NIBIB Workshop on

DEFINING THE STATE-OF-THE-ART IN BIOMEDICAL IMAGING: Research Needs for the Future

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University of Mississippi Medical Center
Jackson, Mississippi

National Institute of Biomedical Imaging and Bioengineering
National Institutes of Health

NIBIB Workshop on Defining the State-of-the Art in Biomedical Imaging: Research Needs for the Future

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Foreword

During the past thirty years, advanced electronics, computer, and communications technologies, and advances in contrast mechanisms have enabled major progress in the diagnosis and management of disease. The results of this workshop confirm that Biomedical Imaging is entering an even more productive phase of development. Indeed, the challenge engaging the new National Institute of Biomedical Imaging and Bioengineering (NIBIB) is the plethora of opportunities enabled by the further capabilities of electronics, informatics, and materials technologies; the rapid progress of biological knowledge; and the increasing integration of "radiologic" techniques in real-time procedures for care. These factors will drive further improvements in the quality, timeliness, and cost of imaging, but they will also stress traditional professional, academic, and industrial models that have created the successes of today. The NIBIB has been created at a crucial time with a critical mission - to hold a position of leadership and consensus and to establish priorities that promote, support, and sustain Biomedical Imaging research and healthcare applications..

NIBIB has a unique focus on technology and its application over a diverse clinical base. There was a strong emphasis throughout the meeting on the need to better support careers in this field with particular emphasis placed on the needs for fellowship training and mechanisms for support of multi-disciplinary team research. In addition to the spectrum of technology and medical researchers represented at the workshop, this will perforce include the clinical researchers on whose shoulders the validation of novel techniques will rest.

As Biomedical Imaging becomes more integrated with other patient and process information, its benefits will be more clear, but the decision to develop a technological improvement will become more complex given resource constraints. The need for resolution of clinical ambiguity through focused examinations will be countered by the ability of many modern imaging systems to generate more information than can be

viewed or assimilated easily by human readers. A major role of NIBIB will then involve balancing priorities for improving sensors, processing, display, and post-processing (including fusion of images and data; comparisons with archives, atlases, and models; etc.) while sustaining the research, training, and healthcare missions. A concomitant role will be to develop methodologies for the scientific assessment of imaging systems and algorithms to ensure that they provide demonstrable and quantifiable improvements for specific tasks or biomedical research.

The workshop identified several areas of concentration for consideration as NIBIB priorities in Biomedical Imaging. In the planning meeting and in the two days of the workshop, there was a strong sense of consensus on the major elements, but also a recognition that Biomedical Imaging seems to capture, in one discipline, almost all of the currently "hot" areas of science and medical technology. (With the addition of the Bioengineering side of the NIBIB mission, there may be close to complete coverage.)

The participants in the workshop are to be commended for rising to the challenge of expressing this research agenda and reducing it to manageable form. The hosts of the meeting from the University of Mississippi Medical Center provided a gracious and highly supportive environment for the sessions. We hope that you will find this report both interesting and stimulating, will contribute to improving the research plans, and will participate in meeting the goals.

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Executive Summary

The National Institute of Biomedical Imaging and Bioengineering (NIBIB) of the National Institutes of Health (NIH) conducted a workshop on "Defining the State-of-the-Art in Biomedical Imaging: Research Needs for the Future" on March 16-18, 2003. The meeting was hosted by the University of Mississippi Medical Center (UMMC) and was held at the UMMC Conference Center in Jackson, Mississippi. The objective of the workshop was to identify future research needs appropriate for the NIBIB that can maximize the impact of biomedical imaging and related technologies on healthcare and research. The program consisted of plenary presentations aimed at providing overviews of imaging research in general, clinical needs, research needs, and multi-disciplinary approaches to research; five topical sessions which addressed important components of biomedical imaging (sources and sensors, targeted agents, data reconstruction and informatics, data evaluation and objective assessment, and emerging technologies and applications); and a closing presentation on the future of biomedical imaging research. Approximately 55 people participated in this workshop including extramural (non-NIBIB) imaging researchers and clinicians; program and administrative staff from the NIBIB; staff from other NIH research institutes; representatives of other federal agencies, and UMMC affiliates. General Chairs of the workshop were Drs. Harrison Barrett (University of Arizona) and Kirby Vosburgh (CIMIT). Workshop Coordinators were Drs. Richard Swaja (NIBIB) and David Dzielak (UMMC).

The workshop provided a comprehensive assessment of the critical components of biomedical imaging and recommendations for research needs that can enable the realization of the potential benefits of imaging on healthcare and biomedical research. Results of the workshop produced during the meeting consist of recommendations of research focus areas appropriate for the NIBIB for each of the five component areas. Subsequent to the workshop, priority focus areas based on voting by the extramural participants were determined for each of the five topical areas and overall for the meeting. The top eight overall priority recommendations (highest number of votes first) resulting from this workshop include:

1. Imaging training programs - The need for the NIBIB to support inter-disciplinary biomedical imaging research training was emphasized throughout the meeting. Participant consensus was that the maximum impact of imaging research and development can be realized if an adequate number of investigators capable of conducting cross-cutting, integrative, and collaborative research is available; if effective incentives are developed to encourage and support inter-departmental cooperation; and if basic scientists can be attracted to and retained in imaging research.

