Report of the Joint Working Group on Image-Guided Diagnosis and Treatment

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Acronyms

2D, 3D, 4D	two-, three-, and four-dimensional
ACRIN	American College of Radiology Imaging Network
CAD	computer-aided diagnosis
CAIS	computer-assisted interventional systems
CAS	computer-assisted surgery
CT	computed tomography
DICOM	Digital Imaging and Communications in Medicine
FDA	U.S. Food and Drug Administration
fMRI	functional magnetic resonance imaging
HIFU	high intensity focused ultrasound
IGT	image-guided treatment
ILP	interstitial laser photocoagulation
LITT	laser-induced thermotherapy
LSM	least squares template matching
MEMS	microelectromechanical systems
MR	magnetic resonance
MRI	magnetic resonance imaging
MRS	magnetic resonance spectroscopy
NCI	National Cancer Institute
NIH	National Institutes of Health
NSF	National Science Foundation
PDT	photodynamic therapy
PET	positron emission tomography
PHS OWH	U.S. Public Health Service's Office on Women's Health
RF	radio frequency
VR	virtual reality

Planning Committee

The U.S. Public Health Service's Office on Women's Health and the National Cancer Institute gratefully acknowledge the members of the planning committee, who devoted time and effort to the development of the conference agenda.

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Session 5:	**Machine Design and Clinical Framework**	
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Introduction

In March 1996, the U.S. Public Health Service's Office on Women's Health (PHS OWH) established a Federal Multi-Agency Consortium for Imaging and Other Technologies to Improve Women's Health. This consortium facilitates technology transfer from laboratories to patients. The membership of the consortium includes, but is not limited to, the National Cancer Institute (NCI), Food and Drug Administration (FDA), 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, industry, and academia for the advancement of novel breast imaging for early diagnosis of cancer, such as digital mammography, magnetic resonance imaging (MRI) and spectroscopy (MRS), ultrasound, nuclear medicine, and positron emission tomography (PET), as well as related image display, analysis, transmission, and 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 1-2, 1997.[1] During this meeting, consortium members developed recommendations for the scientific and technologic projects critical for advancement of novel breast imaging.

Subsequently, PHS OWH and NCI jointly sponsored the establishment of several working groups to define 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:

- Functional imaging (e.g., PET, MRI and MRS, and optical imaging and spectroscopy) for the achievement of comprehensive in vivo cellular and ultimately molecular biologic tissue characterization[2]
- Image processing, computer-aided diagnosis (CAD), and three-dimensional digital display for enhanced lesion visualization and radiologic image interpretation[3]
- Telemammography, teleradiology, and related information management[4]
- Digital X-ray mammography, with an emphasis on digital display technologies and workstation design for image interpretation[5]
- 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.[6]

This article summarizes the results of the Conference of the Joint PHS OWH/NCI Working Group on Image-Guided Diagnosis and Treatment. Almost 70 international scientific leaders, representing clinical practice, academic research, government agencies and laboratories, and medical imaging system manufacturers, attended the meeting held April 12-14, 1999, in Washington, D.C. This article describes the group's findings and recommendations.

Goals of the Joint PHS OWH/NCI Working Group

1) To review the state of the art in image-guided diagnosis and treatment, including current and future clinical applications and technical challenges and the potential impact on critical diseases, with an emphasis on women's health.
2) To outline short- and long-term research priorities to advance imaging tools for guidance, planning, control, and monitoring of interventional procedures.
3) To consider "ideal" characteristics of equipment and the framework for image-guided diagnosis and treatment.
4) To identify technical limitations and develop problem statement(s) seeking new or emerging technologies.

To achieve these goals, the meeting consisted of the following sessions.

Session 1: Current and Future Clinical Applications of Image-Guided, Computer Assisted Interventions addressed clinical applications across a range of medical specialties and organ systems, including brain; breast; gastrointestinal; gynecology; head and neck; spine; liver; orthopedics; plastic surgery; and ear, nose and throat.

Session 2: Medical Image Computing for Image-Guided Treatment reviewed the critical role of state-of-the-art 2D and 3D image processing and visualization technologies in image-guided interventions.

Session 3: Computer-Assisted Interventional Systems included a series of presentations illustrating such technologies as telepresence/telesurgery, surgical simulators, therapy planning systems, and medical robotics.

Session 4: Treatment Modalities reviewed current practice and emerging opportunities with new treatment modalities, including radiation therapy, thermal ablation, focused ultrasound, and gene therapy.

Session 5: Machine Design and Clinical Framework provided an opportunity for both academic and industrial participants to provide their perspectives on the key issues surrounding broader implementation of image-guided interventions and the characteristics of "ideal" equipment for image-guided diagnosis and treatment.

Session 6: Summary Roundtable of Professional Societies developed a statement on the organizational and training issues surrounding image-guided diagnosis and treatment.

Working Session: Working group members met to formulate consensus reports describing (1) the state of the art and current 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.

Summary Session: The consensus reports were presented during the summary session.

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.

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Session 1: Current and Future Clinical Applications of Image-Guided, Computer-Assisted Interventions

Several applications of image-guided and/or computer-assisted interventions already have had a large impact in many clinical areas. This article focuses on the technical challenges and validation requirements of new investigational applications that have yet to enter the clinical mainstream. Research priorities are outlined for imaging tools for guidelines, treatment planning, control, and monitoring of interventional procedures. In particular, the session participants identified current and future clinical challenges that can be addressed by the advancement of image-guided diagnosis and treatment.

Clinical Applications

Brain

Diagnosis and treatment of brain disorders have a long history of image-guided interventions and associated devices. For example, image-guided stereotatic biopsy is accepted in clinical practice. Most recently, MRI has been investigated as a guidance tool in disease management in the following areas: stereotactic brain biopsy and electrode placement, image-guided tumor resection, and image-guided tumor ablation. Using MR as the roadmap, tools such as the MR-compatible neuroendoscope may have a dramatic effect on minimally invasive neurosurgery.

MRI is now recognized as one of the most promising imaging techniques for the detection of intracranial pathologies. With the development of the MR-compatible stereotactic frame, stereotactic brain biopsy based on MR imaging data is now routinely performed in many institutions. Stereotactic coordinates and the optimal angle of the probe insertion are calculated with high accuracy based on MR imaging. New interventional MR magnets with an open design and in-room monitors now enable frameless stereotactic brain biopsy and minimally invasive treatment.

With appropriately equipped, open-design MR systems, several groups are using MR during surgical procedures such as craniotomy. The ultimate value and indications of the technique remain to be defined.

Image-guided thermal ablation of brain tumors thus far appears to be a safe, minimally invasive treatment that deserves further study. Unlike radiation, it is not associated with cumulative toxicity and may serve as a palliative alternative for end-stage patients not wishing to undergo open craniotomy.[1]

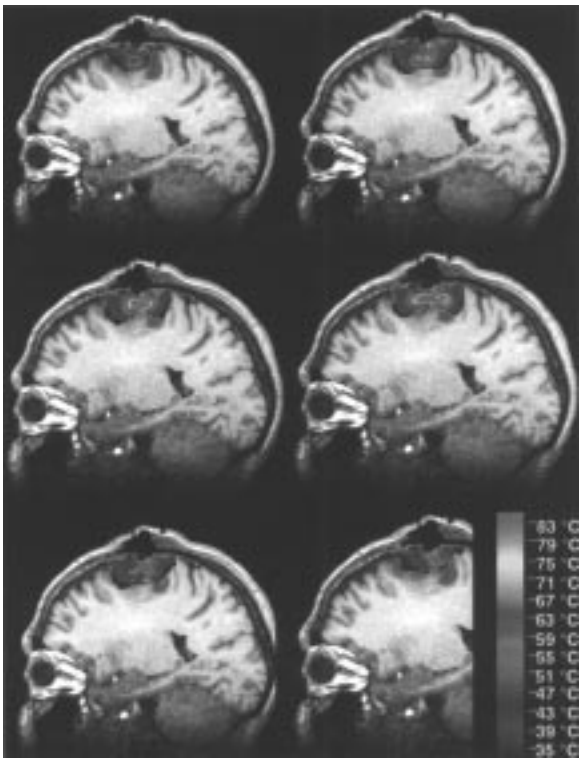

Figure 1-1: MR images during and after laser-induced thermotherapy of an intracranial metastasis.

Source: In vivo MRI thermometry using a phase-sensitive sequence: Preliminary experience during MRI-guided laser-induced interstitial thermotherapy of brain tumors. Thomas Kahn, M.D.; Thorsten Harth, Ph.D.; Jürgen C.W. Kiwit, M.D.; Hans-Joachim Schwarzmaier, M.D.; Christoph Wald, M.D.; and Ulrich Mödder, M.D. *JMRI*. Copyright © 1998, ISMRM. Reprinted by permission of Wiley-Liss, Inc., a subsidiary of John Wiley & Sons, Inc.

For example, Figure 1-1 shows postprocessed, phase-sensitive, two-dimensional, fast, low-angle shot MR images acquired and displayed during and after laser-induced thermotherapy (LITT) of an intracranial metastasis. The calculated temperatures are color-coded, gradually increasing the heat-affected zone with increasing maximum temperatures. Images A through D were acquired during LITT 1, 4, 8, and 10 minutes after starting the laser therapy. Images E and

F show the temperature distribution 2 and 4 minutes after switching off the laser. The temperature returned to baseline values; however, some scattered pixels remain unchanged during cooling.

