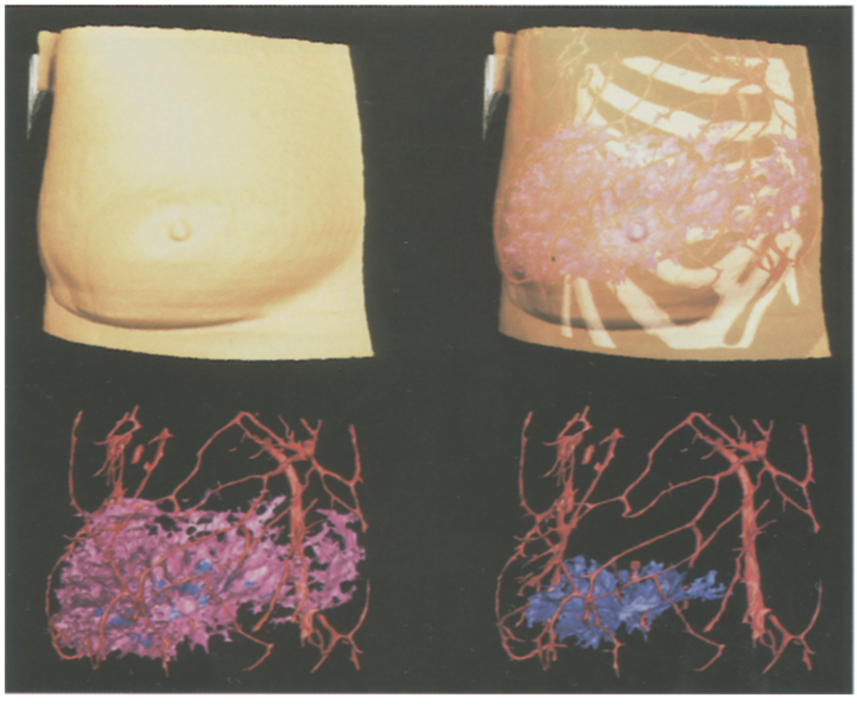

Figure 3. 3D segmentation and rendering of registered MRI, CT, and anatomy image data.

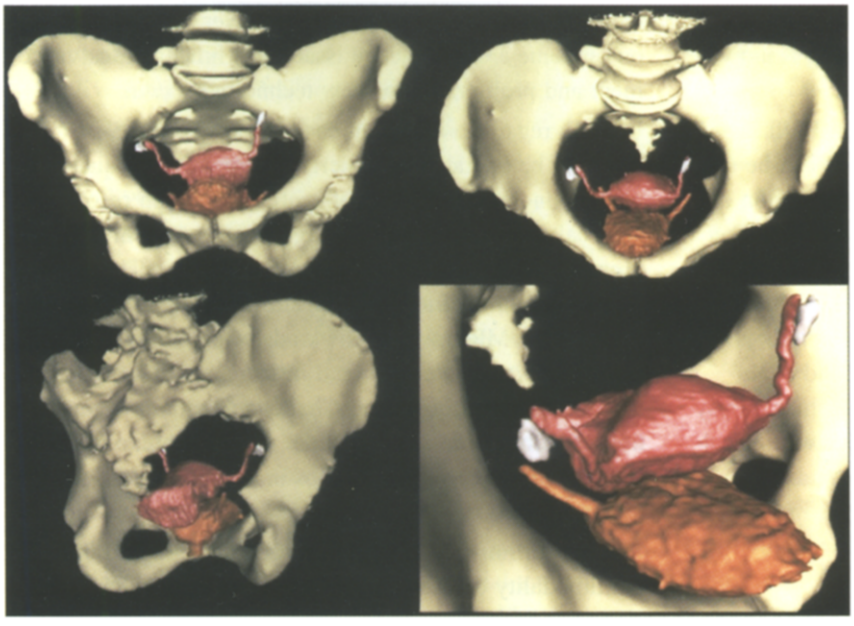

Figure 5. 3D modeling from registered CT and MRI data.

