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The National Institute of Biomedical Imaging and Bioengineering: History, Status, and Potential Impact

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Abstract—This paper describes the history, current status, and objectives and potential impact of the new National Institute of Biomedical Imaging and Bioengineering (NIBIB). Three of the authors (Hendee, Chien, and Maynard) have been involved over several years in the effort to raise the identity of biomedical imaging and bioengineering at the National Institutes of Health. The fourth author (Dean) is the Acting Director of the newly formed NIBIB. These individuals have an extensive collective knowledge of the events that led to formation of the NIBIB, and are intimately involved in shaping its objectives and implementation strategy. This special report provides a historical record of activities leading to establishment of the NIBIB, and an accounting of present and potential advances in biomedical engineering and imaging that will be facilitated and enhanced by NIBIB. The National Institute of Biomedical Imaging and Bioengineering represents a "coming of age" of biomedical engineering and imaging, and offers great potential to expand the research frontiers of these disciplines to unparalleled heights. © *2002 Biomedical Engineering Society.* [DOI: 10.1114/1.1433491]

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INTRODUCTION

The National Institute of Biomedical Imaging and Bioengineering (NIBIB) was established through legislation passed by the Congress of the United States, and signed into law by President Clinton in December 2000. This event is a milestone in the effort to increase the visibility and recognition of biomedical imaging and engineering within the National Institutes of Health (NIH), with the goal of enhancing the contributions of these disciplines to the public's health and well being. The dedication of leaders in the engineering and imaging communities to achieve these goals extends back more than 25 years. Encompassed within this history are the contributions of many pivotal individuals who held leadership positions in a number of scientific and professional organizations over the last three decades of the twentieth century.

QUEST FOR A HOME FOR BIOMEDICAL IMAGING AND BIOENGINEERING AT NIH

Biomedical Imaging

In the mid-1970s, under the leadership of Herbert Abrams of Harvard and Russell Morgan of Johns Hopkins, a group was established to represent the diagnostic imaging community to Congress, the NIH, and other federal agencies. This group, called the Conjoint Committee on Diagnostic Radiology, was sponsored by the American College of Radiology, Association of University Radiologists, and Society of Chairmen of Academic Radiology Departments. The Conjoint Committee was chaired initially by James Youker of the Medical College of Wisconsin and subsequently by Charles Putman of Duke University.

Over the next two decades, the Conjoint Committee played an important role in several developments related to imaging research at the NIH. Among these developments was the transfer of imaging research from the National Institute of General Medical Sciences (NIGMS) to the National Cancer Institute (NCI). This move was accomplished in 1978 in the belief that imaging research would receive greater attention in the NCI than in the NIGMS, and with the understanding that the NCI would support noncancer as well as cancer imaging. The result

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of this move was small but steady increases in funding of imaging research over the next several years. The Conjoint Committee also led the effort to create the intramural Laboratory of Diagnostic Radiology Research (LDRR) at the NIH in 1992, and in 1994 helped organize a NIH-sponsored Conference on Developing a Long-Term Plan for Imaging Research.[7]

Over time, the need for a more permanent organization to replace the Conjoint Committee became apparent to leaders in the imaging community. In 1995, the Academy of Radiology Research (ARR) (http://www.acadrad.org/) was created to focus attention on biomedical imaging and, more specifically, to work towards establishing a new institute for imaging research at the NIH. The ARR began as an alliance of 19 scientific and professional societies (currently 25 organizational members) representing more than 40,000 radiologists and imaging scientists who reflect a broad cross section of interests in biomedical imaging. The first president of the ARR, Charles Putman, was followed by Stanley Baum of the University of Pennsylvania and C. Douglas Maynard of Wake Forest University.

