DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

National Institute of Biomedical Imaging and Bioengineering

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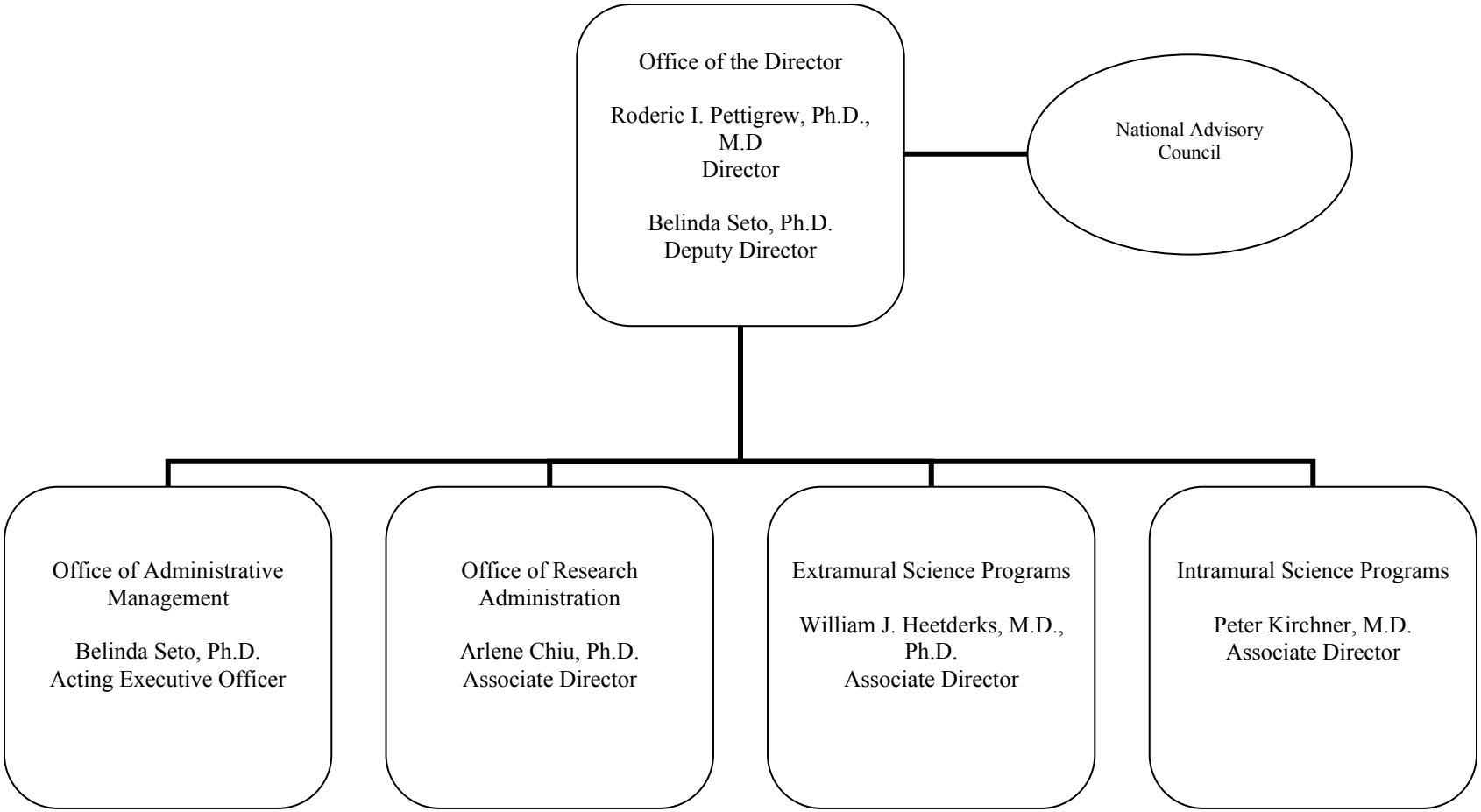

## NATIONAL INSTITUTES OF HEALTH

NATIONAL INSTITUTE OF BIOMEDICAL IMAGING AND BIOENGINEERING

For carrying out section 301 and title IV of the Public Health Service Act with respect to biomedical imaging and bioengineering research, [$300,647,000] *$299,808,000.*

[Departments of Labor, Health and Human Services and Related Agencies Appropriations Act, as enacted by the Consolidated Appropriations Act for Fiscal Year 2005]

**National Institutes of Health**
**National Institute of Biomedical Imaging and Bioengineering**

**Amounts Available for Obligation 1/**

| Source of Funding | FY 2004 Actual | FY 2005 Appropriation | FY 2006 Estimate |
|---|---|---|---|
| Appropriation | $288,900,000 | $300,647,000 | $299,808,000 |
| Enacted Rescissions | (1,771,000) | (2,438,000) | --- |
| Subtotal, Adjusted Appropriation | 287,129,000 | 298,209,000 | 299,808,000 |
| Real transfer under NIH Director's one-percent transfer authority to other ICs | (445,000) | --- | --- |
| Comparative transfer to NIBIB for Radiology Program | 1,733,000 | --- | --- |
| Comparative transfer to Buildings and Facilities | (32,000) | --- | --- |
| Comparative transfer to/from other NIH ICs for NIH Roadmap | 445,000 | --- | --- |
| Subtotal, adjusted budget authority | 288,830,000 | 298,209,000 | 299,808,000 |
| Unobligated Balance, start of year | --- | --- | --- |
| Unobligated Balance, end of year | --- | --- | --- |
| Subtotal, adjusted budget authority | 288,830,000 | 298,209,000 | 299,808,000 |
| Unobligated balance lapsing | --- | --- | --- |
| Total obligations | 288,830,000 | 298,209,000 | 299,808,000 |

1/ Excludes the following amounts for reimbursable activities carried out by this account:
FY 2004 - $518,000 FY 2005 - 3,000,000 FY 2006 - $3,000,000

## Justification

## National Institute of Biomedical Imaging and Bioengineering

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Authorizing Legislation: Section 301 of the Public Health Service Act, as amended. Reauthorizing legislation will be submitted.