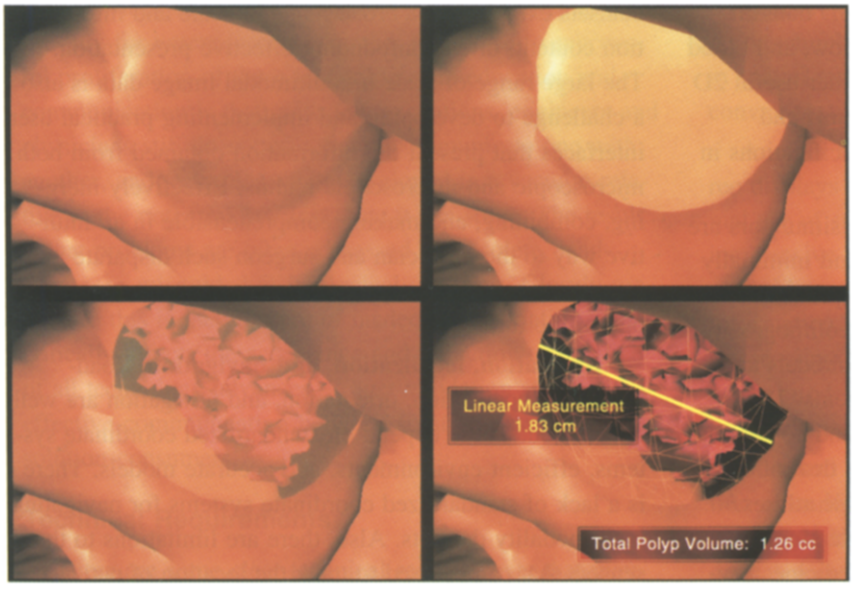

Figure 6. Virtual endoscopic view obtained from spiral CT scan.

bined datasets is implemented by a variety of techniques, some as simple as side-by-side, superimposed, and/or overlay transparency or involving more sophisticated mathematical registration and fusion of the images for simultaneous display of multiple elements of information, such as relative tissue characteristics. Fused multimodality datasets also are used in enhanced or augmented reality implementations, where on-line image data streams can be registered and merged with preoperative datasets. The preoperative image data can be modified based on the on-line data to reflect more accurately the current status in 3D. An example of this is the brain shift problem experienced in neurosurgery, where the preoperative images of the brain are not an accurate representation of the live brain after the skull is opened and the brain is exposed. The brain first decompresses and then sags and shifts relative to its preoperative position in the closed skull. On-line imaging of a portion of the brain during surgery can be used to drive deformation of the high-resolution preoperative image to make it coincide with the operative anatomic size,

shape, and position of the brain so that the image-guided navigation will be accurate. Real-time processing is not yet possible, but is needed.

Orientation, localization, and navigation. Both 2D and 3D correlation techniques that fuse images can be used for path planning. In general, however, the application of these techniques in real time and the real-time realization of dynamic accommodation is poor. The clinical applications of multimodality datasets are primarily limited to rigid structures. Although there are emerging nonlinear elastic solutions, these are still being refined and evaluated. Except for a few successful examples, such as biopsy of the breast and diagnosis of pelvic anomalies where real-time ultrasound imaging is available, the fusion and merging of real-time data streams with preoperative, high-resolution image data has not yet been effectively accomplished.

Augmentation of 2D. Current techniques in MR angiography use maximum intensity projection techniques. This is a 2D display technique of processed 3D data that are useful for looking at vessel beds, blood flow, and blood volumes in various regions of the body. Another useful 2D display of a 3D structure is breast mammograms and tomograms that reveal the morphology of calcifications in the breast.

Communication and education. Various simulators are available for training and teaching surgical and minimally invasive procedures. These include laparoscopic and arthroscopic training systems. There are stereolithography systems that can be used to develop realistic models and plastic casts from the 3D image scans of patients. These can be used effectively in patient education and conveying understanding of procedures. There is a great deal of work being done in the development of 3D anatomic atlases.[1-16] Much of this work is stimulated by the Visible Human Data project from the National Library of Medicine. Several laboratories have developed extensive databases and atlases, mostly of the head and brain, but these are now being extended to other regions of the body. These will continue to be very useful in medical education and training.

Roadblocks to Progress

There are several roadblocks to future advances of visualization technology and user interfaces designed to meet the needs addressed above. Clinical practice itself provides major roadblocks. The financial challenges of managed care, physician acceptance of new procedures, throughput of patients, impact on longitudinal studies, third-party payments for new procedures, cost-effectiveness, and impact on outcome are all practice issues that hinder the advancement and proliferation of new technology.

With regard to image guidance, many of these systems can only be operated by experts. There are inadequate display technologies in terms of spatial and depth resolution and real-time update rates. A significant problem in most promising 3D display technologies is latency. There are problems with instrument compatibility. For example, intraoperative MRI restricts the kinds of positional and spatial trackers and interventional instruments that might be used in the operating room. Challenges remain to realization of fully automated, accurate, reproducible, and rapid segmentation and registration of multimodality medical images.

