

Special Report: Biomedical Imaging Research Opportunities Workshop III. A Summary of Findings and Recommendations

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I. INTRODUCTION

The third Biomedical Imaging Research Opportunities Workshop (BIROW III) was held on March 11–12 in Bethesda, MA. BIROW III was sponsored by the Academy of Radiology Research, American Association of Physicists in Medicine, American Institute for Medical and Biological Engineering, Biomedical Engineering Society, and the Radiological Society of North America, and cosponsored by 19 other medical imaging societies. The purpose of BIROW III [similar to the purposes of earlier BIROW meetings held in 2003¹ and 2004²] was to identify and characterize opportunities for scientific research and engineering development in biomedical imaging. This article presents a summary of the findings and recommendations of BIROW III; a full report of BIROW III is available in the *Annals of Biomedical Engineering*.³

BIROW III focused on four areas of imaging that offer a spectrum of opportunities for scientific research and engineering development. These areas are:

- multimodality image-guided therapy;
- imaging informatics;
- imaging cell trafficking; and
- technology improvement and commercialization.

Each of the areas was addressed in a plenary session in which leaders in the field summarized the state-of-the-art science and presented a perspective of research opportunities. Each of the first three plenary sessions was followed by an audience breakout session in which participants explored research opportunities and challenges. The fourth plenary session on technology improvement and commercialization was not accompanied by a breakout session for participant discussion and is not covered in this summary report. The plenary and breakout sessions for the first three topics led to reports that were synthesized into the paper published in the *Annals of Biomedical Engineering*. The findings and recommendations described in detail in that paper are outlined in this summary report.

II. MULTIMODALITY IMAGE-GUIDED THERAPY

A. Introduction

Multimodality image-guided therapy (mIGT) denotes the acquisition and manipulation of biomedical images from multiple imaging modalities for the purpose of actively guiding medical interventions. A rapidly evolving example of mIGT is the presence of two (or more) imaging modalities in

a single hybrid imaging system that facilitates accurate spatial and temporal registration of information from multiple modalities into one set of images. Examples of hybrid mIGT systems include positron emission tomography (PET)-computed tomography (CT), PET-single-photon emission computed tomography (SPECT), magnetic resonance imaging (MRI)-PET, MRI-US (ultrasound), US-PET, CT-US, Optical-US, US-x-ray mammography, and US-x-ray fluoroscopy.

B. Validation of research opportunities

Derived in part from the National Institutes of Health (NIH) roadmap,⁴ four criteria were identified to validate research opportunities in biomedical imaging. The criteria are:

- deepen understanding of biology;
- stimulate interdisciplinary teams to move fundamental developments into the clinic;
- accelerate medical discovery; and
- improve health.

Participants agreed that mIGT satisfies all four of these validation criteria.

C. Challenges to mIGT development

Several challenges to further mIGT development were noted. They include:

- expense of mIGT technologies;
- need for multidisciplinary expertise in the development and application of mIGT;
- objective validation of clinical usefulness of mIGT;
- interpretation of tissue signatures leading to tissue characterization;
- need for surrogate measures for normal and abnormal tissues;
- uncertainties in translation from animals to humans;
- data overload in image acquisition, display, interpretation, and management; and
- insufficient understanding of how the human mind interprets information.

D. Recommendations for mIGT development

Discussion of mIGT led to identification of a number of recommendations, including:

- develop a dynamic strategic plan that guides the pursuit of promising mIGT approaches and rejects unrealistic or cost-ineffective proposals;
- design robust, accurate, and quick image registration and segmentation algorithms;
- evaluate clinical impact of mIGT initially by comparing with current standards of care and intermediate measures of efficacy;
- over the longer term, evaluate the impact of mIGT on survival and quality of life, supported in part by cost reimbursement agencies in collaboration with government, industry, and institutions;
- conduct clinical trials of mIGT using valid statistical and operations research methods;
- expand multidisciplinary training of engineers, basic and clinical scientists so that individuals in each group understand and communicate with those in other groups;
- address potential limitations in the availability of targeted imaging agents;
- improve three-dimensional position-sensing devices to permit free-hand tracking of imaging and therapy equipment in real time;
- continue to improve performance and reduce cost of mIGT systems used with small animals;
- deploy operations management, process control research, and out-of-the-box conceptualization and design approaches to address the complexity, reliability, and operator use of modern imaging systems;
- identify consensus standards for image-data exchange, classification, and validation of imaging systems, and for statistical algorithms and clinical trials;
- evolve new bioinformatics and image-processing methods to manage massive quantities of data acquired with mIGT;
- shift FDA approval criteria for a new imaging agent from safety and efficacy to risk and benefit, including the risk of not using the agent; and
- relax current regulatory constraints on therapeutic trials employing mIGT, where the systems and agents under evaluation are orders of magnitude less risky than the disease being treated.

E. Conclusions

The consensus of BIROW III participants was that mIGT:

- contributes to the understanding of fundamental biology through more accurate and precise image-based targeting and delivery of therapeutic interventions, and effective post-treatment evaluations;
- requires and stimulates the education and training of interdisciplinary teams, both in research and in clinical applications;
- accelerates medical discovery through interdisciplinary processes that span both basic and clinical science; and

- contributes to the well-being of patients through more accurate and precise interventions that are based on a higher level of understanding of biological processes intrinsic to normal and diseased tissues.

III. IMAGING INFORMATICS

A. Introduction

Medical informatics encompasses every aspect of imaging from scheduling a clinical procedure to data acquisition to interpretation to reporting to archiving to information retrieval. Image informatics is a new profession that is essential to the practice of biomedical imaging. The profession focuses on developing innovative research tools and new algorithms for harmonizing large imaging databases of interest to multiple disciplines. Imaging informaticists transcend the boundaries of organ systems and imaging modalities, and connect radiologists, other physicians, physicists, technologists, and information specialists. Imaging informaticists facilitate acquisition of “just-in-time” knowledge in support of the interpretive process in order to:

- improve the accuracy and timeliness of interpretations in a climate of escalating workloads;
- integrate imaging within the larger healthcare enterprise; and
- improve the contribution of biomedical imaging to detection, diagnosis and therapy in order to enhance patient outcomes and research efforts.

Imaging informatics is contributing in a substantial way to the transition of the radiologist from a passive purveyor of information to an active participant in the care of patients, through deployment of a variety of navigation, manipulation, communication and decision-support tools.

B. Challenges to imaging informatics

The BIROW discussion identified several challenges to the continued development of imaging informatics. These challenges include:

- indistinct character of education in imaging informatics, with few pathways of formal education;
- attention directed primarily to limited aspects of informatics such as PACS and workstations, and not to image transmission and workflow across the healthcare enterprise, barriers to information movement among institutions, and integration of informatics research and analysis into the clinical setting;
- lack of attention to improving receptivity to imaging and informatics research within workstations, reading rooms, or departments;
- limitations of image registration and segmentation algorithms;
- lack of a formal plan for developing uniform protocols to assess the quality and impact of new imaging technologies in a universal language;

- obstacles created by the unreliability of shared imaging data among and across institutions resulting from different data acquisition techniques and reconstruction algorithms employed by institutions and vendors, confinement of imaging platforms to specific vendor-developed computer codes, and inconsistencies in the imaging lexicon that make comparisons difficult;
- inadequate educational resources and training tools to bring users of new digital imaging technologies up-to-speed on the optimal design and use of the technologies; and
- disconnect between the need for research in imaging informatics and the priorities and mechanisms for NIH funding decisions.

C. Recommendations for imaging informatics

Recommendations from the BIROW III discussion are:

- create educational programs in imaging informatics;
- establish a conduit into clinical practice for software tools as plugable modules into imaging workstations;
- design tools and techniques to improve the quality of image informatics technologies;
- develop standards to facilitate interoperability of imaging technologies;
- establish training programs in the routine use of imaging informatics by healthcare professionals and in the incorporation of codified best practices into their practices; and
- embrace imaging informatics at the NIH.

D. Conclusions

Imaging informatics has the potential to enhance the Roadmap themes of the NIH⁴ by:

- creating pathways into heretofore inaccessible reservoirs of retrospective data, identifying ways that image acquisition, processing, and display can be harmonized, contributing to a unified language to describe image interpretations, and participating in efforts to develop a seamless nationwide electronic medical record;
- serving as a locus for development of biomedical research teams that span knowledge bases, disciplines, and research methods and tools; and
- raising clinical research to new levels by integrating research into the clinical environment, introducing data mining and aggregation techniques, and working to embrace knowledge across disciplines.

IV. IMAGING CELL TRAFFICKING

A. Introduction

Cell trafficking, which involves loading cells, including stem cells with a traceable label and following their fate *in*

vivo, contributes in a major way to both basic research and cell-based transplantation medicine. Cell trafficking employs magnetic, radioactive, optical, acoustic, or genetic labels in conjunction with appropriate imaging modalities such as MRI, SPECT, PET, fluorescence and other optical imaging techniques, and ultrasound. Deployment of cell-trafficking methods requires a deep understanding of biology and an interdisciplinary research approach involving biologists, chemists, engineers, and physicists. Imaging and tracking cells bridge basic and clinical research, and are becoming essential to advances in both clinical medicine and research at the cellular level, especially developmental biology and stem cell research.

B. Challenges to cell trafficking

Discussion at the BIROW III meeting uncovered several challenges for research in cell trafficking. These challenges include:

- migration of cellular therapies to nontarget sites where they may have detrimental consequences;
- determination of positive outcomes of cellular therapies that are directly attributable to the presence of cells in the affected tissues;
- development of techniques to establish that labeled cells maintain normal function *in vivo*;
- design of protocols to determine the clearance of contrast agents and other compounds from tissues;
- quantification of how well results in a culture medium translate into the clinical environment and remain effective over reasonable periods.

C. Recommendations

The consensus of the BIROW III participants is that basic and clinical research in cell trafficking can be enhanced by:

- increasing the amount and breadth of funding for cell-trafficking research, including research on imaging probes and methods for stem-cell and other cell-based therapies;
- enhancing cross-disciplinary educational opportunities in cell-based transplantation medicine, probe chemistry, and imaging methods;
- increasing the availability and reducing the cost of micro-PET, micro-CT, micro-SPECT, and animal MRI systems for research;
- designing safe multimodality probes and imaging instrumentation and protocols for cell trafficking studies;
- identifying labels that are retained in the cells, and whose impact can be evaluated in real time;
- developing high-fidelity, nongenetic labels that can track cell populations *in vivo*; and
- establishing a dialog between the scientific community and regulatory agencies focused on the requirements for cell trafficking in the clinical environment.

D. Conclusions

Substantial progress has been made in the development of effective cell-trafficking technologies and applications. An additional research commitment is now needed to transition this progress into clinical regenerative medicine. A major commitment to research funding in cell trafficking is needed to realize the vast potential of this technology.

V. FINAL COMMENTS

The topics of BIROW III were chosen to bring researchers in biomedical imaging together around multidisciplinary themes of interest to scientists, engineers, and physicians. Recommendations from the workshop serve as a guide for

researchers and for funding agencies. The meeting provided a dynamic platform for exploring new ideas, challenges and research opportunities, and added additional leverage for the next Biomedical Imaging Research Opportunities Workshop (BIROW IV).

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²C. L. Partain *et al.*, "Biomedical imaging research opportunities workshop II: report and recommendations," *Radiology* **236**, 389–403 (2005).

³W. R. Hendee and G. S. Gazelle (eds.), "Biomedical imaging research opportunities workshop III: A white paper," *Ann. Biomed. Eng.* (in press).

⁴E. Zerhouni, "Medicine. The NIH Roadmap," *Science* **302**, 63–72 (2003).