As the ARR worked in 1995–96 to build support for biomedical imaging and the creation of a new institute, the NCI agreed to expand its existing Diagnostic Imaging Research Branch into a Diagnostic Imaging Program with David Bragg as interim director. Subsequently, Daniel Sullivan was named permanent director, staff and resources in support of imaging were increased, and the program was renamed the Biomedical Imaging Program (BIP). The BIP has grown steadily since its formation, but has continued to focus almost exclusively on cancer imaging. Both the success of the BIP, which demonstrated the potential of imaging research at the NIH, and its limitation to cancer reinforced the view in the imaging community that a new institute was needed at the NIH to support basic research in imaging science with broad applications to a wide range of disease processes and organ systems.[1,4,5]

Biomedical Engineering

In separate, but parallel activities, the engineering research community worked over many years to secure heightened visibility and impact for biomedical engineering within federal agencies, including the NIH. This effort initially was centered in the Alliance for Engineering in Medicine and Biology (AEMB), an organization that strove for several years to achieve financial viability before dissolving in the late 1980s. In 1991, the American Institute for Medical and Biological Engineering (AIMBE) was created, with financial assistance from The Whitaker Foundation, to continue the AEMB efforts in representing engineering societies on public policy issues of concern to biomedical engineering. AIMBE (http://aimbe.org/index.htm) is an honorary society of, currently, 650 biomedical engineers who are elected to membership, 16 scientific societies representing over 32,000 engineers and scientists, 69 academic programs in biomedical engineering, and an industrial council of related manufacturers and industries. As its major charge, AIMBE assumed responsibility for heightened visibility and impact of biomedical engineering within and beyond the NIH. AIMBE supported the efforts of individual biomedical engineers (BMEs) to engage Congress in the need for increased support for research in biomedical engineering. These efforts yielded a call from Congress for a report on the state of bioengineering research at the NIH (http://becon.nih.gov/nihreport.htm) as part of the NIH Revitalization Act of 1993 (PL 103-43). In response, an External Consultants Committee, chaired by Robert Nerem of the Georgia Institute of Technology, submitted a report in 1995 entitled ‘‘Support for Bioengineering Research’’[9] (http://becon.nih.gov/externalreport.htm). Concurrent with these developments, biomedical engineering was making great strides in merging biology, medicine, and engineering to foster tissue engineering, nanoscience and nanotechnology, functional genomics, smart biomaterials, biosensors and their applications to the prevention, diagnosis, and treatment of disease.

LEGISLATIVE ACTIONS AND NIH RESPONSES

In 1996, Congress responded to the reports described above by including an amendment to the reauthorization legislation for the NIH that directed the Secretary of Health and Human Services to prepare a report to Congress outlining specific plans and time frames for implementing the reports' recommendations. The legislation passed the Senate but was not acted upon by the House. In September 1996, at the urging of the ARR's Maynard, Representative Richard M. Burr (R-NC) first introduced legislation (H.R. 4196) to establish the National Institute of Biomedical Imaging at the NIH. The bill was introduced at the end of the Congressional session and did not advance. The bill was reintroduced in 1997 (H.R. 1715), and a companion bill (S. 990) was introduced in the Senate by Senator Lauch Faircloth (R-NC). These bills also failed to advance. Also in 1997, Senator William H. Frist (R-TN) introduced SR 1030 to create a NIH Center for Bioengineering Research. The biomedical engineering community did not support this bill because the proposed Center had no funding authority and would have been located within a specialty institute, the National Heart, Lung, and Blood Institute. As a result, the bill died in committee. In February 1997, NIH Director Harold Varmus formally established the Bioengineering Consortium (BECON) to be the focus of bioengineering issues at the NIH. BECON, chaired by NIH Deputy

Director for Extramural Research, Wendy Baldwin, was composed of senior-level representatives from each of the NIH centers and institutes, together with representatives of other federal agencies concerned with biomedical research and development.

In 1998, the imaging scientists and biomedical engineers joined forces, and at its annual meeting in March 1999, AIMBE adopted the following resolution: ‘‘AIMBE should represent its constituent societies and its fellows as a unified voice seeking to enhance the identity and support of biomedical engineering at the National Institutes of Health through pursuit of the following objectives: (1) Establishment of a free-standing Center or Institute of Biomedical Engineering with a director with authority equal to that of directors of other NIH centers and institutes; (2) Designation of grant-making authority to the Center of Institute for funds allocated in support of basic science, engineering and mathematics underlying biomedical engineering; and (3) Funding the Center or Institute entirely through new appropriations without transfer of funds from existing centers and institutes.’’