Head and Neck

Image-guided biopsy and endoscopic sinus surgery are in use and widely accepted. MRI is rapidly replacing computed tomography (CT) in image-guided aspiration of head and neck lesions because MRI permits precise needle placement into comparatively inaccessible areas, such as the skull base and submandibular region, where beam-hardening artifacts limit the effectiveness of CT. Another advantage is the superior tip localization of MR by obtaining an oblique or orthogonal image along the course of the needle, similar to that of ultrasound.

Palliative management options for recurrent head and neck cancers are limited by the proximity of vital vascular and neural structures and the aggressive nature of these tumors. Wide local resection of these lesions may result in functional and cosmetic deformities. Most head and neck tumors are usually treated by surgery and/or radiation therapy. MR-guided minimally invasive thermal ablation could someday be another alternative if thermal energy delivery would be controlled and monitored accurately with imaging.[2] Nodal metastases to the head and neck (prior to radical neck dissection) provide a valuable model for image-guided thermal ablation of such metastases throughout the body. Although the efficacy of interstitial laser therapy needs to be demonstrated further in larger series, preliminary clinical trials have shown promising results.

Breast

Breast carcinoma is a leading cause of death for women in the United States and Europe. Because of high soft tissue contrast, MR has been able to detect breast carcinomas not visible with the usual mammographic techniques.

The most common clinical scenario that leads to MR-guided breast biopsy is the detection of additional enhancing lesions on breast MRI performed for local staging of breast cancer. In this setting, MRI localization wires may be placed so that these lesions can be excised during excision of primary lesions. This technique also may be used to clearly define the margins of abnormal enhancement so that a lesion with its surrounding intraductal component may be excised in one setting. With the recent development of breast biopsy surface coils, the breast now can be compressed and stabilized while the patient is in a prone position. Although experience is limited to date, successful MR-guided biopsy has been performed on lesions that are not detectable or easily localized by other modalities.

In recent years, management of breast cancer has moved toward breast conservation, with the goal of maximized cosmesis without compromising overall survival. Several ablation techniques have been investigated for treatment of breast tumors. A recent preliminary clinical trial of interstitial laser photocoagulation (ILP) for breast cancer, followed by surgery, showed excellent correlation of MR appearance and pathology.[3] The study suggests that MR-guided interstitial laser photocoagulation for breast cancer is a potentially useful tool. Another study of MR-guided high intensity focused ultrasound (HIFU) therapy for breast fibroadenomas is under way.

Several issues should be addressed before ablation techniques can replace lumpectomy. One reservation concerns the loss of material for histopathologic examination when the whole tumor is ablated, if treatment options may depend on the histologic information. Secondly, the enhancing lesions seen on MRI 48 to 72 hours after ablation may be caused by inflammatory response or residual tumor, thus necessitating multiple biopsies of the treated margin.

Abdomen and Pelvis

Percutaneous interventional procedures in the abdomen and pelvis are mostly performed for biopsies, but they also are done for sympathectomies and drainages. CT-, fluoro-, and ultrasound-guided punctures have been reported in the literature for nearly 30 years. In 1967, Nordenstrom reported the first series of percutaneous fluoro-guided lymph node biopsies.[4] Approaches such as transperitoneal, translumbar, and transvascular procedures using various imaging modalities have been described.

Fine needle biopsies are most often performed for cytologic and histologic diagnosis in the abdomen, retroperitoneum, pelvis, lymph nodes, bones, and joints. In general, the results of percutaneous aspiration techniques are very good. Success rates of more than 80% have been reported for cytologic diagnosis. Sonographic and CT-guided biopsies are established diagnostic techniques. However, ultrasound-guided methods are being replaced more and more by CT guidance. Although new MRI techniques for clinical treatments in the abdomen

Table 1-1: Deep Imaging Techniques in Gynecology and Reproduction

	X-Ray	CT	MRI	US	3D US	Color Doppler US	US plus Ultraguide	Focused US	Other
Uterus									
Endometrium									
Cancer			Op	A	RD	RD			
Hyperplasia				A	F?	F?			
DUB				A	F?				
Myometrium									
Fibroids	A		Op	A	RD	F?		F?	
Adenomyosis			Op	A	RD	F?			
Malformation	A		Op	A	RD				
Ovaries									
Cancer			A	A	RD	A	RD	F?	
Cysts				A	RD		RD		
Fallopian Tubes									
Tubal pathol.	A			A	F?				
Pelvic Cavity									
Metastatic spread			A	A	F?	F?	RD		
Endometriosis			Op	A	F?				
Retro-Periton.									
Node metast.			A	A	F?		RD		
Pregnancy									
Well-being	A			A	RD		A		
Fetal surgery				A	RD		RD	F?	
Assisted Reproduction									
Egg collection				A	RD				
Laser-assisted hatching									Comp. Image

Abbreviations
US = Ultrasound
A = Technique available
F? = Might be available in the future
Op = Optional, but not used routinely
RD = In research and development

have the potential to replace a large number of conventional techniques, they must be used carefully in order to minimize possible injury to vital structures. Biopsies of large tumor masses or abscesses are possible as well as percutaneous tumor therapy with ethanol ablation, radiofrequency (RF), lasers, or cryotherapy.

In the near future, more treatments in the abdomen and pelvis will be performed. Cryogenic, RF, or laser techniques have great potential for treating liver and other tumors, while MR-guided drainage of large cysts and abscesses in the liver, pancreas, retroperitoneum, kidneys, abdominal wall, and pelvis is an area of active investigation.[5] In the future, combined MRI and endoscope therapy, especially for obstetrics, gallbladder, urinary tract, colon, and sympthectomy at all levels of the spines, may be used routinely if endocoils and/or MRI-compatible endoscopic systems are developed.

Gynecology and Reproductive System

Genital organs are relatively accessible for clinical evaluation. Diagnostic tools such as X rays, CT scans, and MR imaging are rarely needed; however, some diagnostic tools, such as ultrasonography and laparoscopy, are used in gynecology more than in any other medical or surgical discipline. In order to understand the background of these trends and possible future developments, one must consider the imaging technologies currently available to the clinician, those that are under development, and the nature of genital organs/disease needs. Most of these technologies are presented in Tables 1-1 and 1-2.

Table 1-2: Surface Imaging Techniques in Gynecology and Reproduction

	Laparoscopy		Hysteroscopy		Colposcopy	
	Conventional	**PDDT**	**Conventional**	**PDDT**	**Conventional**	**PDDT**
Vulva						
Warts					A	RD
VIN					A	RD
Vagina						
Warts					A	RD
VAIN					A	RD
Cervix						
CIN			A	RD	A	RD
Uterus						
Endometrium						
Cancer			A	RD		
Hyperplasia			A	RD		
DUB			A	RD		
Myometrium						
Fibroids	A					
Adenomyosis		RD				
Malformation	A					
Ovaries						
Cancer	A	RD				
Cysts	A					
Ovaries-IVF	Op					
Fallopian Tubes						
Tubal pathol.	A					
Pelvic Cavity						
Metastatic spread	A	RD				
Endometriosis	A	RD				
Retro-Periton.						
Node metast.	A	F?				
Pregnancy						
Well-being	A- Fetosc.					
Fetal surgery	Fetosc.					

Abbreviations
PDDT = Photodynamic diagnosis and treatment
A = Technique available
F? = Might be available in the future
Op = Optional, but not used routinely
RD = In research and development

The deep penetrating imaging diagnostic tools listed in Table 1-1 provide a hard copy documentation. The endoscopic diagnostic procedures listed in Table 1-2 are usually not connected to any objective documentation tool, rendering future evaluation impossible. Although it is easy to store such procedures on videotape, which is standard practice in some clinics, it is not practical to review such tapes in a consultation or to compare current and past images. Moreover, diagnosis based only on the clinician's experience may be inaccurate if not exposed to a second opinion. Recent progress in computer image processing and cost reductions in digital storage call for improved documentation following any kind of minimally invasive procedure with endoscopes.

Bone

The incidence of dislocation following primary total hip replacement surgery is between 2% and 6% and even higher following revisions.[6] It is, therefore, the most commonly occurring early complication following hip replacement surgery. Dislocation of a total hip replacement causes significant distress to the patient and additional costs to relocate the hip. Impingement between the neck of the femoral implant and the rim of the acetabular component can lead to dislocations and also advanced wear of the acetabular

rim, resulting in polyethylene wear debris shown to accelerate loosening of implant bone interfaces. The causes of impingement and dislocation are multifactorial; however, the most common cause of both impingement and dislocation is malposition of the acetabular component.

A system has been developed to permit accurate placement of the acetabular component during total hip replacement surgery. The system includes two components: (1) a preoperative planner and range of motion simulator and (2) an intraoperative image-guided surgery system. The preoperative planner allows the surgeon to specify the position of the implant components within the pelvis and the femur, based upon preoperative CT images. A kinematic range of motion simulator determines range of motion based upon the specific bone and implant geometry and alignment, and predicts the leg positions in which the prosthetic or bone impingement occurs. The feedback provided by the simulator permits the surgeon to determine the optimal, patient-specific acetabular implant alignment for any implant system and determines an "envelope" of safe range of motion.