Budget Authority:

| FY 2004 Actual | | FY 2005 Appropriation | | FY 2006 Estimate | | Increase or Decrease | |
|---|---|---|---|---|---|---|---|
| FTEs | BA | FTEs | BA | FTEs | BA | FTEs | BA |
| 50 | $288,830,000 | 54 | $298,209,000 | 54 | $299,808,000 | 0 | $1,599,000 |

This document provides justification for the Fiscal Year 2006 activities of the National Institute of Biomedical Imaging and Bioengineering (NIBIB), including HIV/AIDS activities. A more detailed description of NIH-wide Fiscal Year 2006 HIV/AIDS activities can be found in the NIH section entitled "Office of AIDS Research (OAR)."

## INTRODUCTION

The mission of the National Institute of Biomedical Imaging and Bioengineering (NIBIB) is to improve human health by leading the development and accelerating the application of biomedical technologies. The Institute is committed to integrating the engineering and physical sciences with the life sciences to advance basic research and medical care. Research in biomedical imaging and bioengineering is progressing rapidly and is becoming increasingly multidisciplinary. Recent technological advances have revolutionized the diagnosis and treatment of disease and provide unprecedented opportunities for furthering understanding of biological processes and for conducting powerful biological investigations. To capitalize on these opportunities, the NIBIB is supporting a robust research program in biomedical imaging and bioengineering that will focus on developing fundamental new knowledge, fostering potent new technologies, supporting promising researchers, and facilitating cross-cutting capabilities. The research conducted and supported by NIBIB is strongly synergistic with the other NIH Institutes and Centers and other Government agencies, and has the potential for direct positive medical application. Ultimately, NIBIB seeks to translate research findings from the laboratory into practical solutions that advance human health by improving quality of life and reducing the burden of disease.

**The Promise of Tissue Engineering**

Tissue engineering has been defined as the application of the principles of life sciences and engineering to develop biological substitutes for the repair and regeneration of tissue or organ function. Tissue engineering uses synthetic or naturally-derived engineered biomaterials to replace damaged or defective tissues, such as bone and muscle, or to generate scaffolds—structural supports that guide the organization, growth, and differentiation of cells to form functional tissue. Research and technology development in tissue engineering promises to revolutionize current methods of health care treatment and significantly improve the quality of life for millions of patients.

*Scientific Advances in Tissue Engineering Research*

*Biomaterials and Tissue Engineering for Degenerative Joint Disease.* Damaged cartilage in knees and joints caused by traumatic injury or the regular wear and tear of age is nearly impossible for the body to repair on its own. Unlike other tissues, cartilage lacks the blood vessels that deliver nutrients and other healing substances to damaged regions. Medical treatment usually aims to alleviate pain and discomfort without mending underlying injuries. However, a newly developed liquid polymer gel that solidifies in 30 seconds when exposed to laser light could help the body use its own resources to replenish damaged cartilage. The biomaterial, which can be injected into torn cartilage tissue, adapts to the contours and size of the cartilage tear. Once cured to a solid, the polymer acts as a scaffold for the body's own cartilage producing cells, which can eventually replace the biomaterial with new and functional cartilage.

*Replacement Parts from Engineered Tissue.* A material developed from the small intestines of pigs has shown remarkable results in supporting the body's own healing process. The material, called SIS (small intestinal submucosa), has been used to treat a wide variety of conditions from ligament reconstruction to incontinence in women. Today, SIS is most commonly used to help the body mend hard-to-heal wounds, such as second-degree burns, chronic pressure ulcers, and diabetic skin ulcers. When magnified, SIS looks like a wild matrix of loosely intertwined collagen fibers with channels and space in between the threads. When a patch of SIS is placed over an open wound, the SIS tissue acts as an anchor for migrating cells, such as fibroblasts, that help synthesize collagen, and macrophages, which fight off bacteria. The patch also supports growing capillaries as they wrap themselves around the collagen fibers like small vines. It is not so surprising that the intestinal mucosa provides such a good platform for growing cells. The cells that line the intestine are regenerated at one of the highest rates of any cell type found in the body. The same factors that are important for rapid replacement of intestinal cells are also important for repair of other tissues. Once established, these capillaries provide oxygen and nutrients to the new tissue. SIS also offers several advantages as a biomaterial. Prior to SIS, skin grafts from human cadavers were routinely used for wound closure and burn treatment. Unlike cadaver tissue, however, the porcine graft is not susceptible to human diseases and viruses, such as HIV or hepatitis. Because SIS is composed of collagen and other materials found in humans, there are no known cases of rejection unlike with some synthetic materials. Scientists are continuing to explore the biochemical mechanisms responsible for SIS's success as a wound healer.

*Future Directions in Tissue Engineering Research*
The NIBIB will continue to support ongoing research in applications for engineered tissues, including three-dimensional human tissue model systems to study questions related to developmental biology, normal physiology, and disease pathogenesis; engineered tissues for monitoring and aiding in the drug development process; and cell-based sensors expected to have broad applications in food testing, animal health, and human health care, including drug discovery and development and disease diagnosis.

**Biomedical Imaging**
Current methods for imaging humans provide predominantly anatomical information or functional information at a macroscopic level. Molecular imaging is an emerging research area aimed at extending existing or novel methods to image specific molecular pathways in the body, particularly those that are key targets in disease processes. Unlike anatomical imaging, molecular imaging displays biochemical and physiological abnormalities underlying disease, rather than the structural consequences of these abnormalities. For patients, combining imaging technologies that can correlate cellular- and molecular-level information with anatomical information will give researchers an extremely powerful tool to diagnose, track, and treat a variety of diseases.