In 1999–2000, the NIH took several steps to address the concerns of the biomedical engineering and imaging communities. Ellie Ehrenfeld, Director of the NIH Center for Scientific Review, created an *ad hoc* working group, chaired by Lee Huntsman of the University of Washington, to recommend ways to make the NIH peer-review process more receptive to non-hypothesis-driven research that is essential to development of new technologies and tools in biomedical engineering and imaging[8] (http://www.csr.nih.gov/bioopp1/select.htm). The Center for Scientific Review also formed an *ad hoc* committee, chaired by Bruce Alberts of the National Academy of Sciences, to restructure the NIH peer review organization into integrated review groups more responsive to the array of research applications received by the NIH (Ref. 6) (http://www.csr.nih.gov/EVENTS/summary012000.htm). In May 2000, NIH established the Biomedical Information Science and Technology Initiatives Consortium (BISTIC), using the highly successful BECON as a model. The NIH also moved toward establishment of the NIH Office of Bioengineering, Bioimaging and Bioinformatics (OBBB, ‘‘OB-cubed’’) in the Office of the Director in response to a Congressional directive in the FY2000 NIH Appropriations Act. These actions by the NIH reflected its recognition of the growing importance of bioengineering and bioimaging research, the close relationship of these fields to other research endeavors, and the need for infrastructure reorganization at the NIH to increase its receptivity to research applications in these fields.

As a result of the AIMBE/ARR coalition, Congressman Burr, with Representative Anna Eshoo (D-CA) as the primary Democratic sponsor, reintroduced his bill (HR 1795) for the third time. This bill, however, called for establishment of a National Institute of Biomedical Imaging and Engineering at the NIH. Shortly later, majority leader Trent Lott (R-MS) introduced a companion bill (S.1110) in the Senate. Introduction of these bills was accompanied by an intense grassroots campaign orchestrated by the ARR to generate legislative support for their passage. The Burr bill was voted upon and passed by the House of Representatives in September 2000, and the Senate passed the companion bill in December. After these actions, Public Law 106-580, the National Institute of Biomedical Imaging and Bioengineering Establishment Act, was signed into law by President William J. Clinton on December 29, 2000. With this action, NIH suspended its efforts to recruit a director of the OBBB and directed attention to development of an operational plan for NIH's newest institute, the National Institute of Biomedical Imaging and Bioengineering (NIBIB).

ESTABLISHMENT OF NIBIB IS PREDICATED ON PRESENT AND POTENTIAL ADVANCES IN BIOMEDICAL IMAGING AND BIOENGINEERING

The establishment of NIBIB was initiated by Congress as a reflection of the remarkable research advances in biomedical imaging and engineering, and the potential of these disciplines to contribute in a profound way to fulfillment of the mission of the NIH. This potential can be expressed as:

- Recognition of biomedical engineering, imaging, and informatics as a matrix infrastructure for biomedical research. Biomedical research is becoming increasingly quantitative and complex as biological understanding evolves from descriptive biology, morphology, and organ physiology, to a deeper level of insight that explores biophysical, biochemical, and genetic mechanisms underlying human health and disease. In this evolution, biomedical imaging and bioengineering gain heightened importance as a knowledge substrate that can support the growing quantitative understanding of biological systems. Solidification of this matrix infrastructure through research in biomedical engineering, imaging, and informatics is essential to the continued expansion of biomedical knowledge about human health and disease at the cellular, molecular, and genetic levels.
- Identification of biomedical engineering and imaging as contributors to future research. In its pursuit of quantitative understanding of biological mechanisms, biomedical research is increasingly dependent on strategic approaches that deploy the analytical tools and techniques of biomedical engineering, imaging, and informatics. This dependence implies that the growth rate in biomedical knowledge about human health and

disease, and the continued development of new methods to prevent, diagnose, treat, and monitor diseases and disabilities, will increasingly be influenced by the ability of biomedical science and engineering to evolve the tools and techniques needed to support the growth. That is, advances in biological knowledge, and successful intervention in diseases affecting various body systems, will increasingly reflect advances in biomedical engineering and imaging.