Correlation of multiple datasets. With regard to multimodality datasets, there has yet to be developed an effective conceptual paradigm, let alone a device, for effective visualization of multimodality datasets. These datasets extend over a broad range of scale and information content, often confounding effective presentation. The large range of scale in multimodal image data is also a challenge to developing and implementing practical user interfaces that present the information obtained from both microscopic and macroscopic realms. Effectively merging, combining, and making comprehensible in an intuitive way to the physician and surgeon such disparate information is an important goal for visualization technology of the future.

Orientation, localization, and navigation. Roadblocks to localization, orientation, and navigation are well understood. These depend on standardized coordinate systems, efficient environments, and accurate models. There is a lack of standardized coordinate systems for navigating multimodality datasets. Also, there are limitations to the sensors that can be used to track the location of patient anatomy, physician hands, and instrument parts in real time during a treatment procedure. The environment depends upon accurate characterization of the datasets available for analysis, and the models depend on accurate and effective segmentation. There is no a priori 3D road map that can guide one through the complexities of anatomy in human beings because of the high degree of normal variability and the unpredictable effect of disease upon anatomic structure and function.

Augmentation of 2D. Roadblocks to augmentation of 2D procedures are not easily addressed. So far there has been insufficient quantification of the value of 3D images

to justify their use either in replacement or augmentation of "conventional" 2D images. There also has been a lack of effective integration of 2D and 3D techniques that work in a synergistic way rather than in a competitive or confusing way. The lack of automation in providing 3D technology in conjunction with 2D technology has also been a barrier to its proliferation and use.

Communication and education. The roadblocks to communication and education include the requirement for effective delivery of multisensory input. These data are not easy to distribute across attractive channels like the Internet and video conferencing technologies. There is too much disparity in the magnitude of information available from multimodality medical and biological image datasets and the current bandwidth available to transmit this information between participants, between teacher and student, or between doctor and patient. Certain social and cultural barriers need to be overcome and should not be discounted in the zeal to promote and advance 3D visualization techniques. Many of these techniques are still regarded as useful only for entertainment. Another hindrance to successful proliferation of these technologies in education and communication is that, with few exceptions, engineers and physicians still do not effectively communicate one with another, and technology gets developed in a vacuum relative to the potential problems that it can solve. The result is that problems are often addressed by obsolete, inadequate, or misguided technological solutions. Closely related to this is the problem of inadequate validation. This critically affects the acceptance and reduction to practice of all technology advances. Proper validation starts with effective communication between solution developers and solution consumers.

Technical Requirements

There are some clear technical requirements that may be specified that will facilitate enhanced developments in 3D image visualization and user interfaces in the near future. These will ensure more readily the success of their implementation and use by the medical profession in helping patients with cancer. The single most important requirement is real-time operation of the visualization technology. This includes the image acquisition, processing, and display phases of the visualization technology, from scanning through 3D reconstruction to automated segmentation, registration, and fusion of multimodality data to rapid and flexible rendering of the processed image volumes so that the displays are presented in real time with interactive manipulation capabilities. Another technical requirement is significantly improved interfaces that are customized to the tasks for which the visualization solutions are implemented, and implemented in a way that is acceptable to the user of the technology. This includes the ability to interact intuitively with the data presented in the displays, such as editing, making measurements, and manipulating the data so as to better understand or use them. An effective interface will facilitate a variety of procedures, simulated or real, that can be tested and final plans made, and even corrections and updates performed on-line to accomplish the desired task.

Yet another technical requirement is higher-quality displays. The magnitude and the quality of information presented by display devices need to increase by two orders of magnitude over today's technology. The amount of information provided in high-resolution medical imaging is still not effectively presented by current display systems. Increased display resolution is related to increased ability to capture both spatial and textural information in scanning technology. The displays need to be not only higher in spatial resolution but deeper in ability to effectively convey texture.

Another technical requirement is to provide better stereo displays that reduce the crosstalk encountered in normal use of stereo displays. Stereo display is generally an inexpensive way to look at images in 3D, but requires device aids such as glasses. Better ways of presenting stereo information without aids are needed, such as in autostereoscopic or holographic displays. This will facilitate greater understanding and usefulness of multimodality 3D image datasets.