*Scientific Advances in Biomedical Imaging Research*
*Better Brain Maps.* With technologies such as functional neuroimaging, scientists can monitor brain activity in animals or humans as they engage in a variety of activities and complex behaviors. Such studies often present a challenge, however, because subjects must be immobilized for the imaging equipment to produce a clear picture of the active brain regions. NIH-supported scientists have created a miniature implantable device called a microbolus infusion pump that releases radioactive tracer molecules into the bloodstream by remote control. When implanted in rats, the pump can be activated to release the tracers just before an animal begins an activity such as running or eating. Scientists can then detect the distribution of the tracer in the brain. The pump opens the possibility of studying functional brain activity of complex behaviors involving animal movement, which has remained largely inaccessible to other brain-mapping techniques. Future studies with the pump will involve investigating animal models of human psychiatric disorders.

*Optical Imaging.* Early research in applying optical imaging techniques to breast cancer research has shown particular promise. Because breast cancer is a molecular disease that has early-stage cellular changes, techniques that can detect these changes may offer a more precise diagnosis and more tailored treatment than do conventional techniques. High-resolution imaging offers an important new method to detect and track breast malignancies that may be difficult to distinguish on conventional mammograms. One such imaging technique is optical coherence tomography (OCT), which relies on near-infrared wavelengths of light to produce an image. OCT is similar to ultrasound, but OCT uses light rather than sound waves to create an image. Light waves can penetrate only a few millimeters into breast tissue, yet the images produced from the light waves can show cellular activity as clearly as images developed from pathology slides. Because of OCT's ability to capture images in real time, the technique may be used to rapidly scan large sections of tissue for suspicious growths; to guide, at the cellular level, surgical removal of malignancy; and to scan tumor margins for the presence of additional disease. Scientists have developed a thin fiber-optic probe that may provide a rapid and accurate alternative to core

needle biopsies for detecting breast malignancies. With core needle biopsies, a surgeon guides a hollow needle into the breast tissue and removes about a dozen tissue samples for analysis, a procedure which has a false-negative rate of up to 7 percent. The new fiber-optic probe can be threaded through the biopsy needle's hollow channel to its tip and placed in the breast directly at the tumor site. The probe then emits near-infrared light into the breast tissue. By monitoring what happens to the light as it travels through the tissue, researchers obtain structural and physiological information about the tissue that indicates whether the needle has hit its mark in the malignancy. Researchers survey multiple areas in the breast by simply rotating the needle, obtaining an immediate picture of malignant tissue that should be biopsied. The probe may work best when combined with another optical sensor for biopsy needles also under development. By detecting the different fluorescence properties of malignant and normal tissue, the sensor can differentiate benign and cancerous breast tissue with 90 percent accuracy in preliminary tests. Although these technologies will not eliminate biopsies, they can provide a more accurate way to locate malignant tissue and ultimately help doctors make an immediate diagnosis.

*Molecular Beacons.* Homing beacons can direct a search and rescue mission and permit the ready discovery of the proverbial needle in a haystack. In a similar way, molecular beacons or probes can highlight specific cells or molecular pathways within cells. Molecular imaging combines new molecular beacons or "probes" with traditional imaging tools to capture pictures of specific biological pathways and processes in the body. These molecular beacons, or imaging probes, are keyed, either structurally or functionally, to the cellular activity or disease process under study. Molecular probes offer researchers a new tool to gather information about the fundamental actions and reactions that occur in cells and molecules. By using fluorescent probes that are compatible with biological material, researchers can obtain color images of cellular and molecular activity. One form of molecular probe that has generated recent interest is semiconductor nanocrystals. These microscopic particles exhibit unique optical properties that offer major advantages over conventional fluorescent dyes for imaging biological samples. Nanocrystals that transmit light near the infrared (IR) region of the spectrum are especially useful for biological applications, because near-IR light penetrates deeply into body tissues and produces little of the background "noise" that can obscure a light signal. Unfortunately, some nanocrystals synthesized to emit near-IR light signals are toxic, unstable, and susceptible to light bleaching. By specially coating these light beacons, a group of scientists has found a way to suppress their toxicity, maintain and improve their ability to transmit light, and limit photobleaching. The new coatings make nanocrystals highly efficient at transmitting light in the near-IR region. Another research group, using molecular beacons, has developed a simple method to measure RNA synthesis in real time. This new approach will aid in the understanding of various mechanisms that control RNA and protein production in cells. Once scaled up to high-throughput formats, the measurement of RNA synthesis will be useful in identifying new drugs that inhibit RNA production by bacteria or viruses. In addition, assays might be developed to identify a specific infectious agent and then quickly determine the most appropriate antibiotic for treatment.

*X-Ray Imaging Sheds Light on Viral Molecules.* A state-of-the-art imaging technique has detailed for the first time how viral DNA binds to and activates an enzyme crucial for viral replication, paving the way for research into new drugs that would fight disease by preventing such binding. The imaging method, known as synchrotron X-ray footprinting, uses high-intensity

X-rays to characterize and display minute structural details of interactions between molecules. NIH-supported researchers applied this technique to human adenovirus, a culprit in common respiratory, gastrointestinal, and eye infections. The scientists focused the synchrotron X-rays on an adenovirus enzyme called human adenovirus proteinase (AVP), a protease enzyme that helps the adenovirus produce new infectious virus particles. DNA from the adenovirus needs to bind to AVP in order for the enzyme to become fully active. The synchrotron data revealed that the viral DNA binds to AVP over a region covering more than half the enzyme molecule, providing ample targets for drugs designed to block that binding. The data also shed light on the molecular changes produced in the protease when it pairs up with the DNA. Armed with these details, scientists have already begun searching for drugs that might treat adenovirus infections by keeping the viral DNA and AVP apart. Since AVP shares features with proteases from many other pathogens, including deadly ones such as HIV, similar imaging studies could potentially help scientists develop better drugs for a variety of serious conditions.