- Transcendence of biomedical engineering and imaging across the structure of the NIH. The NIH is organized in accord with traditional ways of thinking about biomedical research, with a structure of separate institutes focused on specific diseases and organ systems. But the disciplines of biomedical engineering, imaging, and informatics are not organ or disease specific, and cannot be relegated to any one specific institute. The NIH traditionally has invested in bioengineering and bioimaging research as a source of tools and techniques to advance research in specific organ systems and diseases. Although the disciplines do serve this function, their primary need is for recognition and support as substantial contributors to advances in fundamental knowledge about biological processes.
- Diffusion of research in biomedical engineering and imaging across many institutes and federal agencies. Support for applied research in biomedical engineering and imaging is distributed across many institutes at the NIH. In addition, several other Federal agencies support research in these disciplines, including the Departments of Energy, Defense, Agriculture and Commerce, the National Aeronautics and Space Administration, National Science Foundation, the Environmental Protection Agency, and the Centers for Disease Control and Prevention. This uncoordinated dissemination of support creates duplication of effort and impedes the ability of institutes, departments, and agencies to exploit developments occurring elsewhere within the federal hierarchy. Improving the coordination of this distributed effort would improve the productivity and impact of biomedical research.
- Desirability of enhanced training opportunities and funding. Progress in biomedical engineering, imaging, and informatics ultimately depends on a steady supply of young scientists, engineers, and mathematicians who are well educated in the fundamentals and research methods of their disciplines. Sustaining this influx of bright, highly educated young persons into the disciplines requires continuous support for graduate students and postdoctoral fellows.

The bill passed by Congress to establish the NIBIB quoted several findings in support of heightened visibility for biomedical engineering and imaging at the NIH. These findings include:

- Basic research in imaging, bioengineering, computer science, informatics, and related fields is critical to improving health care, but is fundamentally different from research in molecular biology emphasized by the current institutes at the NIH. To ensure development of new techniques and technologies for the 21st century, biomedical engineering and imaging require an identity and research home at the NIH that is independent of the existing institute structure.
- Advances based on medical research promise new, more effective treatments for a wide variety of diseases. New, noninvasive imaging techniques for earlier detection and diagnosis of disease are essential to take full advantage of new treatments and to promote improvements in health care.
- Development of advanced genetic and molecular imaging techniques is necessary to continue the rapid pace of discovery in molecular biology.
- Advances in telemedicine, and teleradiology in particular, are increasingly important to the delivery of high-quality, reliable health care to rural citizens and other underserved populations. To fulfill the promise of telemedicine and related technologies, a structure is needed at the NIH to support basic research focused on the acquisition, transmission, processing, and optimal display of images.
- A number of federal departments and agencies support imaging and engineering research with potential medical applications. A central coordinating body, preferably housed at the NIH, is needed to coordinate these disparate efforts and facilitate the transfer of technologies with medical applications.
- Several breakthrough imaging technologies, including magnetic resonance imaging (MRI) and computed tomography (CT), have been developed primarily abroad, in large part because of the absence of a home at the NIH for basic research in imaging and related fields. Establishment of a central focus for imaging and bioengineering research at the NIH would promote both scientific advance and U.S. economic development.
- At a time when a political consensus exists to add significant resources to the NIH in the coming years, it is appropriate to modernize the structure of the NIH to ensure that research dollars are expended more effectively and efficiently, and that the fields of medical science that have contributed the most to the detection, diagnosis, and treatment of disease in recent years receive appropriate emphasis.
- Establishment of a National Institute of Biomedical Imaging and Bioengineering at the NIH will accelerate development of new technologies with clinical and research applications, improve coordination and efficiency at the NIH and throughout the federal government, reduce duplication and waste, lay the foundation

for a new medical information age, promote economic development, and provide a structure to train the young researchers who will make the path-breaking discoveries of the future.