Technical Requirements

Dramatic advances have been made in image-guided procedures in the brain during the past few years but relatively little attention has been given to other regions of the body. The technical requirements for image-guided procedures beyond the rigid structure of the head are addressed in the following areas:

- Operative planning and surgical simulators
- Intraprocedure imaging and endoscopy
- Registration and segmentation
- Anatomical and physiological modeling
- Surgical instrumentation, tooling, and robotics
- Systems architecture, integration, and user interfaces

Operative Planning and Surgical Simulators

Current models for operative planning and surgical simulators are not sophisticated enough for realistic systems. There are still many research issues in tissue modeling, including deformable modeling. For these systems to be clinically useful, patient-specific models must be incorporated. Finally, for applications where the sense of touch or force is important, better haptic interfaces are needed.

Intraprocedure Imaging and Endoscopy

Hardware developments are required to reduce size and cost while improving imaging resolution. Interventional MRI and the associated instruments are generally seen as too expensive, while other modalities, such as CT and fluoroscopy, involve ionizing radiation.[7] Endoscopy problems include limited visibility, difficulty with knowing where one is in relation to the anatomy, and difficulty in dealing with complications.

Registration and Segmentation

The major technical problems with image registration include the need for manual intervention, limited robustness, the lack of methods for accurate real-time registration of a nonrigid object, and the limited accuracy of fiducial-free registration methods. Segmentation techniques are generally seen as slow and manually intensive. The problem of anatomical motion between imaging and surgery needs to be addressed. Finally, there is a lack of standards for determining performance requirements, assessing accuracy, and validation of algorithms.

Anatomical and Physiological Models

Current models are not realistic enough, and soft tissue modeling is a fundamental problem. Developing an accurate model that incorporates phenomena such as hemodynamics is a complex task. Other issues include the development of patient-specific models, computational efficiency, and validation.

Surgical Instrumentation, Tooling, and Robotics

The major technical challenge is developing technology that is safe, reliable, and easy to use in the operating room. The equipment also should be compatible with imaging modalities such as MRI and CT. Other problems include accuracy, suitable man-machine interfaces, and real-time navigation. Cost, liability, and FDA considerations limit the use of this technology.

Systems Architecture, Integration, and User Interfaces

The major technical challenge is to create a device that is powerful yet easy to use. Many users believe that current image-guided systems remain too difficult to use in the operating room and that a skilled technician usually is required. The user interface is a key issue. Effective user interface design requires collaboration of experts from various fields. Conveying the information that surgeons need in a

format they can use is still a problem. Other factors limiting the use of these technologies include the lack of complete component technologies, economic justification, and liability issues. The use of different file formats by different medical imaging device manufacturers also is a problem, but this might be resolved by the DICOM medical imaging standard.

Research Priorities

Short Term

- Improve resources for multicenter trials (e.g., ACRIN).
- Develop better user interfaces for wide clinical acceptance.
- Improve validation and create uniform standards of thermal monitoring technology.
- Develop better ablation technology to target larger lesions with smaller access.
- Optimize image-guided systems for nonrigid anatomy, focusing on ease of use and registration.
- Improve soft tissue stereotaxis.
- Develop better contrast agents for tumor definition.
- Develop better interactive control of thermal ablation.
- Conduct multicenter cost and/or efficacy studies of the following:
  - Intraoperative MRI of brain
  - Image-guided percutaneous disk ablation versus microdiscectomy
  - Palliation for recurrent head and neck tumors (also study pain control and morbidity)
  - LITT versus liver resection for colorectal metastases
  - LITT versus no treatment following failed treatment for colorectal metastases
  - Image-guided percutaneous ablation versus surgery for hepatoma
  - Percutaneous image-guided thermal ablation of fibroids versus myomectomy
  - Image-guided joint replacement/reconstruction systems.
- Conduct feasibility studies of the following:
  - Image-guided thermal ablation of metastatic lymph nodes in the head and neck
  - Thermal breast cancer ablation followed by surgery
  - Image-guided percutaneous bone ablation and structural repair related to metastases.

Intermediate Term

- Conduct feasibility studies of the following:
  - New treatment effector technologies (e.g., ablation, robots, gene therapy).
  - Pedicle screws, other than thoracic level and percutaneous placement
  - Image-guided percutaneous ablation of gynecologic malignancy prior to definitive surgery.
- Improve target delineation to better determine eloquent brain areas and tumor margins.
- Research safety and quality-of-life issues related to thermal breast cancer ablation without surgery
- Conduct multicenter trials of thermal ablation of breast cancer and fibroadenoma.
- Research the role of growth factor stimulation in surgery versus LITT or other thermal ablation (animal model).
- Automate segmentation of bone-tissue margins.
- Standardize commercial image-guided orthopedic technology components.

Long Term

- Incorporate tissue elastic properties into models of brain tissue deformation; use open MR and other new imaging technologies data to validate these models.

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Session 2: Medical Image Computing for Image-Guided Treatment

The goal of medical image computing in the context of image-guided treatment (IGT) is to create and manipulate three (or higher) dimensional representations of relevant patient data to enhance the ability to detect disease and to plan and deliver therapy. Dimensions beyond three may be temporal (e.g., the synthesis of multiple scans from a single modality at several times or a time sequence of images from a cine modality, such as digital subtraction angiography, ultrasound, or fast MRI). Additionally, the patient representation may include multiple anatomical signals or functional values at each point in space. For example, metabolic information from nuclear medicine, several MRI intensities from multiple image sequences, blood flow information from functional MRI (fMRI), and intensity from CT all might be available and useful. Merging all the relevant portions of this data into a single representation can define a vector-valued field in the 3D or 4D (location plus time) patient space. For the purpose of the present discussion, the components of this vector field beyond the first are equivalent, as far as their computational requirements, to additional dimensions of the patient model.

Examples

Clinical Analysis, Change Detection, and Time Series Analysis

Guido Gerig, Ph.D., University of North Carolina at Chapel Hill

A least squares template matching (LSM) has been used for the precise measurement of patient positioning in a series of digital images. This new development is driven by applying image analysis in order to check patient position during radiotherapy treatment. Accurate information about patient position is gained by employing electronic portal images acquired during radiation treatment sessions. The problem with such megavoltage X-ray imagery is its extremely low contrast, rendering reliable feature extraction a difficult task and thus favoring the LSM approach.

LSM is an iterative and area-based fitting method especially suitable for attaining very high precision or for processing low-contrast, noisy, and blurred images. The automatic quality control—a component often missing in commonly used image matching methods—is achieved by self-diagnostic measures supervising the iterative procedure.

The present system includes both field edge alignment and 2D anatomy displacement measurement. A very promising success rate of over 90% was reported with 500 portal images. Digitally reconstructed radiographs were used as simulated portal images with known ground truth, allowing the measurement errors to be analyzed in more detail. Furthermore, results for the multimodal match between a digitally reconstructed radiograph reference image and therapeutic portal images promise an approach that might significantly increase the accuracy of a treatment.

Real-Time 3D Brain Shift Compensation

James S. Duncan, Ph.D., Yale University

The use of surgical navigation systems has become a standard method to assist the neurosurgeon in navigating within an intraoperative environment an in planning and guiding the surgery. However, these systems are subject to inaccuracy caused by intraoperative brain movement (i.e., brain shift), since commercial systems typically assume that the intracranial structures are rigid. Experiments show brain shift of up to several millimeters, making it the cause of the dominant error in the system.

Addressing this problem requires an image-based brain shift compensation system based on an intraoperatively guided deformable model, such as that under development at Yale University. A set of brain surface points has been recorded during the surgery and used to guide and/or validate model predictions. Initial results show that such a system limits the error between its brain surface prediction and real brain surface to within 0.5 mm. This is a significant improvement over the systems that are based on the rigid brain assumption, which in this case would have an error of 3 mm or greater. Future work is aimed at richer intraoperative data acquisition and nonhomogeneous brain tissue modeling.

Volumetric Display and Analysis of 3D Data

Sandy Napel, Ph.D., Stanford University

The past several years have seen an explosion in the detail and amount of medical imaging data that can be routinely produced during the course of a cross-sectional imaging examination. Ten years ago, a

typical CT examination generated between 30 and 50 images; today's helical CT scanners generate hundreds of overlapping slices for interpretation. Spatial resolution and sampling, particularly in the through-plane direction, also have improved. Similar trends are evident in MR and ultrasound. Although these and other modalities have become more sophisticated, the dominant method for radiological interpretation—that is, visual assessment of each of the cross-sectional images generated by the modality—has not changed. Furthermore, as the number of images increases, so does the time required for interpretation.

While radiologists may be keeping up in 1999, it is doubtful that the current paradigm will be possible in the near future. Consider the introduction of multiple-detector ring helical CT, which can image a contrast bolus as it travels from above the renal arteries to the toes in 1 minute and can generate over a thousand 2.5-mm-thick slices spaced every 1.25 mm. Not only does the time and, therefore, the cost of interpretation significantly increase, but fatigue and other factors might compromise diagnostic accuracy.

The new paradigm of radiological interpretation will be based upon treating the acquired image data as a volume to be explored and from which to extract images and quantitative data that document the condition of the patient. Although several volume visualization techniques have been available for several years (e.g., maximum intensity projection, surface rendering, volume rendering, flat and curved reformatted planes, thin slab renderings), they have been used largely to supplement the diagnosis made by assessment of the primary source images and for conveying findings to referring physicians. In the new paradigm of radiological interpretation, these and other techniques, including segmentation and computer-aided diagnosis, exist as choices that can be made as part of the exploration process. However, the concept of diagnosis based on these methods, perhaps without ever viewing the primary source images, is new and must be validated for every possible diagnosis. Nevertheless, in the new world of 1,000+ images per examination, diagnosis based on review of source images is not yet validated and may not be possible.