*Future Directions in Biomedical Imaging Research*

Biomedical imaging will continue to be an area of high priority for both basic and clinical research, especially with regard to image-guided surgery, biopsies, and minimally invasive therapies. The need to support research and development in the area of image-guided procedures has been documented at multiple workshops co-sponsored by the NIBIB, including a recent Image-Guided Interventions Workshop held in May 2004. The goal of the NIBIB program is to support research on the development of tools and technologies that can replace traditional invasive surgical procedures with minimally invasive, image-guided procedures that serve as standards of care. Critical to the advancement of image-guided interventions is the development of technologies associated with improvements in image acquisition, reconstruction and processing that enable real-time display and analysis of images as well as the development of platform technologies that allow the seamless integration of data from a wide range of clinical applications. In addition, research within the fields of molecular and optical imaging is expected to lead to the capability to do microscopic pathology examinations of some tissue in the operating room without the need for an excisional biopsy and analysis in the pathology laboratory.

The NIBIB will also continue to support research on the synthesis of clinical imaging agents and molecular probes. Research in this area is expected to lead to the development of "modular" probes that can be adapted to new targets, "smart" probes that can be activated by a specific physiological process, molecular probes that enable the simultaneous imaging or detection of multiple biological processes within the body, and imaging agents that have drug delivery capabilities.

**Nanotechnology-Based Diagnosis and Treatment**

The term nanotechnology is used to describe many types of research at the atomic, molecular, or macromolecular level—research where the characteristic dimensions are less than one-thousandth of the diameter of a human hair. Nanotechnology research provides a fundamental understanding of phenomena and materials that enable the creation and use of structures, devices, and systems that have novel properties and functions because of their extremely small size. Today, biomedical researchers are working at the micro- and nano-scales to diagnose disease and to develop new drug delivery methods, therapeutics, and pharmaceuticals.

*Scientific Advances in Nanotechnology Devices Research*

*Miniature Microscopes.* DNA sequencing promises to improve the way in which diseases such as cancer are diagnosed, monitored, and treated. The technology relies on detecting fluorescent signals created when pieces of DNA bind together on a microchip. An emerging technology—electrophoresis on microchips—has aided DNA sequencing by miniaturizing processing technologies. Miniaturization has reduced the time needed to analyze samples and decreased the sample size required for testing. To extend the power of DNA sequencing, a research team has developed a new microscope that can identify fluorescently labeled DNA sequencing fragments that have been separated by microchip technology. Using the new microscope, researchers will gain more information from a single electrophoresis test because more fluorescent dyes can be used and detected. Researchers expect to gain additional insights into the molecular profiles of many diseases as a result of these developments.

**Story of Discovery: Painless Drug Delivery**

Transdermal patches—medicated adhesive pads placed on the skin that release drugs gradually for up to a week—have been available in the U.S. for more than 20 years. The first transdermal patch, approved by the U.S. Food and Drug Administration in 1979, delivered scopolamine to treat motion sickness. Since then, more than 35 transdermal patch products have been approved. Examples include the nicotine patch that helps people quit smoking, the lidocaine patch for relieving pain, and a patch containing hormone derivatives for preventing pregnancy.

Transdermal patches have several advantages compared with other methods of drug delivery: they are painless, the drugs are not degraded in the gastrointestinal tract, and they provide a constant dosage without the need for patients to remember to take their medications. In addition, delivering drugs by way of patches can reduce the side effects of some drugs. For example, estrogen patches, unlike estrogen pills, do not cause adverse effects on the liver when used to treat menopausal symptoms. However, due to permeability constraints of the outer skin layer, the number of drugs that can be administered via transdermal patches is limited.

**Microneedle Arrays Expand Transdermal Applications**

To expand the number of compounds that can be delivered via the skin, researchers are developing novel transdermal technologies, including microneedle arrays that consist of tiny needles with diameters smaller than a strand of hair. The microneedles create micrometer-scale holes in the outer skin layer, thereby allowing passage of large molecules and other compounds that ordinarily could not traverse the skin. The microneedles are painless because they are too small to touch the nerves located deeper in the skin.

Although microneedles were first proposed in the 1970s, the technology needed to make microneedles did not become widely available until the 1990s. Using techniques developed in the microelectronics industry, NIH-supported researchers devised methods for inexpensively mass-producing microneedles from materials such as silicon, metals, and glass. The researchers also showed that microneedles can be made from polymers that will harmlessly degrade in the body, thereby preventing problems should a microneedle break off in the skin. The investigators further demonstrated that microneedles can be constructed to be solid or hollow, and both types can be made with different geometries to allow the administration of different-sized compounds, including drugs, proteins, and vaccines.

One drug-delivery technique uses solid microneedles to create micropores in the skin, and then the drug is applied over this area. NIH-funded scientists recently used this technique to administer insulin to diabetic rats. An array of solid metal microneedles was pressed into the skin, and then a glass chamber filled with insulin solution was placed over the microneedle array. Over a 4 hour time period, blood glucose levels steadily dropped by as much as 80 percent. Another drug-delivery method involves coating solid microneedles with a drug, which is then released from the needles when they are embedded in the skin.

Still another method employs hollow microneedles, which allow drug solutions to be infused through the needles using a microprocessor-controlled pump. NIH-supported scientists recently inserted hollow glass microneedles into the skin of diabetic rats to deliver insulin for 30 minutes. Over a 5 hour period after the insulin was administered, the blood glucose level dropped by as much as 70 percent. Because people would require minimal training to apply microneedles, these devices may prove useful for immunization programs in developing countries or for mass vaccination or antidote administration in bioterrorism incidents.

**Increasing Skin Permeability With Low-Frequency Ultrasound**
Another transdermal technology being developed is low-frequency sonophoresis (LFS), which uses low-frequency ultrasound to create pores in the skin that stay open for several hours. In studies with animals, LFS has delivered insulin to diabetic rabbits and the anticoagulant heparin to rats. Recently, scientists used LFS to administer local anesthetics through the skin to human volunteers. To improve the design of LFS systems, NIH-funded researchers have been studying the mechanisms by which LFS increases skin permeability. Scientists found that an ultrasound frequency of 20 kilohertz induces the formation of low-pressure air bubbles on the skin surface. These bubbles grow rapidly and then collapse violently, producing microjets and shock waves that create temporary micropores in the skin. With this understanding of the mechanism of pore formation, investigators can design LFS systems to focus the ultrasound waves so that they maximize bubble formation on the skin surface.