STATUTORY AUTHORITIES OF NIBIB

As described in PL 106-580, the ''general purpose of the National Institute of Biomedical Imaging and Engineering is the conduct and support of research, training, the dissemination of health information, and other programs with respect to biomedical imaging, biomedical engineering, and associated technologies and modalities with biomedical applications.'' PL 106-580 contains several directives for the new NIBIB. Among these directives are:

- Research into the development of new techniques and devices.
- Related research in physics, engineering, mathematics, computer science, and other disciplines.
- Technology assessments and outcomes studies to evaluate the effectiveness of biologics, materials, processes, devices, procedures, and informatics.
- Research in screening for diseases and disorders.
- Enhancement of existing imaging and bioengineering modalities, including imaging, biomaterials, and informatics.
- Development of target-specific agents to enhance images and to identify and delineate disease.
- Development of advanced engineering and imaging technologies and techniques for research from the molecular and genetic to the whole organ and body levels.
- Development of new techniques and devices for more effective interventional procedures (such as image-guided interventions).

The director of NIBIB is instructed to ''prepare and transmit to the Secretary (of the DHHS) and the Director of NIH a plan to initiate, expand, intensify, and coordinate activities of the Institute with respect to biomedical imaging and engineering.'' The plan shall include recommendations with respect to ''(i) the consolidation of programs of the National Institutes of Health for the express purpose of enhancing support of activities regarding basic biomedical imaging and engineering research; and (ii) the coordination of the activities of the Institute with related activities of the other agencies of the National Institutes of Health and with related activities of other Federal agencies.''

STARTING UP NEWEST NIH INSTITUTE

On January 2, 2001, Dr. Ruth Kirschstein, Acting Director of NIH and her Senior Advisor, Dr. Donna J. Dean, began the first steps to establish NIBIB as an entity within the NIH:

- Designation of a small task force of Institute Directors to assist in defining the mission of NIBIB. The task force was chaired by Steven Hyman (Director, National Institute of Mental Health) and had the following members: Stephen Katz (Director, National Institute of Arthritis, Musculoskeletal and Skin Diseases); Richard Klausner (Director, National Cancer Institute); Claude Lenfant (Director, National Heart, Lung and Blood Institute); and Lawrence Tabak (Director, National Institute of Dental and Craniofacial Research).
- Development of an implementation document for transmission to the Office of the Secretary of the Department of Health and Human Services, to give NIH the basic approval necessary to implement the statute creating NIBIB.
- Formulation of technical enabling legislation to permit transfer to NIBIB of the $1.975 million originally designated for the OBBB in FY01, since no money had been appropriated to NIBIB for FY01.
- Consultation with groups representing the biomedical imaging and bioengineering communities.
- Identification of already-funded grants and activities appropriate for transfer to the new institute.
- Formulation of a budget request for NIBIB for FY 2002.

At the same time, AIMBE and ARR formed a joint committee to assist NIH in formulating a short-term strategy for NIBIB. This committee consisted of Shu Chien, William Hendee, John Linehan, Peer Portner, and Buddy Ratner from AIMBE, and Stanley Baum, Reed Dunnick, Bruce Hillman, Douglas Maynard, and Elias Zerhouni from the ARR. Dr. Chien and Dr. Baum co-chaired the committee.

During January and February 2001, the NIH and the ARR/AIMBE joint committee engaged in several activities focused on moving the new institute forward. Interest in the new institute was widespread in the biomedical imaging and engineering communities, and several individuals raised concerns about its focus and direction. In response, articulation of the NIBIB's mission statement became the primary focus for a series of meetings of the Institute Directors' task force and the ARR/AIMBE joint committee. The groups discussed issues involved in the establishment of a new Institute at NIH, addressed areas of mutual concern, and established communications with interested research constituencies. The NIH task force developed a mission statement for the NIBIB, which was made public on March 5, 2001. A letter addressing the role of NIBIB in the overall context of the NIH, co-signed by Shu Chien and Douglas Maynard, was published in *Science* on March 2, 2001.[2] A statement from that letter articulates a key unifying principle endorsed by constituency groups and NIH senior managers: ''The NIBIB should strengthen and complement (not subtract from or substitute for) research programs in the other NIH Institutes and Centers.''

On April 26, 2001, Dr. Kirschstein designated Dr. Dean to serve as Acting Director of NIBIB. The original four staff members of NIBIB (Dr. Joan Harmon, Dr. Richard Swaja, Ms. Mollie Sourwine, and Dr. Dean) focused on a number of internal implementation steps that include:

- Developing program areas in biomedical imaging, biosensors, biomaterials, bioinformatics, biosystems and integrative biology, and nanotechnology.
- Articulating referral guidelines for assignment of grant applications to NIBIB.
- Finalizing transfer of funded grants into NIBIB.
- Establishing an identity and presence for NIBIB, including a website (www.nibib.nih.gov) and occupancy of NIBIB central offices in NIH's building 31.
- Extending outreach and communications to the potential research constituencies of NIBIB.
- Recruiting additional scientific and administrative staff to NIBIB.

At the NIH, the BECON has been a highly effective mechanism to bring NIH staff responsible for biomedical engineering and imaging activities together at monthly meetings to discuss common interests, problems, and strategies. BECON has developed major NIH grant programs (for example, bioengineering research partnerships and research grants). It also has held four important national meetings focused on specific topics in biomedical imaging and engineering (bioengineering, February 1998; biomedical imaging, June 1999; nanotechnology, June 2000; and reparative medicine, June 2001). The next BECON conference (with biosensors as a topic) is being planned for June 24–25, 2002. The stewardship of BECON is now a responsibility of NIBIB, and a strong emphasis on trans-NIH activities will continue. The help of BECON members has been invaluable in identifying grants for transfer to the NIBIB and in developing draft referral guidelines.

Under Public Law 106-580 NIH must establish an Advisory Council for Biomedical Imaging and Bioengineering to advise the NIBIB Director, and to assist in developing a strategic plan for the NIBIB. The Advisory Council will have 12 scientific members, 6 of whom will be ''scientists, engineers, physicians, and other health professionals who represent disciplines in biomedical engineering and imaging and who are not officers or employees of the United States'' and six who will be ''scientists, engineers, physicians, and other health professionals who represent other disciplines and are knowledgeable about the applications of biomedical engineering and imaging in medicine and who are not officers or employees of the United States.'' In accord with the other Institute Advisory Councils at NIH, an additional six members will represent the public. Ex officio members of the Advisory Council will include the Director of the Centers for Disease Control and Prevention, the Director of the National Science Foundation, and the Director of the National Institute of Standards and Technology (or their designees).

ARTICULATING A MISSION

NIBIB Official Mission Statement

The mission of the National Institute of Biomedical Imaging and Bioengineering is to promote fundamental discoveries, design and development, and translation and assessment of technological capabilities in biomedical imaging and bioengineering, enabled by relevant areas of information science, physics, chemistry, mathematics, materials science, and computer sciences. The Institute plans, conducts, fosters, and supports an integrated and coordinated program of research and research training that can be applied to a broad spectrum of biological processes, disorders and diseases, as well as organ systems. The Institute coordinates with the biomedical imaging and bioengineering programs of other agencies and NIH institutes to support imaging and engineering research with potential medical applications, and facilitates the transfer of such technologies to medical applications.

In support of its mission the Institute will:

- Support research and research training through existing NIH funding mechanisms, and take the lead in exploring novel approaches for funding technology development and interdisciplinary research.
- Form partnerships with NIH Institutes and Centers to translate fundamental discoveries into research and applications for specific diseases, disorders, or biological processes.
- Coordinate with other government agencies to translate fundamental or cross-cutting discoveries and developments in imaging and engineering, and related areas of information science and technology assessment, into biomedical applications.
- Encourage and support the development of relevant standards and guidelines that will enable widespread adaptability for biomedical imaging, bioengineering, and related information science and technology and computation, by taking a leadership and coordinating role for the NIH.

The mission statement represents the first step in a critical pathway to the Institute's full implementation. The principles outlined above were further elaborated in the FY02 Congressional budget justification for NIBIB. Rich opportunities for research were identified in that document as:

Nanotechnology. The creation and characterization of functional materials, devices, and systems at a scale of 1 to 100 nm (a nanometer is one billionth of a meter), as well as the exploitation of novel properties and phenomena developed at that scale for application to biomedical studies.

Biomaterials and Tissue Engineering. Research on approaches to creating new, perhaps ''smart'' or self-monitoring materials designed specifically for therapies which are cell based, chemical (drug) based, or gene based. Development of (1) efficient methods to assess acceptance of biomaterials by the human body; (2) *in vivo* and *in vitro* models that are predictive and low cost and that permit assessment of reliability and reproducibility; (3) methodology for accelerated testing, analysis, and evidence of failure; and (4) approaches for improved understanding of the biology–biomaterial interface. Research on the processing and manufacture of well-characterized materials, including biostable materials as well as bioresorbable and scaffold materials.

Implant Science. Research to create design principles and approaches; exploratory research of next-generation concepts; studies to prevent adverse events (i.e., chronic inflammation); development of tools for assessing loads and stresses on an implant in the everyday environment; rapid simulation and prototyping methods; lifetime predictive methods and rigorous analysis of technologies both at the time of design and at the time of dysfunction and failure.

Development of Imaging Devices. Research and development of generic biomedical imaging technologies before specific applications are demonstrated.

Contrast Agents. Research on the design, synthesis, calibration, and standardization of contrast agents and molecular probes that link an imaging device to the processes related to a specific disease by selectively targeting a specific region, tissue, lesion, or cell based on some novel aspect of its particular biology or some specific physical property that it has.

Image Exploitation. Development, design, and implementation of algorithms for image processing and information analysis, including advanced methodology for acquisition, storage, and display of images; research and development on image-guided procedures; and techniques for using multidimensional images to understand normal and abnormal function.

Assessment of Imaging Technology. Research on and development of methods for the evaluation and comparison of new and existing imaging technologies to establish their effectiveness, robustness, and range of applicability.

Minimally Invasive Technologies. Basic research involving the use of robotics technologies of actuation, sensing, control, programming, human/machine interface, and the design of mechanisms to determine research end points such as automated or remote diagnosis and treatment of disease.

Biosensors. Research and development of basic biosensor technology including the design, fabrication, and characterization of biocompatible sensors to be used in biomedical research and medicine.

KEY OPPORTUNITIES FOR NIBIB

With leadership from ARR and AIMBE in early 2001, research constituencies in biomedical engineering and imaging characterized several of the research directions that NIBIB could pursue. These directions will serve as useful guidance to the NIBIB Director and Advisory Council in the formulation of a research strategy for NIBIB. Some of the research directions are articulated below.

In Biomedical Engineering

The research goals for biomedical engineering that have been identified by AIMBE include:

- Use of bioengineering approaches, including bioinformatics, to study functional genomics and proteomics.
- Molecular biomechanics: nanoscience and nanotechnology.
- Molecular delivery: Automated and implanted drug delivery; controlled release; targeted delivery.
- Tissue engineering, including biomaterials and stem cell engineering.
- Systems and integrative bioengineering: Combination of experiments and mathematical modeling to quantify, characterize, analyze, and synthesize complex biological systems from molecules to the whole body, and from individuals to populations.
- Development of novel instrumentation: The next generation of laboratory, clinical, and population research methods and tools, e.g., biosensors, remote monitoring, and noninvasive therapeutic intervention.
- Development of systems to reduce medical errors and increase the cost effectiveness and safety of health care delivery.
- Development of infrastructure for research, education, and training in bioengineering: Innovative and interdisciplinary. Combination of quantitative biology with engineering principles and methods.
- Collaboration with biomedical imaging: Studies of bioengineering problems with molecular, cellular, organ, and total body imaging.
- Centers for research training.

- Training grants and research career development awards.
- Clinical trials.

In a recent article, Griffith and Grodzinsky[3] identified the following research frontiers in biomedical engineering: new therapeutic devices, new molecular diagnostic methods, cell and tissue engineering, engineering approaches to molecular genomics/proteomics, biomedical research tools, mathematical modeling of complex systems, and automated and targeted drug delivery.

One of the most exciting of the research frontiers in biomedical engineering is molecular genomics and proteomics, where engineering approaches to data acquisition at the molecular level are providing the capacity to manipulate, sequence, reconstruct, and model proteins and genes. These engineering approaches promise not only to yield deep insights into biochemical and genetic processes essential to life, but also have the potential to greatly improve the design, evaluation, and delivery of drugs and devices important to disease prevention, diagnosis, treatment, and rehabilitation. These contributions include the development of miniaturized tools that integrate mechanical, electrical, and optical systems to provide extremely rapid analytical measurements at the microscopic level. Biomedical engineering, imaging, and informatics all have major contributions to offer to the continued evolution of molecular genomics and proteomics. In addition, biomedical engineering integrates knowledge from genetic, molecular, and cellular research to elucidate structure and function at the levels of tissues, organs, and biological systems, including the human organism. These integrative approaches will contribute substantially to the understanding of physiological functions in health and disease.

In Biomedical Imaging

The research goals for imaging identified by the ARR include:

- molecular imaging;
- small animal imaging systems;
- optical imaging;
- imaging agent/contrast agent development;
- minimally invasive therapies;
- magnetic resonance microscopy;
- centers for research training;
- research infrastructure development;
- clinical trials;
- computational imaging;
- ultrafast cross-sectional imaging;
- novel imaging device development;
- diagnostic and screening clinical trial methodology;
- PACS, teleradiology, and telemedicine development;
- communications and information transfer relating to health care systems reform;
- centers for excellence in imaging research;
- partnerships with other federal agencies; and
- computer-aided diagnosis.

In a recent article, Tempany and McNeil[10] identified the following frontiers in biomedical imaging: new imaging technologies, image-guided therapy, monitoring treatment effectiveness, bioinformatics in support of imaging, molecular imaging, and imaging for disease prediction and prevention.

Arguably the most exciting of these frontiers is molecular imaging, an area rapidly gaining the attention not only of investigators, but also of equipment manufacturers in medical imaging. The growing emphasis on molecular imaging reflects a shifting perspective on human disease and disability to the molecular and genetic levels. This shift is the product of the substantial investment in research in molecular biology and genetics over the past several years, and is expected to accelerate in response to the growing knowledge base about human genetics and the mechanisms whereby genetics controls protein formation in cells. Molecular imaging is also impacted greatly by technological developments such as ever-evolving microfabrication techniques and microchip technology, robotics, bioinformatics tools for database analysis and management, computers and advances in information networking, and imaging technologies with much-improved spatial and temporal resolution, sensitivity, and specificity. But the area of greatest promise for molecular imaging is the development of new chemical compounds with heightened specificity for molecular targets. It is these compounds, used in combination with imaging techniques such as positron-emission tomography, magnetic resonance, and optical imaging, that offer the greatest potential for major advances in molecular imaging.

Optical imaging techniques such as diffuse optical tomography, reflectance diffuse tomography, phase-array detection, confocal imaging, photon counting, and near-infrared fluorescence offer exciting possibilities for imaging at the molecular level.[11] These optical methods rely on fluorescence, absorption, reflectance, and bioluminescence as the source of image contrast. At present, most of these optical imaging methods are confined to imaging small animals under experimental conditions. In the future, however, optical imaging may well become a companion to more conventional molecular imaging methods such as emission tomography and magnetic resonance for studying human health and disease.

CONCLUSION

Formation of the National Institute of Biomedical Imaging and Bioengineering provides an unprecedented opportunity for imaging scientists and biomedical engineers. It represents a ‘‘coming of age’’ of biomedical engineering and imaging as a vital and valuable enterprise that contributes substantially to the infrastructure essential to research advances in the biomedical sciences. The timing could not have been better, because today biomedical imaging and biomedical engineering are expanding rapidly from the detection, diagnosis, and treatment of diseases and disabilities at the level of tissues and organs, to the analysis of structure and function at the molecular and genetic levels. Establishment of the NIBIB demands a strategy that reflects the insightful thinking of the best research scientists and engineers in the disciplines. Development of this strategy should be the first and foremost priority of the yet-to-be-identified Director of the NIBIB and the Advisory Council established by PL 106-580. With proper planning, and a progressive research agenda, the establishment of NIBIB could in future years be recognized as one of the most pivotal events in modern NIH history.

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