Visualization and Virtual Reality (VR) in Image-Guided Surgery

Richard A. Robb, Ph.D., Mayo Foundation and Clinic

Interactive visualization, manipulation, and measurement of multimodality 3D medical images on standard computer workstations has been developed, used, and evaluated in a variety of biomedical applications for more than a decade. These capabilities have provided scientists, physicians, and surgeons with powerful and flexible computational support for basic biological studies and for medical diagnosis and treatment. Comprehensive software systems, ANALYZE and VRASP, developed at the Mayo Clinic have been applied to a variety of biological, medical, and surgical problems and used on significant numbers of patients at many institutions. This scope of clinical experience has fostered continual refinement of approaches and techniques, especially 3D volume image segmentation, classification, registration, and rendering and has provided useful information and insights related to the practical clinical usefulness of computer-aided procedures and their impact on medical treatment outcome and cost.

This experience has led to using virtual reality technology in computer-assisted surgery (CAS). VR offers the promise of highly interactive, natural control of the visualization process, providing realistic simulations of surgery for training, planning, and rehearsal. The Mayo Clinic has developed efficient methods for the production of accurate models of anatomic structures computed from patient-specific volumetric image data (e.g., CT or MRI). The models can be enhanced with textures mapped from photographic samples of the actual anatomy. When used on a VR system, such models provide realistic and interactive capabilities for patient-specific surgical training, surgery planning and procedure rehearsal. VR technology also can be deployed in the operating room to provide the surgeon with online, intraoperative access to all preoperative planning data and experience, translated faithfully to the patient on the operating table. Additionally, these preoperative data and models can be fused with real-time data in the operating room to provide enhanced reality visualizations during the actual surgical procedures.

Virtual endoscopy is a new method of diagnosis using computer processing of 3D image data (e.g., CT or MRI) to provide simulated visualizations of patient-specific organs similar or equivalent to those produced by standard endoscopic procedures. Conventional endoscopy is invasive and often uncomfortable for patients. It can have serious side effects, such as perforation, infection, and hemorrhage. Virtual endoscopy visualization avoids these risks and can minimize difficulties and decrease morbidity when used before actual endoscopic procedures. In addition, there are many body regions not compatible with real endoscopy that can be explored with virtual endoscopy. Eventually, virtual endoscopy may replace many forms of real endoscopy.

Other applications of VR technology in medicine being developed include anesthesiology training, virtual histology, and virtual biology. These techniques provide faithful virtual simulations for training, planning, rehearsing, and/or analyzing medical and/or biological image data.

There remains a critical need to refine and validate three-dimensional (e.g., CAS or VR) visualizations and simulated procedures before they are acceptable for routine clinical use. The Mayo Clinic has used the Visible Human Dataset from the National Library of Medicine to develop and test these procedures and to evaluate their use in a variety of clinical applications.

Table 2-1: Technical Problem Areas

• Data management, communication, and visualization
• Access to computing resources
• Segmentation
• Multimodality registration and fusion
• Realistic anatomical modeling
• Validation
• Atlases
• Plan optimization

Specific clinical protocols are developed to evaluate virtual surgery against surgical outcomes and to compare virtual endoscopy with real endoscopy. Informative and dynamic on-screen navigation guides will help the surgeon or physician determine body orientation and precise anatomical localization while performing the virtual procedures. Additionally, the adjunctive value of full 3D imaging (e.g., looking "outside" of the normal field of view) during the virtual surgical procedure or endoscopic exam is being evaluated. Quantitative analyses of local geometric and densitometric properties obtained from the virtual procedures ("virtual biopsy") are being developed and compared with other direct measures.

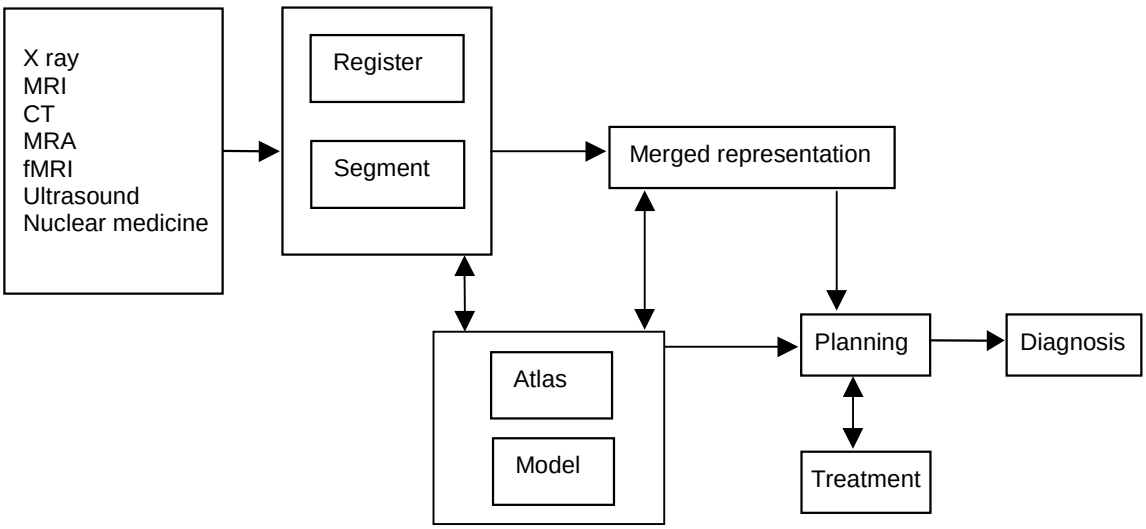

Figure 2-1: Interaction of computing tasks in planning and delivery of IGT.

Preliminary results suggest that these virtual procedures can provide accurate, reproducible, and clinically useful visualizations and measurements. These studies will help drive improvements in and lend credibility to virtual procedures and simulations as routine clinical tools. CAS and VR-assisted diagnostic and treatment systems hold significant promise for optimizing many medical procedures, minimizing patient risk and morbidity, and reducing health care costs.

Technical Problem Areas

The synthesis of many of the individual computing tasks into the planning and delivery of IGT is schematically illustrated in Figure 2-1. The box at the left represents data management and communication, where all relevant patient data are brought into the appropriate systems for subsequent steps. Registration and segmentation are performed to extract the essential components of the multimodality patient model used in treatment planning and delivery. Atlases and patient models inform registration, segmentation, and planning and are in turn informed by the multimodality patient representation. In the case of IGT, the plan optimizes the proposed treatment based on all the available information. In the case of image-guided diagnosis, the merged patient representation may be used in a CAD step. On completion of the plan, treatment might be delivered with image guidance and with iterative modification of the plan as an image-guided procedure unfolds.

As demonstrated throughout this section, computing is pervasive in the planning and delivery of IGT. There are, however, technical problem areas that need additional research support (Table 2-1).

Data Management, Communication, and Visualization

The volume of image data available per study, as well as the number of studies performed, has increased rapidly in recent years, and it is quite reasonable to expect that fully developed IGT regimes will generate and use terabytes of data per year (1 terabyte = 1 million megabytes). Continued research on optimized methods to store and communicate this information is required. The contents of image data archives will not consist solely of the primary image data themselves. Full use of multimodality IGT planning will require saving multiple copies of some datasets that are registered with other datasets and/or developing new, efficient methods to produce registered image datasets on demand. There may be other patient-specific and general information (e.g., functional, pathological, clinical) in addition to the primary image data. Partially processed images, segmentation results, and deformed and synthesized datasets also must be available for timely and efficient use. The sheer volume of these data, and the interactive nature in which they may be used, means that rapid development in data management, communication, and visualization methods are key to the practical realization of IGT. Moreover, communication of information among collaborators, both within institutions and throughout the world, is of extreme importance to continued research progress in areas related to IGT. Continued research and development in compression, communication, and data organization methods is critical to the success of the overall IGT research enterprise.

An important development is the enhancement of capabilities for data manipulation by the IGT planner and therapist. Visualization of IGT datasets, both single-modality and multimodality, requires considerable further research. Although some progress has been made in rendering 2D, 3D, or 4D views of portions of image datasets, more powerful and flexible methods for exploration of all available image data are needed. The techniques of scientific visualization as used in many other application areas should be adapted and developed to suit the particular needs of medical imaging and IGT. Seemingly simple tasks such as navigating a CT dataset will become prohibitive as the number of slices generated by multiring scanners grows to 1,000 and beyond. One aspect of visualization that has not been well enough developed is how to convey to an end user (e.g., surgeon, radiation therapy machine, robot) a useful estimate of uncertainty in the plan, which can be used to optimize the delivery of therapy.

Continued improvement in display methods also is important. The accuracy with which IGT can be delivered depends on (1) the resolution and orientation of acquired image data, (2) the format in which the data are presented to the user, and (3) the quality of the display of information. The demands on display quality, as with many aspects of IGT, are application dependent.