Researchers have also experimented with viscous substances known as porous resins to increase skin permeability during sonophoresis. When dissolved in a solution of water and alcohol, these resins release air bubbles that trigger the formation of larger bubbles when LFS is applied. Investigators discovered that adding a porous resin to the solution surrounding pig skin increased permeability to the drug mannitol during sonophoresis. Mannitol promotes urine excretion, which is useful for treating brain swelling and other conditions that involve excess fluid. The results of this study suggest that adding a porous resin to the fluid that bathes the skin might enhance drug administration by sonophoresis.

**Transporting Drugs Using Electroporation**
Still another transdermal technology under development is electroporation, the application of short, high-voltage electrical pulses to create temporary micropores in the skin. Electroporation has been used to transport several drugs through the skin in humans, including insulin, heparin, and the local anesthetic lidocaine. Studies also suggest that electroporation could be used to deliver compounds that would ameliorate skin aging, such as particular genes or Vitamin C. NIH-supported scientists have found that transdermal drug delivery via electroporation can be enhanced through the use of mild heat, alkaline solutions, and sodium dodecyl sulfate (a detergent used in various household products, including toothpaste, shampoo, and cosmetics).

Because the drug reservoir remains outside the body, transdermal drug delivery devices provide the opportunity to easily adjust the quantity and delivery rate of medications. Transdermal systems could be controlled by a miniature computer, which would allow for accurate dosing as needed by the patient. These systems might also include sensors that monitor blood levels of compounds, such as glucose in diabetics, and then adjust the release of a drug, such as insulin. These and other developments in transdermal drug delivery technologies hold promise for improving patient compliance by making drug administration effortless and painless.

*Future Directions in Nanotechnology Research*

The NIBIB will continue its efforts to support research that encourages technology development projects with the potential to facilitate and accentuate the translation of discoveries in nanoscience and nanotechnology to biomedical products for diagnosis and therapy. For example, the NIBIB will support research aimed at the design and fabrication of electronic, optical, and fluidic components for microelectromechanical systems (MEMS) that enable fundamental studies of multiple biosensing platforms. The goal will be to design integrated systems that provide "sample-to-answer" capabilities—from sample preparation to detection to data processing and output—relevant to a given clinical problem, like blood glucose sensors for diabetes.

**Biosensors for Biodefense**
Knowledge gained through NIBIB-supported advances in nanotechnology will be further leveraged for the development of devices that can be applied to other critical research areas such as biodefense. Biodefense research is aimed at understanding the organisms that might be used as agents of bioterror and how the human body responds to those organisms. NIBIB researchers are developing highly sensitive and selective biosensors for the identification of harmful viruses, bacteria and environmental health hazards.

*Scientific Advances in Biodefense Research*
*New Device May Lead to Virus Detection Systems*. A tiny scale that is sensitive enough to weigh a single virus particle may become the basis for biodefense detection systems that can instantly recognize dangerous viruses. Scientists recently fabricated a microscopic, silicon-based device that looks like a tiny diving board and vibrates naturally at a particular frequency. Researchers measure the frequency by bouncing laser light off the tip of the device, known as a cantilever. Because the cantilever is so small, about one micron wide, or approximately one-hundredth the width of a human hair, it is extremely sensitive to changes in mass, even the addition of a single virus. Researchers succeeded in placing a lone particle of the vaccinia virus on the cantilever, allowing them to weigh the virus. The addition of the virus changed the vibration frequency in a measurable way, signaling a change in weight. The virus weighed in at nine femtograms (quadrillionths of a gram). The next step in development will involve efforts to coat the cantilevers with antibodies that will allow only a single type of virus to stick to the device. This research represents a significant step toward the development of handheld systems that can detect viruses, bacteria, and other airborne microbes in real time. Such biosensors could detect bioterror agents that might be used in attacks, and may be useful for other purposes such as monitoring air quality in hospitals.

*Future Directions in Biodefense Research*
The NIBIB will continue to support innovative research in the area of biodefense. Efforts in nanotechnology and sensors will focus on the development of low-cost, miniaturized, integrated sampling detector systems for field use, including the development of systems that provide "detect-to-warn" capabilities, and that enable the rapid and accurate verification of exposure to harmful environmental agents.

## NEW INITIATIVE: NIBIB QUANTUM PROJECTS

The confluence of our appropriations combined with scientific opportunity has already begun to yield significant results for the NIBIB. For some research areas, promising preliminary results support a more integrated and focused research agenda using multidisciplinary approaches to develop innovative and marketable technologies. The goal of the unique "NIBIB Quantum Program" is to make a (quantum) advance in healthcare by funding research on a specific project(s) that will translate into new technologies and modalities for the treatment, prevention and cure of disease within a reasonable time frame, for example 10 years. In these "bench to bedside" partnerships, a team of multidisciplinary scientists will conduct collaborative research that will result in a prototype product that can be immediately translated into clinical practice. Individuals from academia, Federal laboratories, regulatory agencies, medical care organizations, and industry will work in concert to enable the timely realization of a common goal—to improve

human health by accelerating the development and application of biomedical technologies into the healthcare arena.

## NIH ROADMAP

To transform the nation's medical research capabilities and to speed the movement of research discoveries from the bench to the bedside, the NIH has laid out a series of initiatives known collectively as the NIH Roadmap for Medical Research. The NIH Roadmap provides a framework for strategic investments that NIH needs to make to optimize its entire research portfolio and builds on the tremendous progress in medical research achieved thus far. In setting forth a vision for a more efficient and productive system of medical research, the NIH Roadmap focuses on the most compelling opportunities in three main areas: New Pathways to Discovery, Research Teams of the Future, and Re-Engineering the Clinical Research Enterprise.