2. Stimulation of research collaborations - Considering the multi-disciplinary nature of biomedical imaging research and the regulatory aspects of related applications,

collaborations among academia, national laboratories, hospitals and clinics, federal funding and regulatory agencies, and industry need to be encouraged and supported to facilitate rapid translation of new technologies to industry and rapid deployment of advances to the patient community.

3. Improvements in existing or emerging imaging technologies – This item is especially appropriate for discovery research and where market forces are inadequate to support development of new technologies or translation of existing methods. Included with this effort is the integration of modalities and image-guided interventions.

4. Improved methods for image analysis and segmentation – This effort involves developing (1) more effective and efficient methods for image analysis and visualization and (2) image segmentation frameworks that can be quickly adapted to different applications and deployed as standards for the imaging community to use. Advances in these areas are needed to support digital anatomic imaging in all modalities which has the potential to replace all conventional film and analog imaging methods and to make possible significant improvements in healthcare applications.

5. Data integration and analysis across modalities, subjects, and scales – This item involves extraction, integration, and fusion of information from large databases of different imaging modalities, subjects, spatial and temporal scales, and laboratories. Such an integrative approach will enable derivation of more information from imaging signals and will facilitate development of unique analytic technologies and new acquisition approaches.

6. Understanding the basic science associated with biomedical imaging - Understanding the basic science associated with origin of the signal, imaging physics, and underlying chemical and biological processes is necessary for the development and application of new imaging approaches and modalities and for the development and validation of descriptive computational models and algorithms. Methods for objective scientific assessment of image quality are also needed to facilitate demonstrable progress in the development of imaging technologies.

7. Molecular-level imaging – This item involves imaging at the cellular and molecular spatial scales and applying related technologies to biomedical research or clinical use. Molecular-level imaging offers the potential for significant advances in disease diagnosis and therapy not possible only with anatomical imaging. Concomitant advances in structure-to-function (e.g., anatomic-to-biology) and function-to-structure imaging capabilities can significantly accelerate future advances in the state-of-the-art of healthcare.

8. Involvement of chemists and chemistry departments with imaging researchers – The importance of chemistry in the development of new ligands, probes, contrast agents, and delivery mechanisms was emphasized throughout the workshop. Programs that facilitate interaction of chemists and imaging researchers are especially important for the efficient development of targeted agents that improve specificity and contrast resolution.

Information resulting from this workshop will be used by the NIBIB to develop and evaluate future imaging research and research training programs. A Web site providing details of the workshop including PowerPoint files of most presentations is available at http://www.nibib.nih.gov/events/Jackson/Jackson2003.html.

Workshop Report

The National Institute of Biomedical Imaging and Bioengineering (NIBIB) of the National Institutes of Health (NIH) conducted a workshop on "Defining the State-of-the-Art in Biomedical Imaging: Research Needs for the Future" on March 16-18, 2003. The meeting was hosted by the University of Mississippi Medical Center (UMMC) and was held at the UMMC Conference Center in Jackson, Mississippi. The objective of the workshop was to identify future research needs appropriate for the NIBIB that can maximize the impact of biomedical imaging and related technologies on healthcare and research. General Chairs of the workshop were Drs. Harrison Barrett (University of Arizona) and Kirby Vosburgh (CIMIT). Workshop Coordinators were Drs. Richard Swaja (NIBIB) and David Dzielak (UMMC). Information resulting from the meeting will be used as scientific community input by the NIBIB to evaluate and develop its research programs. This report provides a summary of the workshop including background, participants, program, and results.

Background

The broad mission of the NIBIB is to develop and translate enabling technologies and to conduct and support focused and multi-disciplinary research and research training with the objectives of improving healthcare and addressing national biomedical needs and priorities. Considering the multi-disciplinary nature of imaging research and the mandated commitment of the NIBIB to the field, the Institute is in a unique position to facilitate realization of the potential healthcare benefits associated with biomedical imaging and related technologies. To be optimally effective in developing and implementing its research and research training programs, the NIBIB actively solicits input from the biomedical imaging and the bioengineering communities. In conjunction with these scientific community activities and in support of the Institute's commitment to biomedical imaging, this workshop was conducted to identify future research needs appropriate for the NIBIB that can maximize the impact of imaging and related technologies on healthcare. The UMMC was an appropriate venue for this meeting in view of the current and planned development of their imaging research programs and facilities.

Initial planning for the Workshop was conducted by a twelve-member Advisory Committee of extramural imaging researchers and clinicians who met in Jackson,

Mississippi, on October 28, 2002. Appendix A is a list of Workshop Advisory Committee members and other planning meeting participants, and Appendix B is the agenda for the October 2002 meeting. A preliminary program and a list of participant candidates (chairs, speakers, and session moderators) were developed at the October 2002 meeting, and this information provided the basis for the March 2003 workshop. The five topical areas that represent important aspects of biomedical imaging were also developed during the Advisory Committee meeting.