Standard protocols for visualization and for presentation of multimodality image information need to be developed. Standards are needed both for image formats and for display representations. Such standards will make it possible for technology developers and users to design more effective and useful customized applications that are targeted directly and efficiently at a specific problem. Another clear technical requirement is better object trackers: better tracking of the hand, the eye, and instruments during medical procedures. Immersive displays, true 3D displays, and enhanced reality displays must be available in smaller, lighter forms. For example, they should become like conventional eye glasses or reading glasses, with the same weight and size to which the population is accustomed. Wearing such an unobtrusive immersive display apparatus would provide 3D images in a way that is not

physically constraining or annoying. The visualization technology devices delivered into operating and special procedure rooms need to be sterile. They must provide truly interactive capabilities that are not obtrusive and do not require special accommodations that upset conventional operating room procedures but blend in with the routine of the operating room.

Research Priorities

Short term

- Design and develop standard, real-time interfaces to medical imaging devices.
- Develop higher-quality display technology; this might be evolutionary rather than revolutionary but must be a high priority.
- Develop more effective, intuitive ways to display and manipulate multidimensional image datasets.
- Identify correct clinical scenarios that are as specific as possible with regard to assessment of 3D visualization impact on improved outcome.

Long term

- Develop novel, effective 3D displays for diagnosis and surgery:

  – Spatial resolution increased at least two orders of magnitude

  – Sufficient computational power to edit, manipulate, measure, and analyze the displays in real time.

References

1. Blackwell M, Nikou C, DiGioia AM, Kanade T. An image overlay system for medical data visualization. In: Proceedings of the 1st International Conference on Medical Image Computing and Computer Assisted Intervention, 1998; 232-240.
2. Bruckstein AM, Holt RJ, Netravali AN. Holographic representations of images. IEEE Transactions on Image Processing 1998; 7:1583-1597.
3. Colchester AC, Zhao J, Holton-Tainter KS, et al. Development and preliminary evaluation of VISLAN, a surgical planning and guidance system using intra-operative video imaging. Med Image Anal 1996; 1:73-90.
4. Fuchs H, Livingston MA, Raskar R, et al. Augmented reality visualization for laparoscopic surgery. In: Proceedings of the 1st International Conference on Medical Image Computing and Computer Assisted Intervention, 1998; 934-943.
5. Golland P, Kikinis R, Umans C, Halle M, Shenton ME, Richolt JA. Anatomy browser: a framework for integration of medical information. In: Proceedings of the 1st International Conference on Medical Image Computing and Computer Assisted Intervention, 1998; 720-731.
6. Hanson DP, Robb RA, Aharon S, et al. New software toolkits for comprehensive visualization and analysis of three-dimensional multimodal biomedical images. J Digit Imaging 1997; 10 (Suppl.):1-2.
7. Heinonen T, Visala K, Blomqvist M, Eskola H, Frey H. 3D visualization library for multimodal medical images. Comput Med Imaging Graph 1998; 22:267-273.
8. McInerney T, Kikinis R. An object-based volumetric deformable atlas for the improved localization of neuroanatomy in MR images. In: Proceedings of the 1st International Conference on Medical Image Computing and Computer Assisted Intervention, 1998; 861-869.
9. Nowinski WL, Fang A, Nguyen BT, et al. Multiple brain atlas database and atlas-based neuroimaging system. Comput Aided Surg 1997; 2:42-66.
10. Peters T, Davey B, Munger P, Comeau R, Evans A, Olivier A. Three-dimensional multimodal image-guidance for neurosurgery. IEEE Transactions on Medical Imaging 1996; 15:121-128.
11. Pflesser B, Tiede U, Hohne KH. Specification, modeling and visualization of arbitrarily shaped cut surfaces in the volume model. In: Proceedings of the 1st International Conference on Medical Image Computing and Computer Assisted Intervention, 1998; 853-860.
12. Robb RA. Virtual reality assisted surgery planning using patient specific anatomic models. IEEE Engineering in Medicine and Biology 1996; 15:60-69.
13. Robb RA. Visualization methods for analysis of multimodality images. In: Thatcher RW, Hallett M, Zeffiro T, John ER, Huerta M, eds. Functional neuroimaging: technical foundations. San Diego, CA: Academic Press, Inc., 1994.
14. Serra L, Kockro RA, Guan CG, et al. Multimodal volume-based tumor neurosurgery planning in the virtual workbench. In: Proceedings of the 1st International Conference on Medical Image Computing and Computer Assisted Intervention, 1998; 1007-1016.
15. Skrinjar O, Spencer D, Duncan J. Brain shift modeling for use in neurosurgery. In: Proceedings of the 1st International Conference on Medical Image Computing and Computer Assisted Intervention, 1998; 641-649.
16. Toriwaki J, Mori K. Visualization of the human body toward the navigation diagnosis with the virtualized human body. Journal of Visualization 1998; 1:111-124.