The tie between the NIBIB mission and the NIH Roadmap is direct—the Roadmap will facilitate the development of innovative, novel and multidisciplinary science and technology that has the potential to further advances in health care. Roadmap activities will improve health by providing researchers with tools and capabilities to make new discoveries and to quickly allow basic research discoveries to be translated into new therapies.

A key focus of the Roadmap and NIBIB is molecular libraries and imaging, a component of New Pathways to Discovery. More specifically, the NIBIB is participating in an initiative entitled *Development of High Resolution Probes for Cellular Imaging*. This initiative will facilitate the formation of collaborative research teams capable of generating novel probes for molecular and cellular imaging. The overall goal is to establish programs to create complete tool sets for the detection of single molecule events in living cells and to generate new strategies for dramatically increasing the resolution of imaging dynamic cellular processes. Although the probes initially developed under this initiative will be used for the study of basic molecular and cellular processes, the technology may eventually be adapted for clinical use. The clinical evaluation of specific diseases and how they present in individual patients will enable doctors to obtain personal profiles of molecular and genetic disease markers. Using this information, doctors can then tailor treatments to each patient.

Other areas of immediate interest to the NIBIB under the Roadmap area of New Pathways to Discovery include nanomedicine, new tools for the study of proteomics and metabolic pathways, computational biology, and bioinformatics. Under the Roadmap effort, NIH Institutes and Centers, including the NIBIB, have developed a 10 year plan to create approximately eight National Centers of Excellence in Biomedical Computing to cover key bioinformatics areas such as image processing, modeling, genomics, systems biology, computer-assisted surgery, and computer-aided diagnosis and treatment of disease**.**

The NIBIB also strongly supports the NIH Roadmap theme Research Teams of the Future. For example, in FY 2004 the NIBIB and the National Science Foundation (NSF) co-sponsored a workshop entitled "Research at the Interface of the Life and Physical Sciences: Bridging the

Sciences." The objectives of the conference were to identify opportunities, grand challenges, and issues at the interface of the life and physical sciences that could result in major advances and to develop approaches for bridging these traditionally separate fields. A core of invited extramural scientists served as primary discussants to address the conference objectives. Representatives from appropriate Federal agencies also attended and participated as agency resources. A detailed report describing the program and results of the conference will be prepared and posted on the NIBIB web site.

## INNOVATIONS IN MANAGEMENT AND ADMINISTRATION

Building on planning efforts that took place in previous fiscal years, management and administrative structures continue to be established by the NIBIB.

**Strategic Plan Development.** The NIBIB, in close collaboration with our National Advisory Council and with broad public input, is developing a Strategic Plan reflective of our unique mission and science. Through strategic planning retreats and group discussions, the NIBIB's senior management Working Group identified priorities and scientific opportunities and challenges across the programs of the Institute. The outcome is a plan that defines key goals and outlines strategies to optimize the use of our resources and to install tools and processes for smart management of the Institute in order to help us achieve our mission. The successful implementation of our Strategic Plan will enable the NIBIB to integrate the engineering, physical and life sciences to effect a maximum positive impact on the national health care agenda.

**Continued Administration of the NIH Bioengineering Consortium.** On September 19, 2001, the administration of the Bioengineering Consortium (BECON) transitioned from the Office of Extramural Research, Office of the NIH Director, to the NIBIB. Since its establishment in 1997, the Bioengineering Consortium has been coordinating bioengineering activities at the NIH. The Consortium consists of senior-level representatives from all of the NIH Institutes and Centers plus representatives of other Federal agencies concerned with biomedical research and development. In its administrative role, the NIBIB is committed to maintaining the successful coordination of trans-NIH bioengineering research, training, and related programs. For example, in FY 2004, the NIBIB, in coordination with BECON members, sponsored a symposium entitled "Biomedical Informatics for Clinical Decision Support: A Vision for the 21st Century" as well as the Fourth Annual Bioengineering Research Partnership Grantee Meeting.

**Developing an Intramural Research Program.** The NIBIB has taken several steps toward further developing an intramural research program (IRP). In September 2004, the NIBIB convened a Special Advisory Panel for Intramural Programs—a working group of the National Advisory Council for Biomedical Imaging and Bioengineering (NACBIB). The goal of the Special Advisory Panel was to advise the NIBIB on the size and scope of the Intramural Program. As such, the Advisory Panel will submit their recommendations to the NACBIB for review and discussion of further action. The NIBIB and the Center for Devices and Radiological Health (CDRH) at the Food and Drug Administration signed an interagency agreement establishing a joint Laboratory for the Assessment of Medical Imaging Systems (LAMIS). The purpose of this joint effort is to assess and optimize high-resolution, high-dimensional medical imaging systems. Two laboratory operations previously located within the NIH Clinical

Center—the PET Radiochemistry program and the Imaging Physics program—were reassigned to the NIBIB. The PET Radiochemistry program focuses on the development of new molecular probes to study normal physiology and various disease processes, including the creation of molecular indicators for monitoring biologic stress and for investigating the biochemical changes encountered in aging. Molecular tools developed in this laboratory serve to support research in the intramural programs of several NIH Institutes. The Imaging Physics program focuses on the design and construction of advanced PET/SPECT imaging systems for small laboratory animals and the application of this technology to contemporary biomedical research.

## SUMMARY

The fields of biomedical imaging and bioengineering 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. The establishment of NIBIB was predicated on present and potential advances in these exciting fields. As the Institute evolves in the coming years, our research mission will allow us to capitalize on emerging scientific areas where biomedical imaging and bioengineering approaches can be used to explore promising new directions.