Access to Computing Resources

Incorporating adequate levels of realism in the biomechanics that underlie simulations of IGT will consume computer processing resources. For research

in prototype development, and production use, of IGT systems, it will be necessary to ensure access to leading computing technology. Requests for supercomputer time and state-of-the-art computing hardware should be viewed favorably. The same is true for displays, which as mentioned earlier might limit the utility or accuracy of IGT systems. State-of-the-art visualization hardware might be required to achieve adequate realism in displays at useful interactive rates.

Segmentation

Despite decades of intensive research, segmentation remains an outstanding problem in the continued development of IGT. The magnitude of this "segmentation bottleneck" will become greater as the number and size of image datasets grow. In addition, the problems of segmentation and registration (discussed below) are intertwined, with each depending on and facilitating the other. For example, multispectral segmentation assumes that the various signals have a known geometric relationship to each other and to the patient, which is the essence of registration. Also, many registration methods depend on identifying corresponding points, lines, curves, surfaces, or regions in multiple datasets, which is a function of segmentation.

Two fundamental tasks are required of segmentation methods in the context of IGT. First, image datasets must be labeled—that is, a functional, morphological, anatomical, or other identity must be assigned to voxels or regions in the datasets. Second, datasets must be measured—that is, the geometric shapes and relationships of objects and regions within the datasets must be quantified. Labels and measurements should have credible estimates of uncertainty that should inform the planning and delivery of IGT. Although the generation of these estimates during the segmentation process is assumed to be done, this problem has not been solved, and further research is required. As mentioned earlier, methods for transmitting these estimates in a useful way to end users is of considerable importance.

Continued development of the user interface is required to optimize the user's ability to segment what is seen in images. Humans usually can recognize patterns and perceive objects in images much more effectively than automated segmentation algorithms can. Research therefore is warranted in the development of tools to assist users further and to allow quick and easy labeling and measurement of perceived objects. Also, modeling human processes for perceiving objects in images should lead to further developments in automated segmentation algorithms.

High-level knowledge should be incorporated into the automated segmentation process. Automated algorithms should start out "knowing" what they are looking for, what it should look like, and where it should be found. The classic embodiment of such high-level knowledge is an atlas, which is discussed further later in this section. Given a computationally well defined atlas, the atlas objects can be mapped to, or associated with, regions in the image. Such mappings must consider intersubject variations in the size, shape, and position of organs; distortions due to subject position, pathology, or physiology; and anatomical abnormality. Probabilistic representations of population variability in anatomy and function should be included in such an atlas to aid segmentation and to evaluate the uncertainties in labeling and geometry of extracted features. Continued development of methods for constructing and using atlases should be given a high priority. Another promising means for incorporating high-level knowledge into segmentation is to model the image-formation process, taking into account what is known about the anatomy or biological function being imaged and the physics of the imaging system.

Another promising approach to incorporating segmentation into IGT is to develop probability images that might indicate, for example, the likelihood of finding tumor cells at a certain density at a particular point within a multimodality dataset. Treatment could be tailored to the distribution of risk and response probability resulting from such a "fuzzy" model. This approach will require an understanding of contrast enhancement mechanisms, development of new contrast agents, incorporation of new biological and cellular imaging modalities into existing schemes of multimodality registration and fusion, and development of theoretical models relevant to this conceptual form of segmentation.

Multimodality Registration and Fusion

Registration is the process of determining coordinate transformations that map points corresponding to the same anatomical location in the patient in multiple image datasets. Once the relevant coordinate transformations are known, information from multiple sources can be merged; this synthesis is called image or data fusion. A second important use of registration is to transfer information between an image-based

model of the patient and the actual patient; this is the essence of image guidance.

As mentioned earlier, registration often depends on segmentation. Furthermore, registered datasets may be used to improve segmentation techniques. Research progress in the registration and segmentation fields thus can benefit each other.

One problem is registration in the presence of anatomical motion or distortion. Many methods have been developed for registration of medical image datasets, but none is capable of dealing realistically with distortions between multiple image datasets in such anatomical regions as the breast or the abdomen. Simple models that allow global distortions, such as anisotropic linear scaling, shearing, or warping, have been somewhat successful in dealing with such effects as brain swelling or shrinkage. However, solving general registration problems in every area of the body requires coupling registration with realistic biomechanical models of motion and distortion and/or with atlas-based descriptions of anatomical structure and variability.

A second problem is registration of one 3D dataset with a 2D dataset. For example, a radiograph may be used to infer the position or orientation of a structure or a location defined in the context of a 3D dataset, such as CT or MRI. Since information is lost in the projection onto the plane of the radiograph, the 3D position of objects from a single radiograph cannot be determined exactly except under certain limited circumstances (e.g., when the 3D positions of a sufficient set of landmark points is known and their projections can be uniquely identified). In general, solution for the full 3D orientation of the skull, chest, or pelvis from a single radiograph is an unsolved problem, even when rigid anatomies can be assumed.

Registration of 3D breast images, for example MRI, with radiographs such as mammograms demonstrates both problems. The issues of 2D/3D ambiguity, lack of unique landmarks, and severe anatomical distortion all come together. Further research on these problems should be given a high priority.

As mentioned earlier, incorporating new biological- and/or molecular-based imaging modalities into the more traditional set of modalities may lead to new types of diagnostic and therapeutic approaches. Means for registering new and current modalities need to be developed. This research will be ongoing for many years as newer modalities become available.

An essential stage in the development of any registration method must be a characterization of its accuracy under clinically relevant conditions. Beyond this, ideally it should be possible to give an uncertainty estimate for the accuracy of registration on a case-by-case basis. This information should then be incorporated into the planning process, and a treatment design that is minimally sensitive to the known uncertainties and expected errors in every stage of the IGT process should be used. Many registration methods provide an estimate of uncertainty for each case; however, many others do not. Research into appropriate methods of generating uncertainty estimates and communicating confidence limits to users is important for the success of IGT. Any automated procedure should be able to recognize and report when it has failed to achieve a reliable result.

Realistic Anatomical Modeling

The areas of segmentation, registration, simulation, atlas construction, and planning and delivery of IGT all depend on accurate modeling of the motion and distortion of anatomical structures. The present technique for modeling deformable structures, however, provides the necessary interactivity for only the most limited situations. Considerable progress has been made in modeling cardiac motion, but a complete biomechanical model for characterizing motion and distortion of any part of the body seems many years away. Research in this direction should be given high priority, as should intermediate approaches based on contemporary computer science research that can model the behavior of defined anatomical areas under practically relevant conditions.

As with segmentation and registration, anatomical modeling is intertwined with several of the other research areas described in this section. Segmentation and registration both need realistic modeling to make progress toward more general, highly automated solutions. Modeling treatments during the planning process requires realistic treatment of the motion, distortion, and interactions of anatomical structures. Incorporating uncertainty into the planning process depends on the ability to predict where and how objects will move during procedures and on the probable differences between the static patient model defined during planning and the actual position of the anatomy during therapy. Presentation of information during IGT should use realistic representations of

anatomy, including deformation of anatomical structures by the intervention.

Anatomical modeling is an area where access to high-performance computing resources will be of particular importance.

Validation

All of the steps in planning and delivering IGT must be characterized as to their accuracy, reproducibility, reliability, and robustness in the presence of expected deficiencies in input data. A database of standard "ground truth" data against which to test newly developed segmentation and registration methods would be an important community research resource. Such a database could consist of well-characterized image data and simulated data incorporated with known information. For example, a standard lesion database for tumor detection could have simulated lesions of known size, contrast, and other features. Similar databases of normal anatomy with agreed-upon labeling could be used to test segmentation methods. Such a database would need to incorporate realistic intersubject variability in size, shape, position, and image appearance of anatomical structures. This corresponds closely to the development of population-based atlases, which is discussed below.

Validation databases for registration should include well-characterized examples of intra- and intermodality combinations of images. Determining ground truth usually is difficult except, for example, in brain images where stereotactic frames or fiducials can be used to establish a trusted registration. The availability of high-quality standard datasets for testing multimodality registration methods, together with best estimates of the "correct" registration, would be very useful.

An area of medical image computing for which validation methods have not been well developed is visualization. There is no accepted standard by which the accuracy of a visualization, or of procedures performed based on visualization, may be characterized. Research should be pursued on how to characterize accuracy of visualizations and how to translate the uncertainties, including those introduced by the viewer's interpretation, into inaccuracies in treatments.

Atlases

The atlas is the embodiment of prior knowledge concerning structure and function as manifested in image data. Even if not perfect, atlases can be useful. They must be computationally tractable—that is, the information they contain must be expressed in a form that can be used effectively by analysis programs. The utility of atlases can be increased by increasing the amount of information associated with each anatomical point (e.g., nomenclature, normal histology, interactions with other organs or systems). Their utility also will be improved by including information concerning the range of normal variability of structure and function. This allows confidence limits to be placed on quantities derived from atlas-based analyses and on the decisions based on them.

Frequently, atlases are mapped into the coordinate system defined by a particular subject's image studies in order to carry the atlas labels into the image data. Assuming the atlas is valid and the mapping is correct, this step alone can accomplish a good deal of the segmentation task, because many voxels will be labeled. This mapping process is a registration task because the coordinate transformation must be defined to map homologous anatomical points. Depending on the complexity of the anatomical motion and deformation that must be modeled to adequately map the general anatomy of the atlas onto the specific anatomy of the patient, further research may be needed to perform this step adequately.

Most of the attention in atlas construction has focused on brain atlases, where the motions and distortions from the atlas to the individual subject are moderately complex and where the benefits of atlas use in complex segmentation tasks were first appreciated. What will be needed in the future are atlases covering the head and neck, thorax, abdomen, pelvis, and extremities. Development of extracranial atlases, and the tools needed to construct and use them while taking account of shape variability and distortion, should be given high priority in the near to intermediate future. Incorporation of as many functional and anatomic modalities as possible will increase the usefulness of atlases and also should be supported. Synthesis of macroscopic and microscopic information in an atlas also will be an important area of research.

Plan Optimization

The link between the virtual space of medical images and the physical space of an IGT procedure is the treatment plan. The planning stage of IGT is highly structured in radiotherapy, for example, where the complete geometry and time course of the irradiation to be delivered is simulated.

Planning or simulation integrates results from segmentation, registration, atlases, modeling, and visualization in order to provide the planner with the information needed to understand the treatment situation and to design a plan. Weaknesses in these areas limit the ability to produce complex and optimal plans in an acceptable time frame. Imperfections in segmentation; a lack of rich, timely visualization from multimodality datasets; and the unavailability of sufficiently realistic patient models are particularly limiting.

Radiotherapy also provides an illustration of some limitations of manual planning with respect to optimization. The parameter space within which the plan must be optimized (e.g., size, shape, number and 3D orientation of radiation beams; radiation type and energy; spatial variation of intensity within beam apertures) is too large to allow true optimization. Standard or "forward" planning techniques involve (1) choosing a set of plan parameters that are likely to be good, based on past experience with similar case situations, (2) computing the resulting radiation dose distributions, and (3) evaluating some figures of merit that express the success of the plan at fully treating the targets while minimizing collateral damage to normal organs. In consultation with medical and technical colleagues, the planner identifies how the result might be improved, and the process is iterated until the result is acceptable.

An alternative approach is so-called "inverse" planning, where a desired result (e.g., dose distribution) is specified and an optimization algorithm finds a set of treatment parameters to give that result within specified tolerances. Some work has been done in this area, but the parameter space must be sharply limited in order to produce a plan in a timely manner. Continued research on optimization strategies for automated planning, and on incorporating biological endpoints and clinical acceptability into plan evaluation and comparison, should be supported.

An important aspect of a plan is deliverability—that is, the practicality of the plan. Does it require impossible approaches to the patient? Does it minimize the time for the procedure relative to other acceptable plans? Is it sensitive to small deviations from ideal positioning of the patient or equipment? Is it sensitive to uncertainty in location of an internal anatomical structure whose position cannot be precisely measured at the time of therapy? As mentioned in earlier sections, all available estimates of uncertainty during imaging, segmentation, registration, planning, and delivery should be incorporated into the treatment design. The goal is to deliver a treatment whose probability of success will be minimally impacted by the known uncertainties.

Research Priorities

Short Term

- Develop validation databases for registration. Real and synthetic datasets, known truth, and standard validation methodology should be developed and a mechanism for their dissemination should be provided.
- Develop validation databases for segmentation and for lesion detection.
- Improve capabilities for image registration incorporating deformation. Both 3D/3D and the more difficult 3D/2D problems must be addressed.
- Expand access to state-of-the-art computing and visualization.
- Improve capability for navigation of extremely large image datasets.
- Investigate methods for estimating uncertainty at each stage and for propagating through the entire IGT process. Investigate means for ensuring delivered treatments are minimally sensitive to likely uncertainties.
- Improve segmentation capabilities based on user interface to allow users to classify what they can see with minimal time and interaction.
- Continue developing deformable modeling of anatomical structures using current technologies.

Intermediate Term

- Improve capabilities for realistic modeling of anatomical motion and deformation, including as much biomechanical information as is feasible.
- Develop probabilistic atlases for relevant body regions, including characterization of population

variability in shape and position. Incorporate as much additional information linked to the basic anatomical description as possible.

- Incorporate microscopic, biologically based imaging into standard medical imaging.
- Develop widely applicable segmentation methods based on high-level knowledge.
- Investigate probabilistic descriptions of disease from multiple image modalities and the implications for IGT.

Long Term

- Develop realistic biomechanical models of all relevant regions and organ systems.
- Develop complete segmentation and registration capabilities adequate for all relevant anatomical regions and organs.

Session 3: Computer-Assisted Interventional Systems

Integrating imaging with therapy will enable the next era in medicine's history. As surgery becomes less invasive, new sources of vision are required to examine the area outside the surgeon's portal of view. This vision is provided by imaging. Fundamental to bringing imaging into treatment is the complete integration of computers with interventions. Computer integration enables therapeutic innovation.

The tasks facing the physicians, engineers, and scientists who will bring this next medical era through its evolution must be faced by teams of researchers working together. Medicine is conservative and tradition-bound, with a language which appears obscure to those outside. Similarly, engineering seems foreign and obscure to medical practitioners. As clinical hurdles to innovation are identified, each discipline commonly attempts to leap to a solution from its own perspective. Yet for the sake of efficiency—in time, cost, effort, and time-to-acceptance—the coming problems must be solved by teams of specialists working together. It will serve no purpose to develop solutions devoid of input from the collaborating specialty. The problems to be solved must represent unmet clinical needs. Technology development and related research must be clinically driven.

Computer-integrated therapy systems include simulators for training, pretreatment planning, and rapid prototyping. Systems also include localized therapies—both noninvasive therapy modalities, such as HIFU and radiation beam therapy, and minimally invasive therapies, such as radiation seed implants, localized chemotherapy, RF ablation, and cryotherapy. Despite many differences of detail, there are significant synergies that can be achieved by pursuing solutions that are adaptable to multiple treatment modalities, imaging technologies, and organ systems. Significant research barriers must be overcome to extend current capabilities to mobile and deforming organ systems. Similarly, novel and versatile delivery systems can enable the development of novel therapies requiring accurate and consistent delivery.

The development of computer-integrated therapy systems rests on common research and technology needs, including the following:

- Computer science: image processing, modeling, planning, image registration, real-time computing and communication, and reliability.
- Interfacial technologies: sensors, imaging devices, robotics devices, and user interface.
- Systems infrastructure: test beds and modular components to support research, experimentation, and deployment.

Systems-Oriented, Multidisciplinary, Team-Based Research

A program of systems-oriented research on computer-assisted interventional systems (CAIS) should be established. Such research should address both fundamental engineering and scientific problems associated with CAIS, with specific activities motivated or driven by realistic clinical problems. This research is inherently multidisciplinary in nature, and it is best pursued through collaborative efforts incorporating both clinical and engineering researchers. Clinical application cannot be an afterthought, and clinicians should be involved in all phases of the work. Similarly, it is important that engineering researchers not be treated as mere implementers for the clinicians. There are fundamental algorithmic and technology barriers that must be addressed within the context of CAIS and test beds.

One fundamental challenge is finding a means to fund and support such team-oriented research activities. Although there are some potentially pertinent programs within government agencies (e.g., National Science Foundation [NSF], National Institutes of Health [NIH]), it traditionally has been very difficult to secure the necessary level of financial and institutional support. Means must be found to overcome the institutional and other barriers that have inhibited the establishment of effective clinician-engineer teams.

Many of the technologies associated with CAIS are interdependent, forming a web. They are often best pursued within the context of an overall program or test bed application. For example, developing means to deliver patterns of localized injections accurately into a deforming, mobile organ may require advances in real-time imaging, segmentation, deformable

registration, mechatronics, and biomechanics. Better biomechanical models of such organs will make it possible to plan therapy patterns more accurately and can be combined with real-time force and image sensing to help deliver the planned patterns. Similarly, the availability of accurate force and real-time 3D imaging capabilities can be crucial in developing and validating biomechanical models that can predict organ deformations. Finally, the availability of accurate and repeatable means for delivering patterns of therapy to targeted anatomy can significantly speed up the development and validation of new treatment options by reducing experimental variability.

Some mechanisms for promoting this synergy include

- Creation of jointly funded and jointly reviewed NSF/NIH and other multiagency programs
- Funding shared technology infrastructure research
- Promoting common software toolkits and replicable experimental hardware components
- Encouraging consortia to develop shared test beds and fund the development of such test beds
- Funding standards activities and multi-institutional working groups to define robust system architectures with nonproprietary interfaces and activities for the development and maintenance of these standards
- Actively involving industry and academia in the development of standards, "best practice" guidelines, test beds, and took kits.

CAIS currently is a small market compared to other uses of some of the backbone technologies (e.g., 3D graphics and computing). This can be an advantage, in the sense that other commercial applications can often drive technology and cost reductions. However, this cannot substitute for crucial research and development support for adapting these advances to the CAIS environment. Means need to be found to encourage incorporating such advances into a broadly supported infrastructure for biomedical research. One possibility might be to create a funding mechanism that would allow research proposals to include an explicit task (and appropriate support) for development, testing, and maintenance of the technology backbone.

Specific Technology/Research Needs

A number of specific technology areas are crucial for image-guided CAIS:

- Tissue and organ property modeling
- Integration of planning and control
- Robotics systems for treatment delivery
- User interfaces (e.g., haptic, visualization)
- Sensors for feedback
- Representation standards
- Interface standards
- Validation of systems.

Several of these areas are discussed in greater detail below.

Tissue and Organ Deformation Modeling

Advances in biomechanical modeling of tissue and deformable organs are needed to support therapy planning, real-time control of therapy delivery, and simulation. (The role of such modeling in therapy planning and delivery has been discussed briefly above.)

Tissue modeling will enable the development of realistic simulators for training, rehearsal, and device prototyping. Procedural simulation will become the standard of learning for both novice and experienced physicians, as well as provide engineers a means to perform medical procedures for which they are designing new devices. Such simulators also have an important role in therapy planning.

The development of computer-based simulators for medical learning has not progressed to a level of demonstrable transfer of knowledge gained from currently available simulators. One major hurdle to effective learning is the ability to accurately represent simulated organ characteristics such as weight, elasticity, deformation, and texture. Because there is so little established science in this field, developing this knowledge will require multiyear collaborations among physicians, haptics designers, programmers, and engineers. However, the resulting body of knowledge will be used to assemble procedural simulators that will permit medical learning to take place without putting real patients at risk. Realistic medical simulation also will permit rehearsal of difficult procedures and will open the opportunity for biomedical engineers to perform a procedure for which they are designing new implantable devices,

instruments or drug delivery systems. The infrastructure technologies that such an effort will use include sensors to gather data on organ characteristics; robotics to accurately manipulate organs during study; and modeling science, including haptics interface design and graphics programming.

Infrastructure and Enabling Technology
Advancing tissue and organ deformation modeling is directly synergistic with a number of other areas:

- Sensor technology (see below)
- Real-time imaging
- Robotics
- More general modeling, representation methods, segmentation, and registration.

Research Priorities
Short Term

- Conduct experimental studies on in-vivo organ systems

Intermediate Term

- Characterize normal and abnormal tissues in breast, prostate, and liver.
- Integrate normal and abnormal tissue models into graphics and haptic simulation.

Long Term

- Develop real-time control to drive therapy devices.
- Incorporate real-time image feedback.

Spanning the Time Line

- Develop better representation and computation methods that permit incorporation of uncertainties and approximations with predictable error.
- Establish high-fidelity anatomic representations with embedded physiology, permitting silicon device prototyping.

Sensors for Tissue-Tool Interactions

A variety of sensors, in addition to real-time image sensors, will serve as new diagnostic tools, therapy monitors and force reflectance monitors. Microelectromechanical systems (MEMS) technologies from integrated circuit manufacturing will be used to design biosensors that permit tissue analysis for immediate in situ diagnosis, drug monitoring from steady state delivery systems, and monitoring tissue-tool interactions during minimally invasive therapy. These sensors must be integrated into an overall information infrastructure for their effective use in CAIS.

Infrastructure and Enabling Technology
Advances in sensing are directly synergistic with a number of other areas:

- Tissue property modeling
- Stereotactic navigation
- Real time imaging
- Robotics
- More general modeling, representation methods, segmentation, and registration.

Research Priorities
Short Term

- Develop force and touch sensing (e.g., in injection needles, palpation devices).
- Devise integrated imaging sensors (e.g., catheter-based ultrasound, MR sensors built into needles and catheters).

Intermediate/Long Term

- Build biological sensors into therapy and biopsy devices.

Spanning the Time Line

- Enable tissue identification.
- Integrate navigation and robotic positioning devices with sensors.
- Allow image/sensor “fusion.”
- Allow monitoring and control of therapy delivery.

Image-Guided Localized Therapy

There is a need to develop broadly usable and flexible systems for planning and delivering patterns of noninvasive or minimally invasive local therapies. As discussed earlier, such systems are needed (1) to take advantage of the many potential synergies spanning multiple treatment modalities, image modalities, and organ systems and (2) to promote the more rapid development of novel therapy options. Broadly, moving beyond rigid organs like bones and rigidly contained organs like the brain is needed to accommodate mobile and deforming structures.

Infrastructure and Enabling Technology
The development of such systems for localized therapy is directly synergistic with the entire range of technologies discussed in this session and throughout this article. A systems-oriented approach is vitally needed to advance these technologies and their effective application.

Research Priorities
Short Term

- Enable bone and spine biopsies.
- Facilitate vertebroplasty.
- Focus on other stereotactic interventions where organ deformation may be ignored.

Medium Term

- Transition to nonrigid organs such as the breast, liver, and prostate.
- Integrate advances in tissue sensing and monitoring into therapy delivery devices.

Long Term

- Enable dynamic local therapy in mobile organs, such as the heart.

Spanning the Time Line

- Develop multi-institutional preclinical activities.
- Develop common engineering toolkits and shared test beds.

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While the working group reviewed a wide variety of thermal and radiation treatments, this paper focuses on two examples: (1) laser surgery and (2) radiosurgery.

Interstitial Laser Therapy for Tumors of Solid Organs

Laser beams delivered interstitially via flexible fibers provide a convenient means of treating lesions in the center of solid organs with minimal effects on the overlying normal tissues. In most cases, the fibers can be inserted through needles positioned percutaneously. However, the techniques are critically dependent on imaging to position fibers correctly and to monitor and assess therapy. The key to success is matching the extent of the lesion with the extent of the laser-induced necrosis, and the method is only valid if the true margins of the lesion to be treated can be defined sufficiently accurately. Two forms of tissue destruction can be used: thermal and photochemical. Both have the advantage of no cumulative toxicity, so treatments can be repeated at the same site if the initial treatment proves to be incomplete.

The thermal technique of ILP involves gentle heating of the tissue to coagulate a volume of about 1.5 cm in diameter around each fiber tip, larger volumes being treatable by using multiple fibers or diffuser fibers. All tissue within the treated area (cells and connective tissue) is necrosed, and healing is by resorption of the necrosed tissue with scarring or regeneration. ILP is suitable for lesions in relatively large organs in which the surrounding normal tissue can tolerate minimal thermal damage, such as isolated hepatic metastases. It is being studied as a possible alternative to wide local excision in the initial management of small, localized breast cancers as well as for treating fibroadenomas of the breast, fibroids of the uterus, and benign prostatic hypertrophy.

The photochemical technique is photodynamic therapy (PDT) in which low-power red light is used to activate a previously administered photosensitizing drug. There is no increase in tissue temperature and little effect on connective tissue. PDT therefore is safer than ILP near the edge of small organs because there is less risk to their mechanical integrity. Although most research so far on PDT has been done on tumors of the skin and hollow organs, interest has extended recently to tumors of solid organs, such as the prostate and pancreas, and the peripheral part of the lungs. Animal studies have shown that these tissues and surrounding normal structures can tolerate PDT. Clinical trials have started on localized cancers of the prostate (recurrence after radiotherapy) and pancreas. Tumor necrosis can be achieved with no serious complications, but it is too early to judge what role this may have in the overall management of these patients.

Contrast-enhanced CT or MR scans best identify ILP- and PDT-treated areas as new zones of devascularization, but these are only clearly demarcated a day or more after treatment. Dynamic MR imaging can pick up the temperature changes induced by ILP in real time, and it may prove possible to correlate these changes with the final extent of heat-induced necrosis. Real-time monitoring of PDT is more difficult because there are no temperature changes and new techniques are required, perhaps PET or MRS.

The results available so far suggest that ILP and PDT are simple, safe, and effective and warrant more detailed and extensive studies of their efficacy in a range of solid organs.

Miniature Photon Radiosurgery System for Image-Guided Therapy in the Operating Room

A miniature photon radiosurgery system of 50 kvp X rays suitable for use in the operating room has been described by Dinsmore and colleagues.[1] Briefly, this source consists of an electronics package (16x11x7 cm powered by 12 volts dc) to which is attached a 10-cm long, 3.2-mm diameter probe. When the device is turned on, X rays are emitted from the tip of the probe. When the probe is inserted into tissue, the dose rate varies approximately as the inverse third power of the distance from the source, and at 1 cm the typical dose rate is 3 Gy/minute. The rapid falloff of dose results in sharp boundaries between normal and necrotic tissue.

More than 150 metastatic brain tumors have been treated with photon radiosurgery. In these cases, the probe tip was placed interstitially into the tumor.

Interstitial treatment of breast tumors also is in progress. Animal studies of interstitial treatment of the kidney and liver have been performed in preparation for laparascopic clinical use. Percutaneous treatment of these and other organs also is planned. Skin tumors are being treated by using a conical applicator with a flat end, which serves to position the probe tip above the tumor. Spherical applicators are being used to treat the surgical bed of tumors resected from the breast, brain, and colorectal region. In principle, any surgical bed, wherever located and of various shapes and sizes, can be treated using appropriately designed applicators. An animal study is in progress to evaluate the use of the photon radiosurgery system for the treatment of macular degeneration. In this case, the probe is equipped with a microcollimator with a diameter small enough to be inserted into the eye.

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Session 5: Machine Design and Clinical Framework

System Integration

Following the experimental, scientific evaluation of a potential image-guided procedure, there is a need for system integration, engineering, and validation of the tools and instruments used for a clinical operation. This system integration should precede clinical feasibility testing. Within the framework of a procedure, there are individual components that require product development and regulatory approval. Only after these particular elements are adapted to the entire procedure can full integration be accomplished.

Barriers to Overcome

The lack of standards has been a significant problem in this emerging medical field. The full integration of multiple diverse technologies requires the establishment of standards. The presence of standard components will facilitate and promote system integration and make the process substantially easier.

Rapid integration of the components of image-guided therapy usually results in early clinical evaluation. Early clinical trials are frequently performed without well-defined outcome measures and are essentially restricted to the validation of individual components. The fully integrated system, however, should be validated on short-term outcome measures, such as immediate complications or lack of postoperative symptoms. Yet the reliance on short-term outcome measures to test the effectiveness and feasibility of novel procedures is a major problem. Longer term outcome measures are essential to help estimate the potential versus existing market and to conduct any preliminary research on the possibility of reimbursement.

Clinical Benefits of New Technology

While reduced invasiveness and cost are obvious justifications of a minimally invasive procedure, there must be sufficient clinical evidence that the procedure is safe and results in fewer complications than the conventional procedure. In addition, there is a need to show improved efficacy and clinical outcome not only for peer recognition but for widespread patient acceptance.

Breakthrough Technologies

In the current research and development environment of image-guided therapy, there are demands for better target definition using new imaging techniques, optical imaging methods, functional imaging, tumor-seeking contrast agents, genetic or molecular markers. At the same time, there is a need for improved therapy delivery systems, such as transcutaneus energy deposition, gene therapy, targeted drug delivery, and user interfaces, including data presentation, effectors, sensors, and display systems.

The academic-clinical environment for image-guided therapy is a multidisciplinary, multidepartmental, and, in most cases, multi-institutional effort. There is also a great step from the basic to the translational research endeavor. This type of research benefits greatly from on-site technology development. It sometimes is difficult to focus on clinical implementation of specific applications in the same environment where the bioengineering, computing, and other technology-dependent components are undertaken. Because of the limitation of nonacademic sites to combine technology development with clinical implementation, this type of research is mainly restricted to academic institutions where clinical sciences coexist with biomedical engineering facilities. There is the possibility to use off-site academic-clinical codevelopers.

Industrial partnerships are very important for the integration of multiple technologies, especially when nonmedical technologies are used. Nevertheless, industrial support is needed for technology assessment. This support is relatively easy to obtain when there are multiple test bed applications for a single system by a single manufacturer. It is quite difficult, however, when the integration of diagnostic and therapy devices and computers includes multiple vendors.

The industrial design and architecture of image-guided system requires a high degree of modularity. The industrial architecture and design features should include safety considerations and significant documentation for the reinforcement of regulations. Architecture definition influences standards and interfaces as well.

Industry Panel

Interventional MRI

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Interventional MRI has been in use for one and a half decades. In the mid-1980s, Lufkin (UCLA) started using closed MRI systems for MR-guided needle biopsy and aspiration, surgical planning, stereotaxy, and monitoring laser and RF ablation therapy. Mueller and colleagues (Massachusetts General Hospital) performed MR-guided aspiration biopsy in humans in 1986. In 1988, open MRI became commercially available (Toshiba AKA Diasonics), and Seibel and Groenemeyer used open MRI on patients for biopsies and tumor treatment and, in 1989, published on guidance of a needle-biopsy treatment of tumors with chemicals, catheter insertion, visualization of the distribution of the medication, oblique slices to align with certain structures, monitoring of the treatment, and use of lasers. In 1991, Zamorano (Wayne State), Talton (Dynamic Digital Disp.), Hanwehr (Georgetown), Weghorst (University of Washington) and others at IEEE's Strategic Defense Initiative Technology Applications Symposium discussed intraoperative MRI, automated operation, preplanning, display needs, guidance from the MRI system, radiotherapy monitoring, and system and subsystem configurations and designs. Also in 1991, MR fluoroscopy became commercially available, including in-gantry room display and ghost imaging (Toshiba). GE announced a dedicated interventional MRI system in 1994. As this 1999 meeting proves, interventional MRI is still the subject of academic meetings rather than a practice in the community. Why is this the case?

For Toshiba, the team that designed and manufactured the first open MRI, openness was an accident and interventional MRI an afterthought. The intent was to develop a low-cost, reliable system that was easy to install and maintain. Openness fell out of the design of what was to be a low-cost imaging system, and it quickly found a claustrophobic patient market that made it successful. Nevertheless, an operator can charge more for the use of MRI in an interventional procedure as compared to diagnosis. If that is the case, why are all other widely available open systems designed for imaging instead of intervention? Why is GE the only company with a dedicated interventional MRI system? Evidently, the others do not see a market that merits the investment in a dedicated design. That should be a subject for discussion.

Ideal Characteristics of Equipment

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During the past decade, there has been a significant interest in the development of MR systems for interventional applications. This follows in the footsteps of computed tomography, which was first used in the surgical suite in the early 1980s. CT, however, has failed to establish itself as a routine part of surgical practice outside of a very limited number of centers. With this in mind, one must consider what is necessary for MR to succeed in this forum. The presence of an MR system in a therapeutic environment imposes certain restrictions on both conventional instrumentation and personnel. The benefits offered by the MR system must definitively outweigh these limitations in order for interventional MR to gain widespread acceptance. Thus, it is desirable for the MR system to have the full gambit of capabilities that are exhibited on state-of-the-art diagnostic scanners. This includes MR angiography, diffusion and perfusion imaging, fMRI, real-time imaging, MR thermometry, and MR spectroscopy. Moreover, these capabilities must be offered to the interventionist in a way that is compatible with and integrated into their conventional therapeutic environment.

An ideal system for image-guided diagnosis and treatment must exhibit these properties but also must be cost-effective to both the industrial developer and the clinical user. This implies that the resources required to develop an interventional MR system must be in line with the potential market and rates or reimbursement for these products. Clinicians, however, must demonstrate both the benefits of using the technology as well as its cost-effectiveness. Large capital expenditures make the cost-effectiveness justification much more difficult; thus, there is a strong incentive to contain costs. These considerations argue against the development of a highly specialized interventional MR system. A more prudent approach that is being used by several vendors is to customize existing products to the special needs of the interventional environment. This approach requires the use of a conventional MR system as the starting point.

There are currently two major genre of MR scanners: cylindrical bore and biplanar. The biplanar configuration offers lateral access to the patient while at isocenter, but these systems have limited field strength, which, in turn, negatively affects image quality and imposes functional limitations. Short-bore

cylindrical systems, particularly those exhibiting a flared opening, offer some degree of patient access during scanning and provide all of the benefits that MR has to offer. A platform such as this has the additional advantages of being acceptable for conventional diagnostic scans when not being used for therapy and will be upgradeable with future developments to diagnostic scanners.

System performance, patient access, and cost are mitigating factors that tend to oppose one another and therefore it is difficult to define an ideal interventional MR system. The continuing evolution of applications that may require or benefit from MR imaging guidance also complicates matters. The desirable system features that are realistically achievable are as follows:

- Approximate the capabilities of a current diagnostic scanner.
- Offer acceptable patient access and/or provide fast and easy patient transport.
- Build the interventional MR system upon an accepted diagnostic standard.
- Integrate MR into the existing therapeutic environment (as opposed to vice versa).
- Develop an interactive and intuitive interface.
- Minimize the extent and impact of the magnetic, gradient, and RF fields.
- Minimize acoustic noise production.

Ultimately, the ideal system will be defined by the specific application(s) it will perform. In the interim, when the niche of image guidance in therapy is established, it will be necessary for both industrial and clinical partners to make judicious choices between system properties that are often in conflict.

Session 6: Summary Roundtable of Professional Societies

A paradigm shift in medicine has occured. Imaging has become an important, if not critical, factor in the care of patients beyond simply diagnosis. This has resulted from several decades of advances in the imaging sciences. Developments in hardware and software in CT, MR, ultrasound, and nuclear medicine, in concert with clinician-directed applications, has made this shift possible.

Organizational Issues

A similar paradigm shift in image-guided therapy is beginning. This revolution requires synergistic interactions between scientists, bioengineers, and clinicians from many disciplines. The underlying science that enables this field of study must be rigorously investigated to maximize the delivery of health care. As such, centers of excellence in image-guided therapy are essential to break down the traditional barriers, foster collaborative interactions, and elevate this discipline to include hypothesis-driven science.

Within academic health centers, image-guided and computer-assisted intervention does not have a clearly defined structure or home. Unlike other multidisciplinary and multidepartmental programs (e.g., MRI, neuroscience), image-guided, computer-assisted intervention does not have a single advocate or champion.

Training Issues

This lack of structure in image-guided and computer-assisted intervention makes it difficult to establish an applicant pool and criteria for research and clinical training. At present, people train elsewhere and bring expertise to a clinical program rather than learning the expertise within the program.

Industrial Partnerships

Most academic partnerships with industry tend to be made with departments and schools so that longstanding relationships are established. In image-guided and computer-assisted interventions, the "partnerships" tend to be with individuals and frequently lack long-term commitment.

Recommendations

Organization

It is suggested that the National Institutes of Health establish centers for image-guided diagnosis and treatment similar to what is being done with "In Vivo Cellular and Molecular Imaging Centers." These new centers for image-guided diagnosis and treatment should have the following criteria:

- The center should be established within a department or as a formal collaboration of several departments, thereby having an advocate within the medical center
- The center should be multidisciplinary and have multidepartmental support.
- The center should be able to support on-site technology development with strong basic science and system engineering.
- It is desirable that the sponsoring department have a successful track record in industrial partnerships.

Training

The faculty in the funded center should be encouraged to apply for training grants for graduate students, as well as research and clinical fellows. Support from training grants should be sought from all appropriate federal agencies, as well as industry.