Participants

Approximately 55 people participated in the March 16-18, 2003, workshop including 35 extramural (non-NIBIB) imaging researchers and clinicians; 10 program and administrative staff from the NIBIB; 2 staff from other NIH research institutes; and 8 UMMC affiliates. The extramural participants represented academia, hospitals and clinics, national laboratories, other federal agencies, and technical societies. Appendix C lists the meeting participants and their contact information.

Program

The detailed program for the workshop is given in Appendix D. On the evening of March 16, an orientation dinner was held to describe the objectives, format, and logistics associated with the workshop. The opening session on the morning of March 17 consisted of welcoming remarks and a charge by NIH and NIBIB representatives, the State of Mississippi and UMMC representatives, workshop coordinators, and the general chairs. This opening session was followed by four plenary presentations aimed at providing overviews of imaging research in general, clinical needs, research needs, and multi-disciplinary approaches to research and research training.

Five 90-minute topical sessions were held during the afternoon of March 17 and the morning of March 18 to address important components of biomedical imaging that were identified during the October 28, 2002, planning meeting. Topics of these sessions included sensors and sources; targeted agents; data reconstruction, interpretation, and informatics; data evaluation and objective assessment; and emerging technologies and applications. Each topical session consisted of a lead presentation to define the topic and set the stage for the discussion, three shorter talks to focus on specific aspects of the topic, and a general discussion period to develop preliminary recommendations and results Program staff from the NIBIB were assigned to each topical session to assist the moderator with preparing a summary of results and recommendations.

A session aimed at summarizing results of the five topical sessions and developing preliminary consensus lists of recommendations was held during the afternoon of March 18. The meeting concluded with a charge to the participants regarding the future of biomedical imaging research and research training.

Details of the workshop and PowerPoint files of most presentations are available on the Internet at http://www.nibib.nih.gov/events/Jackson/Jackson2003.html.

Results

The following text presents results of the general discussions and topical sessions based on proceedings during the workshop and input from participants following the meeting. Topical session summaries include the preliminary recommendations for research focus areas developed during the meeting and the top three "priority" recommendations from each session. To obtain the priority recommendations, preliminary results from each topical session were transmitted to the extramural participants subsequent to the meeting. Participants were asked to vote for their top three choices for each of the five sessions and overall considering all discussions. The top eight overall priority recommendations are also included. Responses were received from 29 of 35 extramural participants.

General Discussion

The following items are themes that were discussed formally or informally throughout the meeting and were not specific to any one of the topical sessions:

1. **Training** - The need for the NIBIB to support inter-disciplinary biomedical imaging research training was emphasized throughout the meeting. Participant consensus was that the maximum impact of imaging research and development can be realized if an adequate number of investigators capable of conducting cross-cutting, integrative, and collaborative research is available; if effective incentives are developed to encourage and support inter-departmental cooperation; and if basic scientists can be attracted to imaging research. The following specific items were highlighted as training needs during the workshop:
    a. *Scope* - Imaging research training should encompass all aspects of imaging science including clinical applications and devices, cellular- and molecular-level research, imaging informatics (i.e., image reconstruction, segmentation, interpretation, analysis, and visualization), and objective assessment of image quality.
    b. *Molecular Imaging* - Molecular-level imaging was identified as an important future research focus area at this workshop. Training programs that encourage graduate research education and training collaborations among chemistry, radiology, and molecular biology are critical to ensure that adequately prepared investigators will be available to conduct the necessary research and development.
    c. *Collaboration* - The need to develop incentives for basic science, engineering (including bioengineering), and computer science departments to work closely with clinical departments (including radiology) in imaging research programs is also very important. One possibility to support this

effort is to use shared instrumentation grants to help build research infrastructure and facilitate recruitment of basic scientists.

d. *Resident Training* - The need to develop incentives to attract radiology residents into imaging research careers as opposed to private practice was also emphasized.

Discussion at the workshop reflected the belief that effective multi-disciplinary imaging training programs could be cornerstones for the future of the Institute and the field of biomedical imaging in general.

2. **Collaborations** - Considering the multi-disciplinary nature of biomedical imaging research and the regulatory aspects of related applications, collaborations among investigators, funding and regulatory agencies, and industry are necessary to facilitate rapid translation of technologies to industry and rapid deployment of advances to the patient community. The NIBIB should encourage and support partnerships between academia, national laboratories, hospitals and clinics, federal agencies, and industry in the implementation of its research and research training programs.

Session 1: Image Acquisition – Sensors and Sources

Medical imaging systems sense radiation reflected by, transmitted through, or emitted by the patient's body. Sensor or detector characteristics are often limiting factors with regard to gathering the information necessary for medical purposes. This session surveyed the major types of sensors used in different medical imaging modalities, discussed applicable sources of radiation, and identified areas in which improvements in sensor and source characteristics could have major benefits in healthcare and biomedical research.