*The NIH Neuroscience Blueprint*

**Overview** – The Blueprint is a framework to enhance cooperation among fourteen NIH Institutes and Centers that support research on the nervous system. Over the past decade, driven by the science, the NIH neuroscience Institutes and Centers have increasingly joined forces through initiatives and working groups focused on specific disorders. The Blueprint builds on this foundation, making collaboration a day-to-day part of how the NIH does business in neuroscience. By pooling resources and expertise, the Blueprint can take advantage of economies of scale, confront challenges too large for any single Institute, and develop research tools and infrastructure that will serve the entire neuroscience community.

**FY2005** – For fiscal year 2005, the Blueprint participants are developing an initial set of initiatives focused on tools, resources, and training that can have a quick and substantial impact because each builds on existing programs. These initiatives, with the participation of all Blueprint Institutes, include an inventory of neuroscience tools funded by the NIH and other government agencies, enhancement of training in the neurobiology of disease for basic neuroscientists, and expansion of ongoing gene expression database efforts. The NIBIB will work with NICHD and other Institutes and Centers on the potential expansion of the Pediatric Magnetic Resonance Imaging (MRI) study, which is developing an MRI database that charts development of the human brain in normal children.

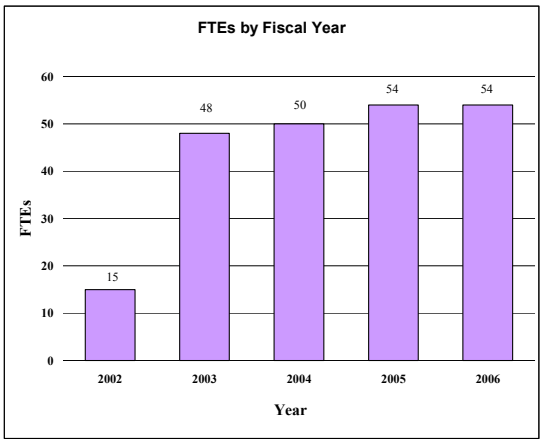
**FY2006** – Advances in the neurosciences and the emergence of powerful new technologies offer many opportunities for Blueprint activities that will enhance the effectiveness and efficiency of neuroscience research. Blueprint initiatives for fiscal year 2006 will include systematic development of genetically engineered mouse strains of critical importance to research on the nervous system and its diseases and training in critical cross cutting areas such as neuroimaging and computational biology. The NIBIB will participate in three Blueprint initiatives as they are

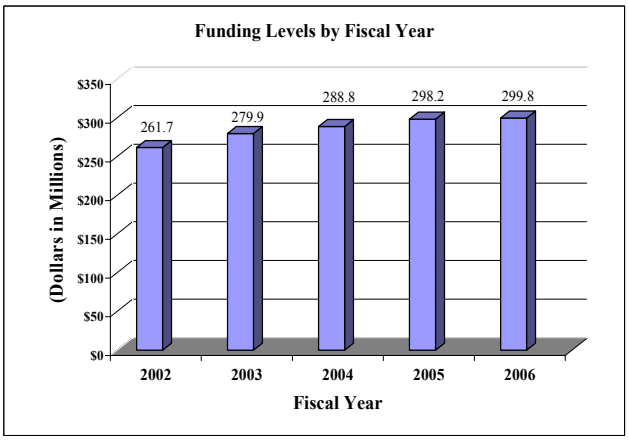
developed and implemented. These include the Neuroimaging Training Program that will develop interdisciplinary neuroimaging training programs, the Computational Neuroscience Training Program that will develop a training environment in which basic neuroscientists and computational modelers work together to develop this new interdisciplinary field, and in the neuroimaging initiatives which will support the development of tools and resources for sharing neuroimaging data and for testing new methods of analyzing neuroimaging data.

## Budget Policy

The Fiscal Year 2006 budget request for the NIBIB is $299,808,000, an increase of $1,599,000 and 0.5% percent over the FY 2005 Final Appropriation. Also included in the FY 2006 request, is NIBIB's support for the trans-NIH Roadmap initiatives, estimated at 0.89% of the FY 2006 budget request. This Roadmap funding is distributed through the mechanisms of support, consistent with the anticipated funding for the Roadmap initiatives. A full description of this trans-NIH program may be found in the NIH Overview.

A five year history of FTEs and Funding Levels for NIBIB are shown in the graphs below.




NIH's highest priority is the funding of medical research through research project grants (RPGs). Support for RPGs allows NIH to sustain the scientific momentum of investigator-initiated research while pursuing new research opportunities. The average cost of competing RPGs will be held at the FY2005 level. There will be no inflationary increases for direct, recurring costs in noncompeting continuation RPGs.

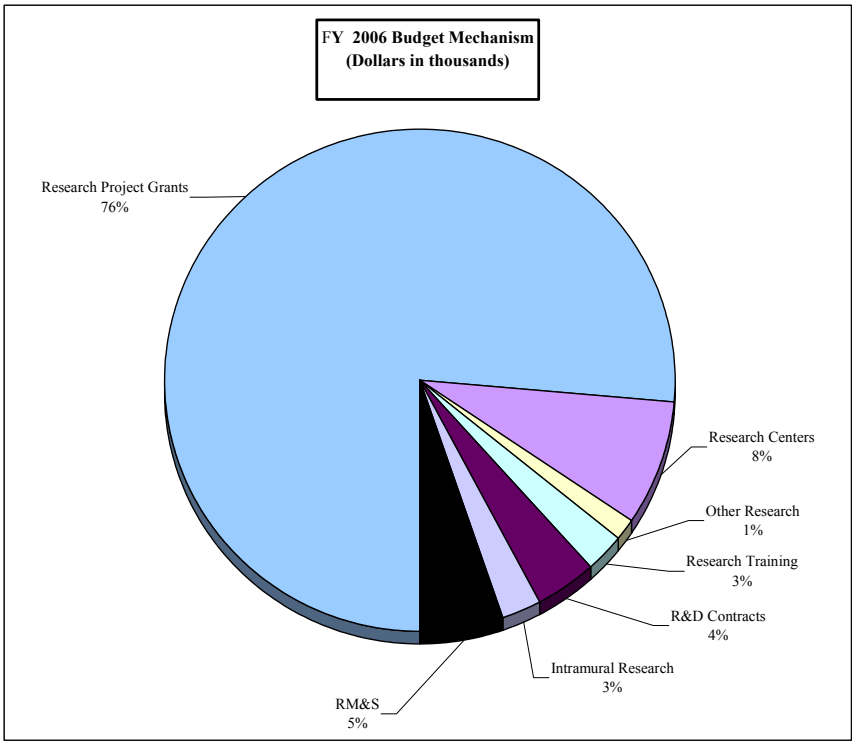
Advancement in medical research is dependent on attracting the best and the brightest to pursue careers in biomedical research. In the Fiscal Year 2006 request, stipend levels for post-doctoral recipients supported through the Ruth L. Kirschstein National Research Service Awards will increase by 4.0% for those with 1-2 years of experience, with all other stipends remaining at the FY2005 levels. NIH will also provide an increase of $500 per post-doctoral fellow, for increased health insurance costs. This increase in stipends and health benefits is financed within the FY2006 request by reducing the number of Full-Time Training Positions by –1. NIBIB will support 171 pre- and postdoctoral trainees in full-time training positions.

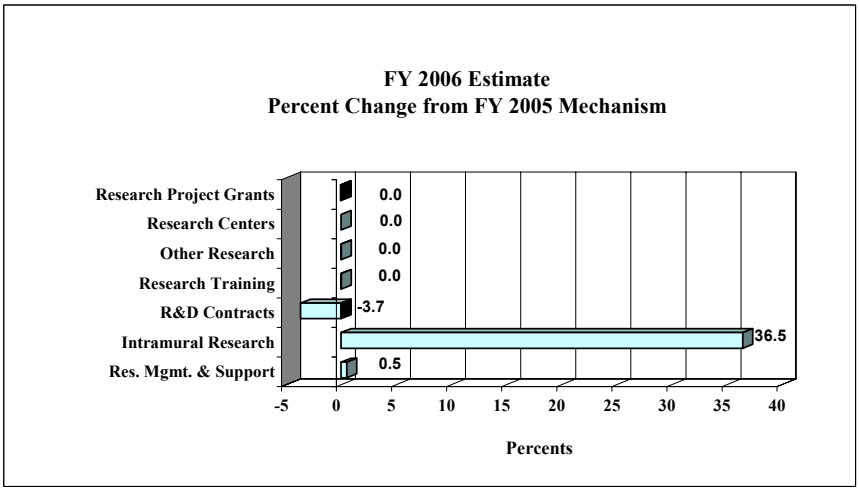
The Fiscal Year 2006 request includes funding for 582 competing and noncompeting research project grants, 24 research centers, and 33 other research grants which include 18 career development awards. Research Management and Support receives an increase of 0.5 percent, the same as the NIH total increase. The intramural research program was formally established with research laboratories on NIH campus in FY05. This was accomplished by the realignment of the PET Radiochemistry Group and the Imaging Physics Section from the Clinical Center to the

Institute. The opportunity to grow this program will be guided by the Board of Scientific Counselors.

NIBIB is participating in the NIH Neuroscience Blueprint. The FY 2006 request includes $100,000 for a variety of Neuroscience Blueprint initiatives, including neuroscience cores, training initiatives, and the Neuromouse project. Initiatives for FY 2006 that are of particular relevance to the NIBIB include the cross-institute neuroscience training initiative in Neuroimaging, the computational neuroscience initiative that will link computational models to neurophysiology at multiple scales, and the neuroimaging initiatives.

The mechanism distribution by dollars and percent change are displayed below:



# NATIONAL INSTITUTES OF HEALTH
## National Institute of Biomedical Imaging and Bioengineering

## Budget Mechanism – Total

| MECHANISM | FY 2004 Actual | | FY 2005 Appropriation | | FY 2006 Estimate | |
|---|---|---|---|---|---|---|
| Research Grants: | No. | Amount | No. | Amount | No. | Amount |
| Research Projects: | | | | | | |
| Noncompeting | 474 | $172,286,000 | 448 | $171,627,000 | 428 | $169,738,000 |
| Administrative supplements | (13) | 452,000 | (14) | 684,000 | (14) | 684,000 |
| Competing: | | | | | | |
| Renewal | 29 | 11,494,000 | 32 | 15,867,000 | 51 | 16,516,000 |
| New | 115 | 33,619,000 | 116 | 31,734,000 | 103 | 32,897,000 |
| Supplements | 0 | 0 | 0 | 0 | 0 | 0 |
| Subtotal, competing | 144 | 45,113,000 | 148 | 47,601,000 | 154 | 49,413,000 |
| Subtotal, RPGs | 618 | 217,851,000 | 596 | 219,912,000 | 582 | 219,835,000 |
| SBIR/STTR | 62 | 9,107,000 | 37 | 8,930,000 | 37 | 8,894,000 |
| Subtotal, RPGs | 680 | 226,958,000 | 633 | 228,842,000 | 619 | 228,729,000 |
| Research Centers: | | | | | | |
| Specialized/comprehensive | 5 | 2,991,000 | 5 | 4,034,000 | 5 | 4,034,000 |
| Clinical research | 0 | 0 | 0 | 0 | 0 | 0 |
| Biotechnology | 21 | 21,928,000 | 19 | 20,809,000 | 19 | 20,809,000 |
| Comparative medicine | 0 | 0 | 0 | 0 | 0 | 0 |
| Research Centers in Minority Institutions | 0 | 0 | 0 | 0 | 0 | 0 |
| Subtotal, Centers | 26 | 24,919,000 | 24 | 24,843,000 | 24 | 24,843,000 |
| Other Research: | | | | | | |
| Research careers | 17 | 2,172,000 | 18 | 2,353,000 | 18 | 2,353,000 |
| Cancer education | 0 | 0 | 0 | 0 | 0 | 0 |
| