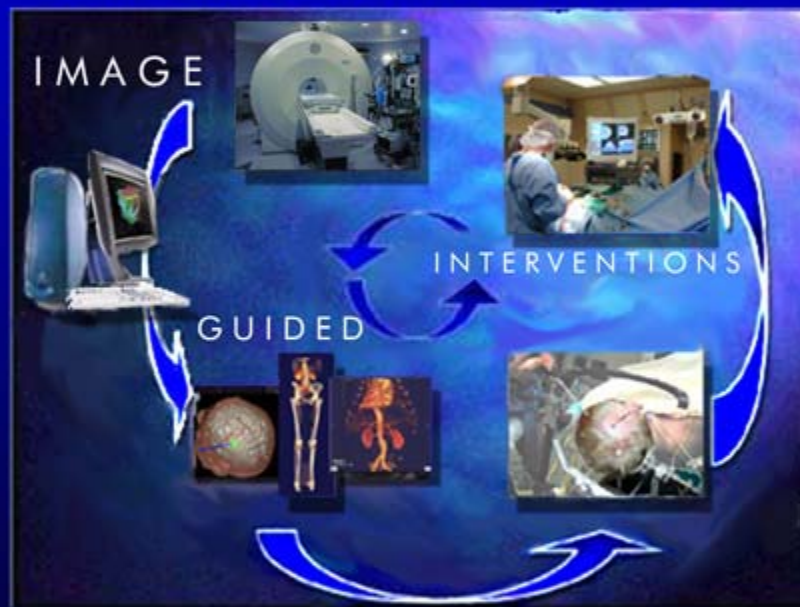


# IMAGE-GUIDED INTERVENTIONS WORKSHOP FINAL REPORT

NIH/NSF WORKSHOP ON  
IMAGE GUIDED INTERVENTIONS  
SEPTEMBER 12-13, 2002



BETHESDA, MARYLAND



National Institute of Biomedical  
Imaging and Bioengineering



**Report of the NIH/NSF Group on  
Image-Guided Interventions  
September 12-13 2002**

*Sponsored by  
National Cancer Institute  
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## **PREFACE**

On September 12-13, 2002 the National Institute of Biomedical Imaging and Bioengineering (NIBIB), the National Cancer Institute (NCI), and the National Science Foundation (NSF) held a workshop on Image-Guided Interventions at the Bethesda Marriott in Bethesda, Maryland. The workshop was co-chaired by Dr. Ferenc Jolesz from Harvard University, Dr. Russell Taylor from Johns Hopkins University, and Dr. Michael Vannier from the University of Iowa. Over 60 researchers, engineers, clinicians and federal officials were in attendance to discuss advances in basic imaging science and engineering as they relate to minimally invasive treatments, biopsies, and surgical procedures that improve human health. The recommendations from this workshop have been and will continue to be used by the NIBIB, NCI, and NSF to enhance programs associated with image-guided interventions.

The purpose of this workshop was to ensure that NIH and NSF programs address important needs and issues associated with image-guided interventions (biopsies, surgery, and other image-guided therapies). To this end, input was sought from the academic community and other developers and users of image-guided technologies used in medicine. This meeting covered the spectrum of technological advances related to image-guided technologies. Information from this workshop continues to be used in the development and evaluation of NIH and NSF research programs.

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## **EXECUTIVE SUMMARY**

### **NIH/NSF Workshop on Image-guided Interventions September 12-13, 2002**

A planning workshop sponsored by NIH and NSF was held to identify the needs, opportunities and issues associated with future advances in image-guided interventions (biopsies, surgery, and other image-guided therapies). A group of academic, industrial and government experts in medical imaging, surgery, and regulatory affairs met on September 11-12, 2002 to advise NIH and NSF on these matters. This meeting covered a broad spectrum of technological advances and applications related to image-guided interventions.

At this workshop, recent progress in the field was reported to identify new opportunities. Clinicians who are experts in their respective fields were consulted to identify unmet needs in this planning meeting.

### **IMAGE-GUIDED INTERVENTIONS (IGI) WORKSHOP RECOMMENDATIONS**

- Surgical robots and biopsy devices that locate targets of interest seamlessly across different resolution scales.
- Intra-operative, real-time, 3D image-guided navigation (4D-IGI) for moving or deformable tissues/organs.
- Develop “fully engineered” components of IGI systems that can be seamlessly integrated for a wide range of clinical applications.
- A technical working group is needed to develop standardized system interfaces.
- Collaborations between academia and industry should be facilitated.
- Establish centers of excellence and resources that exploit grid computing and informatics infrastructure.
- The clinical requirements for IGI are evolving rapidly and should be updated by a periodic forum.

### **CLINICAL REQUIREMENTS FOR IGI**

The clinical breakout sessions recommended a forum that would periodically meet to establish the clinical requirements for Image-Guided Interventions (IGI). The latter would include the development of the IGI protocols and methods for quality assurance and assessment of outcomes of interventions; namely to develop a broad consensus for more standardized approaches for emerging IGI methods. Clinical requirements identified included the development of: (a) IGI methods that can be implemented across different commercial imaging platforms and organ systems, (b) validation methods and related standards early in the development phase, and (c) a means for collaboration between academia and industry to encourage the development and more timely

dissemination of IGI systems as required for multi-center clinical trials. Greater transparency was suggested for clinical validation studies by academic institutions, device and drug industry, namely to facilitate an improved understanding of emerging requirements for FDA approval.

Two clinical models were reviewed that highlighted the need for improved IGI methods, specifically the diagnosis and treatment of lung and prostate cancer. Common requirements were identified, including: (a) further advances in molecular, functional and hyper-spectral imaging using an array of imaging modalities or combination technologies to improve the sensitivity and specificity for disease detection, classification, and microscopic target identification, (b) improved trajectory planning that includes image guidance (IG) methods, robotics, and biopsy devices required to locate and sample the target(s) of interest seamlessly across different resolution scales, and (c) real time feed back methods to assess the IGI method(s) employed. Recommendations confirmed that many components of IG systems are generic and the optimization of methods for targeted applications may often be disease- specific.

### **INTEGRATED SYSTEMS APPROACHES AND VALIDATION**

The technical breakout sessions recommended the development of ‘fully engineered’ IGI systems, recognizing that most IGI systems today are not fully optimized and are often targeted for a narrow range of clinical applications. The systems approach recommended for IGI included: (a) the identification of appropriate performance standards for all the emerging system components, and the development of standardized interfaces, (b) the development of component technologies that can be more readily implemented across different commercial imaging platforms, and (c) open source software platforms that may facilitate the development of more harmonized IGI protocols. A comprehensive list of operational standards was developed.

The recommendations included the establishment of a second technical working group to periodically meet to encourage the development of standardized system interfaces, with representations from both academia and industry. It was recognized that IGI technologies are rapidly evolving and that it is important to include emerging systems for anatomical, functional and molecular imaging that may require some re engineering of IG methods. It was also recognized that IGI methods might require multi-modality image guidance, including imaging at the cellular scale. Thus issues such as development of more standardized interfaces and methodologies and validation methods were well recognized as becoming increasingly complex. Similar recommendations and observations were made for image-guided therapy (IGT) and image-guided surgery breakout sessions (IGS).

### **RESEARCH CENTERS AND RESOURCES FOR IGI**

Finally, the breakout session on research centers proposed a number of top-down mechanisms to implement the above clinical and technical recommendations. They included the support of centers of excellence, or virtual centers or resources using GRID Internet based interaction. Implicit in these recommendations was the need for active networking between the academic and the device and drug industry community.

## OVERVIEW

### NIH / NSF Workshop on Image-guided Interventions September 11-12, 2002

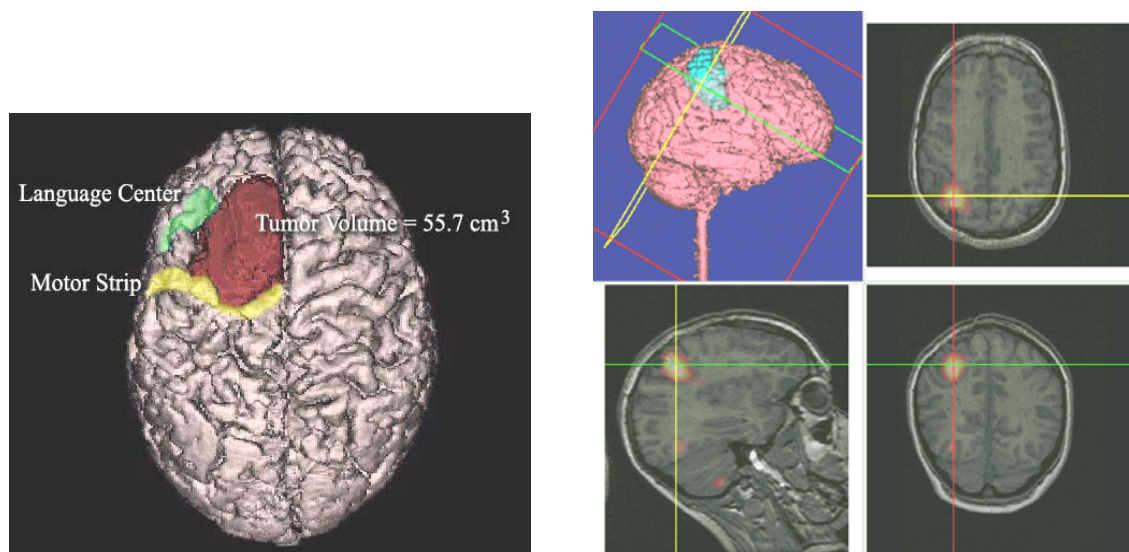
The Image-Guided Interventions (IGI) workshop was convened to cover the spectrum of technological advances related to image guided technologies used to localize human disease and injury, navigate human anatomy, provide diagnostic tissue, administer treatment, and monitor responses to therapeutic interventions. The requirements for IGI have been evaluated in the past.<sup>1,2</sup> At this workshop, recent progress in the field was reported to identify new opportunities. Clinicians who are experts in their respective fields were consulted to identify unmet needs in this planning meeting.

For the purpose of this workshop and report, IGI is defined as a patient encounter where images are obtained (within or immediately before a procedure) and used for guidance, navigation and orientation in a minimally invasive procedure to reach a specified target under operator control. Common requirements for all IGI are a source of images, real time interactive display linked to the intervention with a means of target definition in the context of real 3-D space (as distinguished from the abstract image space).

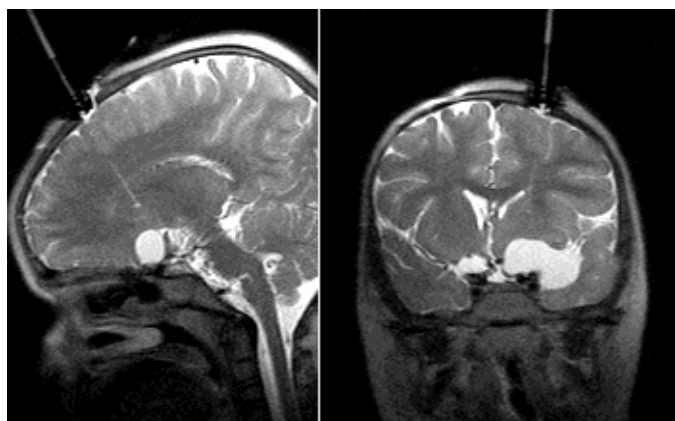
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<sup>1</sup> Industry Canada assembled a Medical Imaging Technology Roadmap Steering Committee in 2000 that included Working Group 4 on Image Analysis and Visualization. Their report, issued in June 2000, was intended to provide a market-driven forecast on technologies needed to improve patient care and enhance the global competitiveness of the Canadian medical imaging sector. (<http://strategis.ic.gc.ca/medimage>) Working Group 4 reported that image guided surgery and therapy offers a less invasive, less costly approach to patient care for a number of common procedures, but that the requirements for a successful system are demanding. They specifically analyzed systems for tracking instruments in the body; flat-panel stereoscopic display systems; head-up display systems; automatic patient-image registration; force feedback technologies for visualization; surface matching and bone-mounted markers with a wide variety of user interface tools.

<sup>2</sup> In the USA, the Scibermed Virtual Institute ([www.scibermed.com](http://www.scibermed.com)) was formed by the Biomedical Research Foundation of Northwest Louisiana in conjunction with Sandia and the Department of Energy to develop technology and policy objectives and formulate roadmaps for minimally invasive therapy, imaging, and energy delivery. Their technology objectives include: 1) to develop image-based methods of tissue identification and characterization and multimodal image display technologies, 2) to enhance and expand innovative methods of tissue reconstruction and ablation, 3) to develop methods to accomplish therapy using the least invasive access route feasible, and 4) to develop a system for rapidly disseminating new, effective minimally invasive therapies.



**Figure 1. IGI techniques used to target brain tumors.** Image courtesy of R. Robb, plenary presentation.



**Figure 2. Real time cyst drainage using IG techniques.** Image courtesy of Peter Luyten, from University of Michigan.

The global market for minimally invasive image-guided interventions is currently over \$3 billion, though less than 15% of all surgeries are performed using a minimally invasive, IGI approach.<sup>3</sup>

IGI has several advantages and a few disadvantages. The most positive features of IGI are its less invasive nature and efficiency – both in time and cost. The higher precision of IGI may result in fewer complications and less normal tissue damage, with assurance that the procedure has been completed as intended, thus reducing the need for rework. And the public prefers a high technology approach whenever possible, leading to rapid clinical acceptance. The disadvantages are that IGI may add unnecessary complexity and cost

<sup>3</sup> Source: AdvaMed; The Lewin Group; The Gartner Group – 2001



when the procedure can be accomplished without images – such as in the case of palpable lesions. Images may be over interpreted, leading to unnecessary procedures due to overdiagnosis. Some IGI systems do not have the ability to update the images in the midst of a procedure, so the images being used may be incorrect. IGI procedures may place special demands on the operator for experience and training, and special equipment is required that may not be widely available.

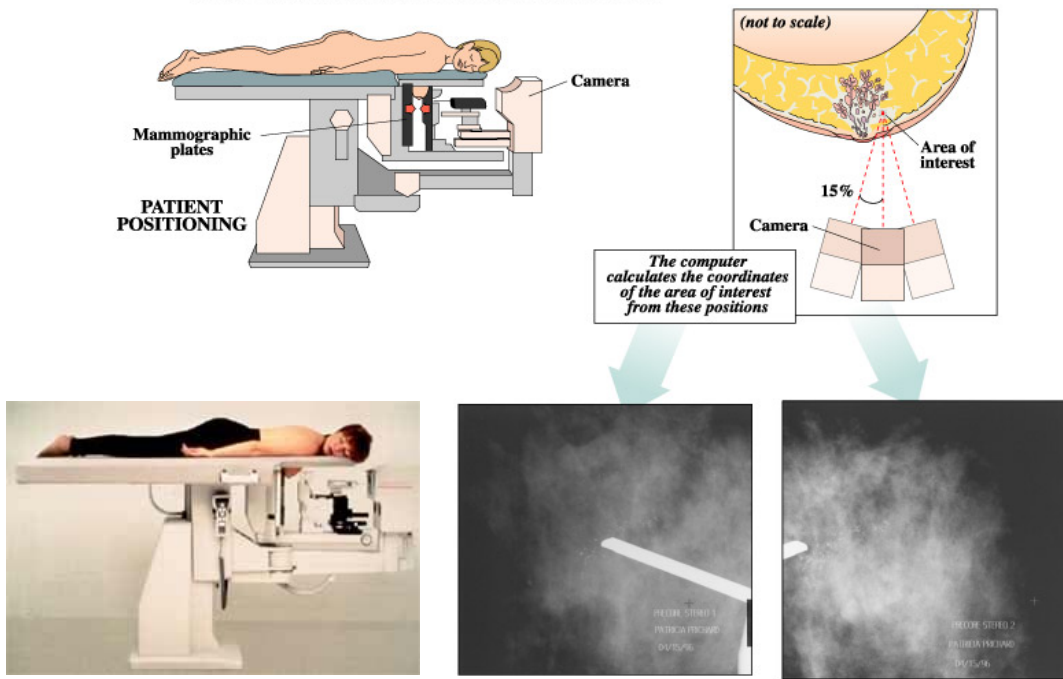
In some clinical applications, IGI is the standard of care. This is true, for example, in laparoscopic cholecystectomy, stereotactic breast biopsy, stereotactic radiosurgery, functional endoscopic sinus surgery, and 3D conformal radiotherapy to name a few. Clinical trials of IGI have been reported, and among these the RTOG found that image-guided 3D conformal radiotherapy of the prostate with dose escalation increased the cure rate without excess complications in a multicenter trial.

A new imperative for IGI arises as a result of screening tests for cancer and other diseases (especially coronary artery disease) where a diagnosis is needed and treatment administered in an asymptomatic at risk population found to have early disease. In such cases, IGI is virtually the only alternative for management of individuals who have a positive screening result but no overt signs of disease. Given that false positive screening test results are common (e.g., 75% of positive screening mammograms are falsely positive), and patients with positive screening tests suffer high anxiety and stress from knowledge they may have cancer or heart disease, a rapid, reliable and cost-effective means of diagnosing these individuals is needed. IGI is most promising, since (in cancer, for example) a diagnosis can only be made and treatment started when histopathological results are available that must come from tissue sampling. The biopsy procedure may be combined with the administration of therapy. Stereotactic breast biopsy is a common example. Screening mammograms are done, followed in positive cases by a biopsy. In the past these biopsies were done in the operating room with a lumpectomy. Today, it is common to diagnose breast cancer with a core needle biopsy rather than open procedure, lowering the cost and associated invasiveness. Similar procedures for the lung are needed, as CT screening progresses and candidate small lung cancers are identified. At present, many of these lung CT screening patients will undergo a mini-thoracotomy and partial lung resection. An image-guided minimally-invasive procedure would be preferable, however. The scenario for lung cancer screening is complicated by the detection of “incidentalomas” in the liver and especially adrenals. These benign lesions cannot be diagnosed by imaging alone, so IGI is necessary.<sup>4</sup>

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<sup>4</sup> Adrenal incidentalomas have become a serious problem with widespread use of CT and this issue can increase in importance with screening for lung cancer (which often metastasizes to the adrenals). An NIH State-of-the-Science Consensus statement on Management of the Clinically Inapparent Adrenal Mass (Incidentaloma) was formulated and issued in 2002.

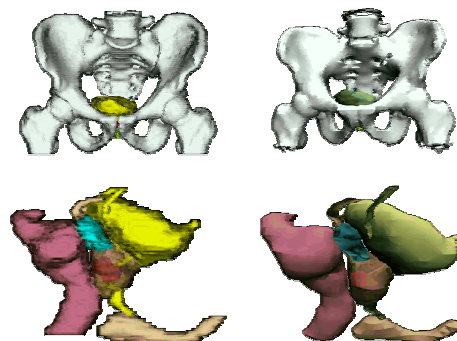
## STEREOTACTIC BIOPSY



**Figure 3. Stereotactic biopsy of breast tissue.** Image courtesy of M. W. Vannier, plenary presentation.

IGI can provide a new option for care of patients, such as the screening of detected lesions described above, which may not exist today. Given the benefits of IGI in breast cancer diagnosis and prostate radiotherapy, many patients and their clinicians would opt for this approach if it were available. Thus, there is strong motivation to adapt and extent current IGI technology for use in new applications, especially common diseases where the options for interventions do not currently include IGI.

It is clear that image guidance improves therapy as demonstrated by the improved survival in prostate cancer treated with IGI 3D conformal radiotherapy (RTOG trial), and by the widespread acceptance and use of IGI stereotactic breast biopsy in patients with positive screening mammograms.



**Figure 4. Image of normal and cancerous prostate produced from MRI and CT scans.** Volume rendering is shown at left and volume modeling at right. Cancerous tissue is shown in red. Courtesy of Richard Robb, plenary presentation.

The specific medical applications that can benefit from the application of IGI technologies are 1) patients with positive screening tests – who are asymptomatic individuals at high risk for having early stage disease, such as cancer or coronary artery disease, 2) neurosurgery, 3) orthopedics, 4) vascular surgery, and 5) general surgery. Virtually any open procedure could be converted into an IGI with appropriate technology.

The challenges and issues associated with image-guided diagnosis and therapy include exploitation of IGI in areas where there is no currently widely accepted minimally invasive alternative. The goal should be to establish IGI as the standard of care, which will require convincing proof of benefit – both in cost and outcome – that can only be established by clinical trials. The design of IGI systems should bear this requirement – that the system itself facilitates trial procedures for data gathering, quality control, consistency, reduction of intra- and inter-operator variability, and widespread availability at a cost competitive and preferably lower than current practice.

Among the specific technologies and methods that show promise for advancing IGI and need to be developed and applied to diagnostic and therapeutic procedures are demonstration projects using the “operating room of the future” where imaging modalities are integrated with all other OR technologies in a seamless fashion. Many of the opportunities have not been fully developed and evaluated, including advanced CT (or CT/PET) and MRI systems in OR environments, multimodality imaging in real time, synergies among various technologies, and better standardization of interfaces and control structures. The issues of user interface design and evaluation, reuse of surgical experience captured by the informatics infrastructure, training of new operators and augmentation of human performance (by robots, for example) are among the most important priorities in future IGI development.



**Figure 5. IMR Suite at University of Michigan.** Image courtesy of Peter Luyton, plenary presentation.

The NIH and/or NSF should actively address the challenges and facilitate the realization of the benefits associated with IGI by sponsoring research in this area. Realizing that an integrated approach is necessary where multiple technologies (real time multimodality imaging and display, surgical robotics, high performance computation and networking) are necessary for success, the establishment of a national persistent infrastructure led by centers of excellence is strongly recommended. These centers (and more than one is needed) should engage collaborators at multiple institutions to pursue a broad portfolio of technology development and applications projects. Work in IGI is intrinsically multidisciplinary, and support provided by NIH and NSF should emphasize the development of teams to pursue these objectives in a decentralized fashion with special attention to the interfaces between their components and existing technologies or components developed by others. As such, coordination of effort with standardization of communications protocols, expertise in man-machine interfaces, and special attention to the needs of clinical trials that will test and evaluate the technology in real world applications are unique aspects of IGI.

For the surgeon or the therapist to make a decision it requires that the IGI tools are inserted precisely and the coordinates of the problem areas are well defined. This means that the image taken by the instrument is appropriately reconstructed and might require some image enhancement and compression for image reconstruction, image transmission, and image display algorithms.

Imaging, information and instrument-aided decision making is at the heart of many programs that involve imaging as a means for the detection, diagnosis and treatment of a variety of diseases. We therefore need to develop research strategy and activities in support of tools and technologies for rapid and automated image acquisition, image enhancement, image reconstruction and display for non-invasive diagnosis, through biopsies, surgery and image-guided therapy.

These could include:

- Development of special image sensors and sensor systems, associated algorithm development for image reconstruction, transmission, and display.
- Special set of endoscopes and targeted probes and other non-invasive
- Surgical tools that could in-situ diagnose if the tissue was malignant or non-malignant. The MEMS, NEMS and many other devices designed and fabricated using biomaterials have a great potential in these areas.
- Molecular imaging techniques that provide imaging and in-vivo analysis of tissues under examination.
- Nanosystems on a chip that diagnose and deliver treatments.
- Modeling and simulation of novel biomaterials and systems integrated on a chip
- Development of common standards for image acquisition, biopsies, and surgical treatments using IGI.

- Methods and modules for acquisition, and management of data. This would involve quick retrieval and on the spot comparison of the IGI information with stored data.

Support is needed for research and development for image-guided interventions, including biopsies, surgery, and image-guided therapies. Research areas for image-guided interventions include technologies for detecting, monitoring, locating, navigating and treating disease and injury. Research areas should emphasize the multidisciplinary nature of the research.

Examples of research areas are:

- New technologies for tracking anatomical targets and instruments/delivery devices.
- Development of tools used with targeted probes, including tools for both better target definition and real-time applications.
- Improvements in image co-registration, image fusion and deformable models for image-guided interventions.
- Integration of optical/endoscopic with other radiologic images.
- Image segmentation tools that enhance visualization in image-guided systems.
- Improve 3D visualization software and hardware to communicate critical information used in image-guided interventions (e.g., vascular mapping, functional areas).
- Minimally invasive imaging devices or other probes, which can distinguish malignant from non-malignant tissue.
- Imaging technologies development including MRI guidance, improved use of ultrasound, biodegradable fiducials, etc.
- Real-time treatment monitoring.
- Computer-assisted, real-time control of interventional devices.
- Mathematical and computer models to aid diagnosis and treatment decision-making.
- Physiological and predictive models used in image-guided interventions.
- Development of robotics, artificial intelligence, smart algorithms, and/or expert systems for image-guided interventions.
- Development of steerable devices including catheters, endoscopes and needles.
- Microfabricated instrumentation for in vivo tissue analysis and image-guided treatments.
- Development of multi-purpose tools for image-guided interventions across medical specialties, across multiple organ systems, and across pathologies.
- Real-time therapy monitoring (e.g., tissue viability, temperature measurement).

## SPECIFIC RECOMMENDATIONS

### 1) Platforms For Operational Standards For IGI

This work group identified several issues for consideration of funding by NIH and NSF to address several important and unsolved problems in IGI. The committee unanimously agreed that better models for IGI system design and development were needed to enable and expedite the use of IGI in more institutions. Particularly effective models will accelerate the transfer of IGI methods from laboratories to clinical applications. The committee identified a critical need for improved and flexible operational interfaces, for both equipment and software. In this regard, the dissemination and replication of experimental platforms for development and evaluation of IGI technology could greatly facilitate progress. With regard to software, the user interface is often the most neglected, least optimal component of an image-guided application or system. The design of the user interface must be carefully organized and managed with frequent evaluations of user satisfaction. These design and evaluation reviews should include a detailed analysis of the application, design of the dialogue between man and machine, design of the graphic screen layout, an iterative approach to prototyping the interface and perhaps both subjective and objective evaluations of usability. Another critical issue identified is latency – the time required for transmission of data and procedural commands between system components in an IGI system. Acceptable latency was defined as the maximum allowable time for completion of aggregate procedural steps that does not interfere with the normal routine of the user (e.g., surgeon or physician). The role of a national computing grid in IGI collaboration was discussed, but no definitive paradigms or mechanisms emerged to specifically characterize the utilization of the grid in IGI. The committee agreed that such a resource, however, should continue to be considered.

The committee identified robust validation as an important issue. In this regard, there should be support for development of common and robust figures of merit, for standardized test phantoms and datasets, and for formal and secure methods of validation. A significant, often overlooked, component of validation is inadequate representation of uncertainty – that is the “*error bars*” on accuracy and/or precision. Quantitative characterization of uncertainty will help developers target systems to acceptable accuracy in performance required of IGI systems designed for specific tasks. A need was identified to provide study of and mechanisms for “scale space stitching”. Multidimensional and multispectral images of structure and function in the human body are being obtained over a large scale of size, ranging from microscopic to macroscopic. Cogent integration and interactive access to all structures and associated functions across this scale space will be important to realizing the ultimate potential of IGI systems. For example, as we learn more from the identification and dissemination of the human genome, characteristics of normal function and of specific diseases will be identified at the genetic and cellular level, each having correspondence in expression at the organ and system level. Knowing the unique relationships and connecting pathways between these “cause and effect” biologic, physiologic and anatomic elements will improve diagnosis

and guide development of effective treatments based on IGI technology.

The committee identified a number of other critical needs to bring IGI to routine clinical success. These include quality assurance of each IGI system and its particular application, and useful data exchange standards so that multiple investigators in multiple disciplines at different institutions can work on similar problems and have meaningful exchange, understanding and comparison of results. Specific standard operational procedures and modules should be defined and developed as “plug-and-play” wherein linkable modules could be selected from a comprehensive library and used to rapidly prototype different IGI systems. All such modules would interconnect faithfully and pass information back and forth in standard formats and data types. The role of open source code to expedite the development of IGI systems was discussed, but it was generally agreed that success of this software development strategy in expanding and expediting progress in IGI remains to be demonstrated, but has sufficient promise to be considered further. In this regard, it may be possible to more rapidly and efficiently develop middleware (layered software that connects foundation level system components and algorithms to top-level user interfaces and applications) to expedite the development and dissemination of IGI systems. Finally, the committee recognized at this stage of evolution of IGI systems that ongoing communication among those involved in the field is required, and that working groups should be established to meet regularly to discuss progress, compare and adjudicate approaches, and develop strategic plans and tactical mechanisms to move IGI forward into routine clinical practice.

Recommended funding areas for important and unsolved problems and issues in IGI:

- Systems Modeling
- Operational Interfaces
- Role of the Grid in IGI Collaboration
- Data Transmission/Latency
- Representation of Uncertainty
- Scale Space Stitching
- Validation
- Figures of Merit
- Test Phantoms/Data Sets
- Formal & Secure Methods for Systems Validation
- Quality Assurance
- Data Exchange Standards
- Operational Procedures
- Role of Open Source
- Dissemination & Replication of Experimental Platforms
- Middleware
- Working Group (meet regularly)

## **2) Translation Of Clinical Requirements To Technical Requirements At The Component And System Level**

Clinical requirements identified included the development of: (a) IGI methods that can be implemented across different commercial imaging platforms and organ systems, (b) validation methods and related standards early in the development phase, and (c) a means for collaboration between academia and industry to encourage the development and more timely dissemination of IGI systems as required for multi-center clinical trials. Greater transparency was suggested for clinical validation studies by academic institutions, device and drug industry, namely to facilitate an improved understanding of emerging requirements for FDA approval.

### **Recommendations regarding Components**

- Develop organ / disease specific imaging contrast agents and optimize related imaging system components to enhance specificity (MR and ultrasound in particular).
- Develop minimally invasive probes that can distinguish malignant from non-malignant tissue (e.g., optical coherence tomography). May require facilitation of technology transfer from other industries.
- Focus on low-cost / low-tech solutions for the “masses”
- Develop imaging techniques for improved resolution (i.e., at the cellular / nucleus level).
- Develop 3D visualization hardware components and software techniques to optimize the communication of relevant information to the clinician.
- Develop techniques for automatically registering and tracking deformable tissues.
- Develop new technologies for tracking anatomical targets and instruments / delivery devices.
- Explore tera-hertz imaging and other new imaging modalities.

### **Recommendations regarding Systems/Applications**

- Encourage initiatives that include strong systems engineering components.
- Develop clinical accuracy requirements on a per procedure basis and create associated “gold standards”.
- Prioritize the need for minimally invasive techniques. This will help identify the specific technology problems that must be addressed.
- Develop new methodologies and criteria for the cost-benefit analysis of IGI systems.

### **Recommendations regarding Process**

- Assist both investigators and industry to resolve conflicting Federal Agency requirements (e.g., FDA data requirements vs. HIPAA).
- Establish grant mechanisms that require collaboration between engineering and biology.
- Support education of clinical/technical liaisons (e.g., MD- PhDs).



### **3) Future Clinical Requirements and Translational Research Barriers**

The future clinical requirements group recommended a forum that would periodically meet to establish the clinical requirements for Image-Guided Interventions (IGI). The latter would include the development of the IGI protocols and methods for quality assurance and assessment of outcomes of interventions; namely to develop a broad consensus for more standardized approaches for emerging IGI methods.

#### **Barriers**

- Safety of new interventional devices: who is responsible
- Liability of new IGI procedures
- Lack of demand (ROI)
- Physician acceptance
- Cost of acquisition of rapidly evolving technologies
- Reimbursement & payment for IGI procedures (oper. cost)
- Differing workflow and project planning among disciplines
- Proof of concept (does this work, ? adverse patient selection)
- Study design issues (e.g., how specific to site, path, modality)
- Methodologies: Randomized trials vs. alternatives
- Measures of success and failure
- Generalization of trials among various degrees of expertise
- No support for limited dissemination of technologies
- For validation

#### **Recommendations**

- Rapid & automated image fusion & display
- With real-time elastic, deformable registration
- Including integration of optical/endoscopic & radiologic images
- Goal is platform-independent methods
- Broad clinical roadmap for academic/industry development:
- First, inter-modality single vendor segmentation & registration
- Next, inter-vendor single modality segmentation & registration
- Then, common display and other characteristics
- Development & integration of imaging & therapy
- Requirements/standards – an IGI “DICOM” that works
- Inter-disciplinary forums to make recommendations on clinical requirements for IGI - to include pertinent physician, scientist, vendor communities
- Collaboration among imaging & interventional device manufacturers
- Development of multi-purpose IGI tools (commonalities)
  - Cross specialty
  - Cross organ systems
  - Cross pathologies
- Funding that encourages such collaborations

- Maintain organ system & pathologic specific validation
- Standardized toolkits for module validation (phantoms)
- Support for limited dissemination of “home grown” systems
- High-tech to low-tech IGI transfer
- Development of pseudo real-time alternatives to open interventions
- Validate the anatomic sites and conditions appropriate for such IGI
- Use these early successes to build demand for the next steps
- Congruity of treatment & target border/volumes
- Reliable and repeatable positional information
- Development of adjunctive tools for targeting, monitoring, assessing IGI results
- Contrast
- Combination imaging and therapeutic agents
  - Virtual reality training systems

#### **4) Research Centers And Resources For IGI**

The breakout session on research centers proposed a number of top-down mechanisms to implement the clinical and technical recommendations. They included the support of centers of excellence, or virtual centers or resources using GRID Internet based interaction. Implicit in these recommendations was the need for active networking between the academic community, device developers and drug industry.

##### **Research Centers**

- IGI Centers (NIH, NSF)
  - Big (~10M) to Small (~1M)
  - Joint review and joint funding should be explored
  - with a single to few focuses
    - Multi Clinical/ Multi Technology partnership
    - Education
    - Clinical Test
    - Commercialization - consortium - this can be a center of its own
  - Asking all of goals - too much (?)
  - Evaluation criteria and methods
  - Cooperative agreement with simplified oversight

##### **Resources to Promote Clinical/Technology Interaction**

- Extend Training grants
- Extend/create MD/PhD Program Fellowship
- Research funds explicitly supporting clinical-technology collaboration
  - Clinical resident/fellow (100%) + attending (x%)
  - Postdoc/grad student (100%) + eng. faculty (x%)
  - Funds for eng./materials/lab
  - Support for visiting faculty
  - Collaboration initiation grants

### **Resources for Dissemination and Shared Development**

- Centralized Clearing House
  - Database
  - Hardware - Tools, Devices
  - Software
- Market studies
- Open Software development of designated areas
- Limited dissemination of experimental prototypes
  - Middleware
  - Software
  - Tools, devices
  - Includes funding for modest reengineering/replication/support
- Virtual environments -- as appropriate
- GRID type shared computing, data, etc resource for IGI
  - Develop and make available to IGI grantees
- Shared facilities for small scale validation and test
- Working groups & consortia

### **Funding Recommendations**

- Support more personnel
  - Clinician's time
  - Fellowships to exchange people among different organizations
  - Engineering support (NSF does not support "engineers")
- Research grant structure
  - Single (NIH requirement) vs. Co-Pis
  - Required co (C+T)-Pies
  - Review process - getting appropriate reviewers, study section
- Industrial partners as participants in grants
  - IGI is a small division of a large company
  - Industrial funds and matching funds
  - Explicitly fund engineering for support of integration (e.g., open interfaces)
- Support for working groups and consortia

### **5) Clinical Models - Lung and Prostate Cancer: Biopsy and Percutaneous Methods**

Two clinical models were reviewed that highlighted the need for improved IGI methods, specifically the diagnosis and treatment of lung and prostate cancer. Common requirements were identified, including: (a) further advances in molecular, functional and hyper-spectral imaging using an array of imaging modalities or combination technologies to improve the sensitivity and specificity for disease detection, classification, and microscopic target identification, (b) improved trajectory planning that includes image guidance (IG) methods, robotics, and biopsy devices required to locate and sample the

target(s) of interest seamlessly across different resolution scales, and (c) real time feedback methods to assess the IGI method(s) employed. Recommendations confirmed that many components of IG systems are generic and the optimization of methods for targeted applications may often be disease- specific.

#### **Clinical Model: Lung IGD**

- Diagnosis/management of small nodules
- Target area of abnormality
  - Multi-modal fusion
  - Molecular markers & functional imaging
- Trajectory planning
  - Percutaneous & endo-bronchial approach
  - 3D & multi-planar visualization
  - Real-time tip-specific tracking /imaging
- Development of steerable devices
  - Catheters & endoscopes & needles
- Collaboration among imaging and device industry
- Development of Cath-based tissue specific devices (i.e., OCT)
- Development of image-guided robotics
- Risk reduction and management (PTX control)
- Real-time therapy monitoring (temp., tissue viability)
- Simultaneous vascular mapping

#### **Clinical Model: Prostate IGD**

- Improvement of target definition:
  - MR: MRSI, CED MRI
  - Ultrasound techniques: contrast agents / 3D & Doppler
  - Optical spectroscopy
  - Molecular / physiologic tumor markers
- Guidance / Planning
  - Multi-modality image fusion
  - Interactive image navigation software
- Physiologic & predictive models for bx/tx decision-making
- Real-time feedback mechanism
- Delivery systems: computer-assisted device manipulation
- Real-time treatment monitoring: Reduction of side-effect profile

### **6) Image-Guided Therapy And Radiosurgery**

#### **Barriers and Recommendations**

- Molecular Imaging
  - Tissue and organ specific probes / contrast
  - Microfabricated instrumentation for in vivo analysis and tx
- Mechanisms for collecting clinical data are needed.
  - Potential support for a distributed database with appropriate security

- Mechanism for quick Phase 1 clinical trials of IG procedures (NIBIB?)
- Mechanisms for Equipment funding, Technology development  
(tune existing, develop new mechanisms)  
contrast DOD vs. NIH experience
- Intellectual property / conflict of interest difficulties – can agencies help to resolve these? Some universities are very good at this, some very inept. In Europe, government facilitates IP development
- Difficulty in getting relevant information (images, coordinates, etc) out of commercial systems
- Technology needed
  - Disposable MRI guidance
  - Deformable registration – full organ system modeling
  - Pre-op with intra op image registration
  - Image to physical space registration has not been recognized on the national level. Different from image-image registration.
  - Biodegradable fiducials
  - Improved use of US
- Study section behaviors
  - Reluctance to fund technology development
  - Reluctance to fund equipment
  - Confidentiality / conflict

## **APPENDIX I: WORKSHOP PARTICIPANTS**

NCI – National Cancer Institute  
NBIB – National Institute of Biomedical Imaging and Bioengineering  
NHLBI – National Heart, Lung and Blood Institute  
FDA – Food and Drug Administration  
NSF – National Science Foundation

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## APPENDIX II. WORKSHOP AGENDA

### NIH/NSF Workshop on Image-guided Interventions September 12-13, 2002

#### Thursday, September 12

- |                |   |
|----------------|---|
| 7:30 - 8:00 AM | Continental Breakfast   |
| 8:00 - 8:20 AM | Introductions and scope of the workshop<br><i>NIH Program Staff</i> |

#### Plenary Session I: Clinical Requirements And Barriers For IGI

- |                  |   |
|------------------|---|
| 8:20 - 8:40 AM   | <b>Image-Guided Therapy Delivery Systems<br/>Future Performance Requirements for IGI</b><br><i>F. Jolesz (Harvard University)</i>   |
| 8:40 - 9:00 AM   | <b>Image Guided Neurosurgery:<br/>Clinical Requirements and barriers</b><br><i>Elizabeth Bullitt (University of North Carolina)</i> |
| 9:00 - 9:10 AM   | <b>Multimodality Image Guided Interventions</b><br><i>Robert Maciunas (Case Western University)</i>                                 |
| 9:10 - 9:25 AM   | <b>Overview of IGI: Current and future requirements</b><br><i>Michael Vannier (University of Iowa)</i>                              |
| 9:25 - 10:10 AM  | <b>General Discussion: Review current and future requirements<br/>for IGI</b><br><i>Facilitators: F. Jolesz and M. Vannier</i>      |
| 10:10 - 10:25 AM | <b>Coffee Break</b>   |

#### Plenary Session II: Integrated Systems Approaches And Validation

- |                  |  |
|------------------|--|
| 10:30 - 10:50 AM | <b>Computer Integrated Surgery and Robotics</b><br><i>Russell Taylor (Johns Hopkins University)</i>        |
| 10:50 - 11:10 AM | <b>Integrated Image Guided Diagnosis and Therapy</b><br><i>Timothy Ryken (University of Iowa)</i>          |
| 11:10 - 11:30 AM | <b>Multi Modality Integration: Barriers to commercialization</b><br><i>Peter Luyten (Phillips Medical)</i> |



11:30 - 11:50 AM	<b>System Approach to Validation and Regulatory Approval</b>
11:50 - 12:30 PM	<b>General Discussion</b> <i>Facilitators: Russell Taylor and Robert Galloway</i>
12:30 - 1.30PM	<b>Lunch</b>
<b>Plenary Session III:</b>	<b>Standards For Interfacing Components And Information Interchange: Integrated Software Systems Approaches And Validation</b>
1:30 - 1:50 PM	<b>Needs and Requirements for Integrated Software Systems in IGI</b> <i>Richard Robb (Mayo)</i>
1:50 - 2:10 PM	<b>Integration of Software Systems: Validation of Clinical Application.</b> <i>Ramin Shahidi (Stanford)</i>
2:10 - 2:30 PM	<b>Application specific and general software platforms: Open source distribution.</b> <i>William Lorensen (GE)</i>
2:30 - 3:10 PM	<b>General Discussion:</b> <i>Facilitators: Richard Robb and R. Kikinis</i>
3:10 - 3:25 PM	<b>Coffee Break</b>
<b>Breakout Sessions 1-3 (Day One)</b>	
3:25 - 5:30 PM	<b>(Sessions are Concurrent)</b>
Session 1 (Red):	<b>Platforms For Operational Standards for IGI</b>
Session 2 (Green):	<b>Translation Of Clinical Requirements to Technical Requirements at the Component and System Level</b>
Session 3 (Blue):	<b>Future Clinical Requirements and Translational Research Barriers</b>

**NIH/NSF Workshop on Image-guided Interventions  
Friday, September 13, 2002**

7:30 - 8:00 AM	<b>Continental Breakfast</b>
8:00 - 8:30 AM	<b>Presentations of recommendations from previous breakout sessions (Three 10 min reviews)</b>
8:35 - 10:00 AM	<b>Break out Sessions 4-6 (Day Two)</b>
Session 4 (Yellow):	<b>Research Centers And Resources For IGI</b>
Session 5 (Purple):	<b>Clinical Models - Lung and Prostate Cancer: Biopsy And Percutaneous Methods</b>
Session 6 (Orange):	<b>Image Guided Therapy and Radiosurgery</b>
10:00 - 10:25 AM	<b>Coffee Break</b>
10:30 - 11:00 AM	<b>Presentations of recommendations (Three 10 min reviews)</b>
11:00 - 11:45 AM	<b>Discussion</b>
11:45 - 12:00 PM	<b>Final Summary</b> <i>Michael Vannier</i>
12:00 PM	<b>End of workshop</b>
1:00 - 3:00 PM	<b>NCI/NSF/NIBIB:</b> Review Inter-agency/NIH inter-institute collaboration. What can the NIH and/or NSF do to address the challenges and facilitate the realization of the benefits associated with IGI?

## **APPENDIX III. BACKGROUND INFORMATION**

**Summary Information for the NIH/NSF Workshop on Image-guided Interventions  
Bethesda, Maryland  
September 12-13, 2002**

### **Sponsors**

National Cancer Institute, National Institute of Biomedical Imaging and Bioengineering,  
National Science Foundation

### **Purpose**

The purpose of this workshop was to ensure that NIH and NSF programs address important needs and issues associated with image-guided interventions (biopsies, surgery, and other image-guided therapies). To this end, input was sought from the academic community and other developers and users of image-guided technologies used in medicine. This meeting covered the spectrum of technological advances related to image-guided technologies. Thus, input was sought from the community regarding advances in basic imaging science and engineering as they relate to minimally invasive treatments, biopsies, and surgical procedures that improve human health.

### **Expected/Deliverable Outcomes**

1. Formulation of recommendations by the end of the workshop.
2. Publications of Workshop Results to be included in the journal Academic Radiology and National Institute of Biomedical Imaging and Bioengineering (NIBIB) website.

### **Participants**

1. Over 60 scientists from engineering, imaging sciences, clinical imaging, surgeons and physicians, commercial firms, NIH, FDA and NSF staff.
2. Representatives from 22 universities, 7 commercial firms and 3 federal agencies.

### **Charge to Participants**

The NIH and NSF sought specific recommendations from the community regarding advances needed in image-guided (IG) procedures, as well as recommendations regarding basic imaging science, engineering and medicine as they relate to IG therapies, minimally invasive treatments, IG biopsies, and IG surgical procedures. Questions identified were intended to drive the development of new technology in areas related to image-guided interventions.

## **Background Materials Supplied to Participants**

Image-guided (IG) technologies are rapidly advancing along parallel paths namely, IG biopsy, IG Therapy and IG surgery as required for screening, diagnosis and treatment of different diseases. IG technologies are very complex and multi faceted as they include:

- (a) Cutting edge imaging methods for image guidance, including anatomical, functional and recently molecular imaging methods. Imaging methods may include external tomographic approaches and/or localized imaging probes or other image-guided sensors. Also included are computer software and other components that are all part of the 'integrated IG system'.
- (b) Physical IG biopsy methods where there is a critical need to improve sampling techniques for verification of the disease status of an organ system or lesion (for example, to permit correlation of molecular signatures using tissue array analysis with in vivo molecular or other imaging/spectroscopy signatures).
- (c) IG imaging/spectroscopy, in vivo biopsy methods as an alternative to conventional physical biopsies (laboratory pathological/histological methods) In vivo methods might include such things as optical fiber, catheter-based systems and/or miniaturized US or MRI for localized measurements. Both endogenous contrast and or use of molecular probes could be included in these measurements.
- (d) Therapy methods that use various energy forms for localized treatment such as physical based methods that require IG (optical, RF, focused-US or cryo-therapy) or the use of systemic or locally administered drug interventions such as gene therapy.
- (e) An emerging array of surgical tools for a priori and real time intraoperative image guidance, visualization, or other intervention systems including robotic methods to improve precision of surgical tools and real-time feedback methods to verify the success of the treatment or surgery

## **Generic Scientific Issues:**

- (a) There are numerous components of existing image-guided technologies that are generic with relation to clinical applications. Some examples of the generic aspects of image-guided therapies and interventions include:
- (b) Image acquisition - Improvements in image acquisition (3D techniques, quality, resolution, accuracy, etc.) and imaging devices will inevitably lead to improved image guidance.
- (c) Image processing - Segmentation of critical structures, enhanced image processing, the application of electronic atlases, deformable models, etc. can be used to deliver important information at the point of patient care.

- (d) Optical or Electromagnetic Guidance Systems - Infra-red tracking of the 3D position of surgical instruments or electromagnetic tracking of catheters or other devices inside the body are examples. Tracking of instruments is done to relate real-world anatomy to the virtual anatomy of the image.
- (e) Clinical examples of image-guided therapies that do not include cancer biopsy/treatment include embolization of arteriovenous malformations (AVM), vertebroplasty (injection of bone cement into vertebra), laparoscopically-assisted surgery, stent placement, pedicle screw placement and many others.
- (f) There are many common elements among methods of image-guided interventions. There is a potential for promoting a more comprehensive engineering system approaches for their design, including shared modular design approaches, dissemination and implementation on similar platforms.
- (g) The development of molecular imaging will greatly impact target identification and assessment of the intervention. The premise of a well-defined target for treatment will be challenged. Thus molecular as well as functional spectroscopy imaging (CSI) will set higher performance standards for IG both in terms of hardware and software and the need for real time execution.
- (h) There is a critical need to include the next-generation of image processing and IG software methods, as well as pattern recognition methods for image data interpretation. Next-generation methods will include real time implementation.
- (i) Barriers that impede the progress for IG technologies and their dissemination include the need to develop a broad consensus for: (1) characterization of system response and system validation methods and related standards, (for example in terms of the accuracy and precision of IG software and hardware components), (2) methods and standards for assessment of tissue deformation and related hepatics, (3) visualization methods and standards including 3D displays and virtual reality, and (4) methods and standards for verification of therapy or interventional methods (i.e.; verification using feed back methods such as a measurement of the biological effectiveness of the intervention).
- (j) The performance metrics of IG methods are very different from the methods for the evaluation of diagnostic imaging systems in that there are significant constraints on overall system performance. Furthermore, there are specific requirements for real-time implementation in the therapist's, interventional radiologist's or surgeon's environment.
- (k) The clinical outcome metrics for IG interventions are very difficult to measure and the variability of IG methodology and assessment methods adds to this difficulty.

## Cancer Specific Scientific Issues

- (a) The clinical Impact of Molecular Imaging: There is an opportunity to take advantage of recent advances in functional and molecular imaging methods that may provide a means for IG systems to improve: (1) the sensitivity for identification of the spatial distribution and number of target lesion(s), (2) the detection of microscopic cancer involvement in the vicinity of the tumor bed, (3) the specificity for cancer diagnosis and characterization (benign verses malignant), (4) the prediction of response to any form of IG intervention, and (5) methods that support deterministic means for patient selection for IG therapy.
- (b) Logistical IG Issues: There are many IGI issues that may be cancer-specific including: (1) what to biopsy within the field of the imaging sensor, (2) ability to scale through different FOV's to target different lesions in near real time, (3) where to biopsy within a given lesion, since it is often not homogenous, as required for tissue array analysis, (4) feasibility for diagnosis and treatment within a given clinical protocol, that would require real-time diagnosis, (5) specific treatment selection for a given lesion, (e) ensuring all lesions are similarly treated and (6) inter- and intra-operator variability in performing IG procedures for treatment of multiple lesions as opposed to a single target site.
- (c) Suggested Targeted Applications: Improved methods for (a) IG biopsy for lung cancer classification (to include small nodule or focal opacity characterization, of less than 5 mm in size) that may require robotic methods or other advances to improve localization and sampling accuracy (modalities: CT/PET), (b) IG inter-operative biopsy methods for the determination of microscopic cancer such as from prostate, for example, using MRI/MRS, TRUS or molecular imaging methods (PET/optical probes), (c) IGB, IGT and IGS for the liver, breast, and kidney cancer, each of which pose different procedural problems.
- (d) Feedback Mechanisms: There is a need to develop methods for measuring the biological effectiveness of any form of IG intervention. Are there associated metrics for possible intermediate "IG" surrogate outcomes? For example, there may be an opportunity for real time tissue array analysis and correlation with in vivo finding for small animal cancer models.

### **General Questions**

1. Does image guidance improve therapy? If so, how is this demonstrated?
2. What are specific medical applications that can benefit from the application of IGI technologies?
3. What are the challenges and issues associated with image-guided diagnosis and therapy?
4. What specific technologies and methods show promise for advancing IGI and need to be developed and applied to diagnostic and therapeutic procedures?
5. What can the NIH and/or NSF do to address the challenges and facilitate the realization of the benefits associated with IGI

### **Specific Questions**

6. What are the barriers to developing IGI techniques?
7. How do we get IGI techniques through the regulatory agencies/
8. How do we create public/private/government initiatives to move this field forward?
9. Are there any IP issues that are unique to this field/?
10. What methodologies should be used to evaluate these techniques?
11. How do we get patients to agree to these trials? What are the consent and IRB issues?
12. What are the clinical challenges for translation research associated with image-guided diagnosis, biopsy, surgery and therapy? Page: 31  
What are the performance requirements for IGI?
13. What are the clinical requirements for improved target recognition using functional and molecular imaging?
14. What will be the impact of improved resolution and other aspects of imaging system performance (especially contrast)?

15. How will monitoring and evaluation IGI (e.g. response and outcome measures) of IGI be accomplished?
16. What are the differences in requirements for mega systems and smaller scale systems? What are the IGI requirements for integrated systems?
17. What is the multidisciplinary nature of IGI and its social/cultural effect on medical and technology areas?
18. What are the resource requirements for IGI research?
19. What are the standards for performance, translation and dissemination of critical technologies?
20. How will clinically useful IG technology be developed?
21. What are the target issues of system engineering?
22. Discuss the systems approach for software development, validation, standardization, distribution, and open source software distribution.
23. What is the potential for grid based distributed research resources?
24. How will software technology be transferred?
25. What is the potential for real time implementation platforms?
26. Does Image Guidance Improve Therapy? If so, how?