The top three priority research areas (highest votes first) associated with this topic based on voting subsequent to the meeting include:

1. **Improvements in existing or emerging imaging technologies** – This item is especially appropriate for discovery support as opposed to development support by the NIBIB. It is also especially important where market forces are inadequate to support the development of new technologies or the translation of emerging advances. Specific possibilities discussed during the meeting include:
    a. *High-field magnetic resonance imaging (MRI)* – The demonstrated detection of lower concentrations of MRI contrast agents (CRs) at higher magnetic fields has implications for lowering the injected dose and for detecting targeted CRs in the concentration range of their targets. At sufficiently high magnetic fields, the potential exists for targeted MRI contract agents to perform similar to those in nuclear medicine without the radioactivity effects and without the low spatial resolution. Research

support in this area should include the purchase of high-field MR instruments.

b. *Near-infrared (NIR) imaging* - NIR methods have exhibited excellent specificity and sensitivity for a variety of imaging applications. The potential exists for substantial improvements for a relatively small investment compared to more mature technologies.
c. *Monoenergetic X*-rays – A monoenergtic x-ray beam coupled with small-angle diffraction imaging could create significant improvements in x-ray imaging and could produce new contrast mechanisms such as those based on coherent scatter. New computerized tomography (CT) reconstruction and beam hardening correction algorithms will be necessary to realize the diagnostic imaging benefits associated with a high-efficiency source of monoenergetic x-rays.
d. *Optical technologies* – Optical technologies show significant promise especially for imaging at the cellular and molecular levels. Application of approaches such as bioluminescence, mitochondrial signals, disease-specific tracers, and optical probes and contrast agents could produce substantial improvements in spatial resolution for research imaging.
e. *Nuclear medicine* – Improvements in timing, energy, and spatial resolution for nuclear-based modalities such as positron emission tomography (PET) and single-photon emission computerized tomography (SPECT) could produce significant advances in related diagnostic imaging. Improvements are also needed in algorithmic methods for correcting for system defects and for incorporating patient-specific information such as attenuation and scatter.

2. **Understanding the basic science associated with biomedical imaging** - This item involves understanding the origin of the signal, the basic physics associated with the complete imaging process, and the development of descriptive computational models and algorithms. The overall objective of this issue is to improve the understanding of the basic science underlying imaging modalities in a unified manner and to provide models for evaluating new technologies. Key to this effort is the development of figures of merit for image quality that are specific to the end use of the image.

3. **Fusion of modalities –** The integration of imaging modalities to take advantage of synergisms and complementary performance characteristics can produce significant improvements in spatial, temporal, and contract resolution for diagnostic and research applications. Examples of single modalities that exhibit possible complementary characteristics include MRI, PET, MRS (magnetic resonance spectroscopy), X-ray, NIR, and US (ultrasound).

Other recommendations for future research focus areas that were developed during this session include:

1. **Materials discovery and development** - Research aimed at developing new materials for scintillators, photodetectors, solid-state detectors, NIR fluorophores, and magnets could significantly contribute to improved performance on imaging systems.

2. **Encourage research partnerships and collaborations** – Encouraging and supporting collaborations among academia, national laboratories, federal funding and regulatory agencies, and industry was identified as an important focus area to facilitate the timely translation of novel technologies to industry and the rapid deployment of new imaging methods and instruments to the patient community.

Session 2: Image Acquisition – Targeted Agents

A class of pharmaceuticals called "targeted agents" is used to either produce or increase the contrast of biologically-significant components in the body. The ultimate aim of this topic is true imaging at the molecular level in which biological molecules are targeted for imaging purposes. This session surveyed the field of targeted agents, identified limitations of current pharmaceuticals, and suggested directions for future research.

The top three priority research focus areas identified for this session include:

1. **Stimulate the involvement of chemists and chemistry departments with imaging researchers** – The importance of chemistry in the development of new ligands, contrast agents, delivery strategies, and probes was emphasized in this session and during other discussions throughout the workshop. Programs to stimulate and support the necessary collaborations between chemists and imaging researchers are necessary to facilitate these developments.

2. **Develop targeted tracers to provide images of physical and chemical parameters as a function of time** - In addition to the development of targeted tracers, methods are needed to assess whether images provide adequate information to (l) help prevent or diagnose disease or (2) plan, guide, affect, or monitor treatment.

3. **Relate molecular imaging to disease diagnosis and treatment –** Imaging at the cellular and molecular levels could provide opportunities for detecting diseases at the earliest stages (i.e., well before clinically-observable indications or before detection by current diagnostic techniques). The development of appropriate targeted agents and detectors that would allow the use of molecular-level imaging methods for diagnostic purposes is critical to realizing the benefits of this advance.

Other recommendations and research focus areas identified during this session include:

1. **Develop combinatorial libraries for contrast agents** - Comprehensive databases containing information about the structure, manufacture, and performance of contrast agents for all modalities could be valuable resources for efficient development of new agents and application of existing agents.

2. **Encourage collaborations among academia, biotech/pharmaceutical industries, and the Food and Drug Administration (FDA) -** Such collaborations will facilitate getting new imaging agents into clinical use as quickly as possible. This item also involves working with the FDA and local human investigation committees to develop new guidelines for imaging procedures in patient care.

Session 3: Data Reconstruction, Interpretation, and Informatics

Medical imaging is inextricably linked to computer science and informatics in that large quantities of data must be stored, managed, and analyzed. The data often must be transformed by computer from their raw form (i.e., tomographic projections) to a form usable by the diagnostician (i.e., a 3-D image). After the information is in suitable form, further computer operations are necessary to assist with the diagnostic process. This session assessed the capabilities and limitations of current computer hardware and software all along the informatics chain, and identified important needs for future research and development to advance the field.

The top three priority items for this topical session include:

1. **Methods for image analysis and segmentation –** This item involves processing and analyzing the detector signal to extract information in a form useable to the clinician or investigator. To identify structures in the anatomy, view them in 3-D, etc., the structures must be segmented (labeled or outlined). With regard to segmentation, two primary needs exist – (1) focused efforts to develop segmentation frameworks that can be quickly adapted to specific applications (e.g., computer-aided diagnosis) and can be quickly deployed as standards for the imaging community to use and (2) development of downloadable segmentation evaluation frameworks complete with application-specific image data, true segmentations, evaluation metrics, and software that incorporates standard segmentation methods.

   Digital tomographic imaging of anatomy and related function has the potential to replace all conventional film and analog imaging methods even at resolutions approaching a few microns or milliseconds. This will enable effective 3-D and "real-time" imaging of such structures as very small nerves, ligaments, membranes, blood vessels, capillary beads, and working organs. Digital anatomic imaging in all modalities has the potential to make possible less invasive diagnostic tests and treatments, to permit focus on high-incidence problems (e.g., aging), to evolve into many image-guided therapies, and to inspire alternative

contrast agents that have tissue-selective properties.

2. **Reconstruction methods –** Image reconstruction methods involve 3-D, 4-D, and 5-D algorithms for special data acquisition geometries and strategies; compensation for physics aspects of the imaging process; and parameter estimation and calibration methods for high-resolution image reconstruction.

3. **Data mining of image and patient information and methods for feature extraction** - Considering the large amounts of imaging and patient data available for a wide variety of applications, methods to improve the informatics associated with accessing and analyzing this information are necessary. This item primarily involves new methods to conduct outcomes research. Efficient methods and optimization techniques for feature extraction, selection, and classification are also needed to obtain information from the image.

The following items were also discussed during this session:

1. **Methods for computer visualization –** This topic involves (1) rendering acquired image data and providing intelligent display of real-scene imagery and (2) integrating these data into specific applications (e.g., viewing just relevant information, faster rendering, patient evaluation, surgical planning and training, and image-guided interventions).

2. **Shared, high-quality databases –** Efforts related to this item will facilitate delivery of image information to the clinical workflow across institutions. In the context of this item, "high-quality" refers to rigorously confirmed truth and "databases" refers to image banks.

3. **Improved display devices –** The development of hardware and equipment that supports transmittal and display of high-resolution images (especially 3-D displays) is important with regard to clinical and molecular-level research applications.

4. **Simulation tools for image/system evaluation and validation –** This item involves the development of realistic 2-D to 4-D computer-generated phantoms, accurate projection methods, and data simulations using Monte Carlo techniques.

5. **Training programs in image reconstruction, interpretation, and informatics –** The need for training programs related to this topic was emphasized. The inter-disciplinary training required for image reconstruction and informatics will involve collaborations between statistics, mathematics, computer science, and clinical departments.

Session 4: Data Evaluation and Objective Assessment of Image Quality

Medical and research images are acquired for specific purposes or tasks, and a meaningful evaluation of image quality must consider how well the task is performed. This need has resulted in an important aspect of biomedical imaging in which tools and principles of statistical decision theory are applied to objective assessment of image quality. This effort encompasses such topics as receiver operating characteristic (ROC) analysis, model observers, and statistical modeling. This session surveyed statistical decision theory approaches to medical imaging, identified unsolved problems with related methodologies, and recommended future research needed to address the problems.

The top three priority items for this topical session include:

1. **Data integration and analysis across modalities, subjects, and scales** – Combining and correlating different observations at different spatial and time scales, across modalities, and across objectives (structure/function, molecular/systems, and micro/macro) as well as subjects and even laboratories offers considerable promise for deriving even more information from the signals. Appropriate methods to extract and integrate information from large databases containing data on imaging modalities, subjects (population diversity), and spatial and temporal scales are needed to support effective extrapolation, analysis, and evaluation of information from different sources. Experience from disciplines that routinely deal with large databases such as astronomy and geography could be useful. Such integrative approaches will not only encourage unique analytical technologies but could also promote the development of new acquisition approaches.

2. **Statistical methods for molecular and functional imaging data** – Considering the potential for imaging at the cellular- and molecular-levels to improve healthcare and research capabilities, effective statistical methods for analyzing data from molecular and functional imaging are necessary.

3. **Design of clinical trials** – This item involves the need to design imaging clinical trials that (1) are relevant, valid, reproducible, and generalizable; (2) speed the transition of novel methods and technologies to clinical testing; (3) speed the translation of test results to clinical practice; (4) consider factors appropriate for the study design such as prevalence and variation, hierarchical models, and Bayesian models; and (5) involve collaborations with other institutions and organizations. Methods to effectively and efficiently extrapolate from surrogate endpoints to health outcomes are needed to support modeling and simulation studies. Efforts should be made to train radiologists in clinical trials and other clinical research.

Other items discussed during this session include:

1. **Relate technical efficacy to diagnostic efficacy to patient management** – To facilitate technology assessment without lengthy clinical trials, methods that relate technical efficacy to diagnostic efficacy to patient management and health

outcomes are needed. Such methods will enable the use of intermediate outcomes to reduce the length of clinical trials.

2. **Human observer models** – This item involves bridging the gap between the ideal observer and the human observer. Areas that need to be addressed include visual psychophysics, anthropomorphic models, and appropriate CAD algorithms for image visualization and display.

3. **Realistic models and computational power –** For image processing, analysis, and objective assessment of image quality, realistic models and adequate computational capability are necessary. Collaborations between clinical investigators and computer scientists will be important to address this item.

4. **Shared resources** – With regard to imaging data evaluation, this item involves the interoperability of systems from different sites, shared software, and common data access and analysis platforms.

Session 5: Emerging Technologies and Applications

The most significant advances in biomedical imaging often are associated with identifying new signals that convey information about biological function or applying new technologies that allow more precise measurements of known signals. Several applications of imaging technologies show significant promise for the future in areas associated with biomedical research or healthcare. This session focused on emerging technologies and potential biomedical applications that need to be considered in the future.

The top four priority items (items 3 and 4 received the same number of votes) resulting from this session include:

1. **Molecular-level imaging –** This item involves imaging at the cellular and molecular scales and applying related technologies to biomedical research and clinical use. Realizing the potential impact from imaging at the molecular-level will require research and training collaborations between radiology and molecular biology departments. Specific areas that need to be addressed include understanding of cell function, gene expression, drug and vector development and delivery, and *in vivo* protein interactions across diseases and organ systems. Programs for developing (1) image quality assessment tools and (2) disease-specific tracers and probes targeted to molecular imaging are also necessary.

   Molecular-level imaging offers the potential for significant advances in diagnosis and therapy not possible with only anatomic imaging. Concomitant advances in structure–to-function (e.g., anatomy-to-biology) and function-to-structure imaging capabilities can significantly accelerate future advances in the state-of-the-art of healthcare.

2. **Discovery, validation, and development of image-enhancing agents and multi-modality imaging strategies** – The development of new detectors, contrast agents, single or multiple imaging modalities, and model systems for molecular-level imaging can provide more effective imaging tools for research and clinical applications. Efficient methods to validate the new systems and strategies also need to be developed. With regard to molecular-level imaging, platforms for imaging and contrast agents that seek to deploy multiple modalities for combined anatomical and functional imaging are necessary. These efforts can begin with small animal imaging and be translated to the clinic.

3. **Fusion of image scale and feature space** – The fusion of image scale and feature space is necessary to integrate imaging modalities and analyze data from different sources. This effort is aimed at seamless fusion of virtual-to-real spaces, function-to-structure, genome-to-phenome, and macro-to-micro (across spatial scales). An integrative approach will enable derivation of more information from signals from a variety of sources and will facilitate the development of unique analytical technologies and new data acquisition methods.

4. **Optical imaging** – Advances promised by the application of optical technologies to biomedical imaging will be facilitated by the development of new targeted, activatable, and amplifying contrast agents and associated novel detection mechanisms. Research and development partnerships that involve the pharmaceutical and dye industries may be very effective in the development of these targeted agents.

Other items discussed during this session include:

1. **Small animal imaging** – The development of new techniques for imaging small animals and translating the results to diagnostic applications is very important for testing and validating new imaging systems and deploying the techniques for clinical use.

2. **Image-guided interventions –** The application of imaging technologies and computer-based systems to surgical or therapeutic interventions offers significant promise with regard to new minimally- or non-invasive techniques. This item involves the development of software systems, visual display techniques, and multi-modal technologies for the imaging and interventional aspects of the procedure.

3. **Software systems to model quantitative shapes –** The need for real-time imaging and visualization is important for the clinical application of emerging technologies. Software systems are needed to model quantitative shapes, process complex data, and describe complex behavior of structures in real time.

Overall Priority Recommendations

The top two overall priority recommendations for future NIBIB focus areas based on extramural participant votes were:

1. **Imaging training programs**

2. **Stimulation of collaborations among academia, national laboratories, federal agencies, and industry**.

In addition to receiving the most extramural votes, the fact that these issues were discussed to some degree during all topical sessions and informally throughout the workshop reflects their importance to the biomedical imaging community. Both items are discussed in detail in the "General Discussion" section of this report.

The next six priority recommendations (items 7 and 8 below received the same number of votes) include:

1. **Improvements in existing or emerging imaging technologies** – This item is especially appropriate for discovery research and where market forces are inadequate to support development of new technologies or translation of existing methods. Included with this effort is integration of modalities and image-guided interventions.

2. **Improved methods for image analysis and segmentation –** This effort involves developing (1) more effective and efficient methods for image analysis and visualization and (2) image segmentation frameworks that can be quickly adapted to different applications and deployed as standards for the imaging community to use. Digital anatomic imaging in all modalities has the potential to replace all conventional film and analog imaging methods and to support significant advances in healthcare.

3. **Data integration and analysis across modalities, subjects, and scales –** This item involves extraction, integration, and fusion of information from large databases of different imaging modalities, subjects, spatial and temporal scales, and laboratories. Such an integrative approach will enable derivation of more information from the signals and will facilitate development of unique analytic technologies and new acquisition approaches.

4. **Understanding the basic science associated with biomedical imaging -** Understanding the basic science associated with origin of the signal, imaging physics, and underlying chemical and biological processes is necessary for the development, objective assessment, and optimization of new imaging approaches and modalities and for the development and validation of descriptive computational models and algorithms.

5. **Molecular-level imaging –** This item involves imaging at the cellular- and molecular spatial scales and applying related technologies to biomedical research or clinical use. Molecular-level imaging offers the potential for significant advances in disease diagnosis and therapy not possible only with anatomical imaging. Concomitant advances in structure-to-function (e.g., anatomic-to-biology) and function-to-structure imaging capabilities can significantly accelerate future advances in the state-of-the-art of healthcare.

6. **Involvement of chemists and chemistry departments with imaging researchers –** The importance of chemistry in the development of new ligands, probes, contrast agents, and delivery mechanisms was emphasized throughout the workshop. Programs that facilitate interaction of chemists and imaging researchers are important for the efficient development of agents to improve specificity and contrast resolution.

Summary

The workshop provided a comprehensive assessment of the critical components of biomedical imaging and recommendations for research needs that can enable the realization of the potential benefits of imaging on healthcare and biomedical research. Results will be used by the NIBIB to develop and evaluate future imaging research and research training programs. By their nature, workshops of this type are typically incomplete primarily because investigators consider their own research as the most deserving of support and expansion – which is expected and justified. The broad scope of imaging research represented at this meeting, the formal and informal discussions, and the "priority" voting somewhat mitigated this effect, and the workshop produced many valuable ideas and recommendations. Considering the objectives of NIBIB research programs, recommendations from this workshop may be more useful as implementing objectives rather than specific research priorities. Coalescing the ideas under overarching goals may make the results more effective for determining specific Institute research directions and opportunities. Results of this workshop reflect the perspectives of a very respected and dedicated group of participants and will provide valuable input for future NIBIB imaging research programs.

Acknowledgements

The workshop coordinators and chairs extend special thanks and recognitions of the superhuman efforts of Ms. Lorine Oberhausen of the UMMC in coordinating local arrangements and logistics and Ms. Mariaileen Sourwine of the NIBIB in the development, conduct, evaluation, and follow-up of the workshop. Their performances and contributions were critical to the success of the meeting, and the dedication and competence that they exhibited under occasional extremely stressful conditions are recognized and appreciated by the authors. Sincere thanks and recognition are extended to the UMMC staff for first class hospitality, cooperation, and coordination of meeting

logistics. A special acknowledgement is extended to Dr. Stanley Baum (Penn) who delivered a most appropriate and thoughtful closing presentation for the workshop. The efforts of Drs. Thomas Brady (MGH), Henry Wagner (JHU), Maryellen Giger (Chicago), Bruce Davis (NASA), and Ronald Price (Vanderbilt) who provided excellent leadership and focus as moderators of the topical sessions are also gratefully acknowledged. Thanks are extended the following NIBIB staff for their assistance and contributions: Mr. Stephen Green for supporting the development of the program and preparing the distribution materials; and Drs. John Haller, William Heetderks, Peter Kirchner, and Mary Pastel for serving as NIBIB representatives for the topical sessions. Finally, sincere thanks and recognition are extended to all the workshop participants for their efforts and contributions. The competence, dedication, enthusiasm, and genuine concern exhibited by the participants throughout the entire process from pre-meeting planning to post-meeting evaluation were overwhelming and encouraging. The field is in excellent hands.

Appendix A

BIOMEDICAL IMAGING ADVISORY COMMITTEE MEETING

October 28, 2002
Jackson, Mississippi

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Appendix B

BIOMEDICAL IMAGING RESEARCH ADVISORY COMMITTEE MEETING

October 28, 2002
University of Mississippi Medical Center
Jackson, Mississippi

PURPOSE

Plan for a workshop titled "Defining the State of the Art in Biomedical Imaging" scheduled for March 17-19, 2003, in Jackson, Mississippi.

AGENDA

7:00 AM – Continental Breakfast (Fairview B&B)

7:45 AM – Depart for UMMC Student Center

8:30 AM – Introductions and Charge (UMMC Student Center Board Room)
- Dr. Donna Dean – Deputy Director - NIBIB
- Dr. David Dzielak – Associate Vice Chancellor for Research - UMMC

8:45 AM – Session 1
- March 2003 workshop objectives
- Workshop format
- General areas to consider
- Specific topics to be addressed

10:00 AM – Break

10:30 AM- Session 2
- Specific topics and candidate speakers
- Emerging technologies to consider

12:00 Noon – Lunch

1:15 PM – Session 3
- Emerging technologies to consider
- Industry participation
- Federal agency participation

Training issues
Information dissemination
Conclusion and summary

2:30 PM – Adjourn Advisory Committee Meeting

3:00 PM – NIBIB and UMMC Discussion
Results of Advisory Committee Meeting
Course of action

4:00 PM – Adjourn NIBIB and UMMC Discussion

END

Appendix C

NIBIB Workshop on

DEFINING THE STATE-OF-THE-ART IN BIOMEDICAL IMAGING: RESEARCH NEEDS FOR THE FUTURE

March 16-18, 2003
University of Mississippi Medical Center
Jackson, Mississippi

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Appendix D

NIBIB Workshop on

DEFINING THE STATE-OF-THE-ART IN BIOMEDICAL IMAGING: RESEARCH NEEDS FOR THE FUTURE

March 16-18, 2003
University of Mississippi Medical Center
Jackson, Mississippi

PROGRAM

March 16 (Fairview Bed and Breakfast)

5:30 PM Reception

6:30 PM Orientation Dinner

Welcome – *A. Wallace Conerly (UMMC)*
Opening Remarks – *U. S. Representative Roger Wicker (Mississippi)*
Charge and Objectives – *Roderic I. Pettigrew (NIBIB Director)*

March 17 (UMMC Conference Facilities)

7:00 AM Continental Breakfast

8:00 AM Workshop Opening – *Roderic Pettigrew (NIBIB)*

8:05 AM Welcome – *US Senator Thad Cochran (Mississippi)*

8:15 AM Opening Remarks – *Elias Zerhouni (NIH Director)*

8:30 AM Orientation and Logistics

Workshop Coordinators – Richard Swaja (NIBIB) and David Dzielak (UMMC)
Workshop Chairs – Harrison Barrett (Arizona) and Kirby Vosburgh (CIMIT)

9:00 AM Perspectives on Biomedical Imaging Research and Applications – *William Hendee (Wisconsin*)

9:30AM Break

10:00 AM Clinical Needs for Biomedical Imaging – *Bruce Rosen (MGH)*

10:30 AM Research Needs for Biomedical Imaging – *Michael Vannier (Iowa*)

11:00 AM Multi-Disciplinary Approaches to Biomedical Imaging Research – *Philip Alderson (Columbia)*

11:30 AM Lunch

12:30 PM Session 1: Image Acquisition – Sensors and Sources

Moderator: Thomas Brady (MGH)
*Speakers: William Moses (LBNL)**
Britton Chance (Penn)
John Gore (Vanderbilt)
Gary Glover (Stanford)
NIBIB Staff Representative: Peter Kirchner

2:00 PM Break

2:30 PM Session 2: Image Acquisition - Targeted Agents

Moderator: Henry Wagner (JHU)
*Speakers: Tom Meade (Northwestern)**
Sam Gambhir (UCLA)
Dean Sherry (UT Dallas – Southwestern)
Charles Springer (BNL)
NIBIB Staff Representative: Richard Swaja

4:00 PM Break

4:30 PM Session 3: Data Reconstruction, Interpretation, and Informatics
Moderator: Maryellen Giger (Chicago)
*Speakers: Ben Tsui (JHU)**
David Channin (Northwestern)
Henry Fuchs (North Carolina)
Jay Udupa (Penn)
NIBIB Staff Representative: William Heetderks

6:00 PM Adjourn for the day

7:00 PM Dinner

March 18 (UMMC Conference Facilities)

7:00 AM Continental Breakfast

7:45 AM Agenda for the day – *Conference Coordinators and Chairs*

8:00 AM Session 4: Data Evaluation and Objective Assessment
Moderator: Bruce Davis (NASA – Stennis)
*Speakers: Bruce Hillman (UVA)**
Kyle Myers (FDA)
Art Toga (UCLA)
Alicia Toledano (Brown)
NIBIB Staff Representative: Mary Pastel

9:30 AM Break

10:00 AM Session 5: Emerging Technologies and Applications

Moderator: Ronald Price (Vanderbilt)
*Speakers: David Piwnica-Worms (Washington University)**
Ron Kikinis (BWH)
Richard Robb (Mayo Clinic)
Eva Sevick-Muraca (Texas A&M)
NIBIB Staff Representative: John Haller

11:30 AM Lunch

12:30 PM Summary and Recommendations – *Session Moderators, Conference Chairs*

1:40 PM The Future of Biomedical Imaging Research – *Stanley Baum (Penn)*

2:00 PM Adjourn Workshop

*Lead speaker

END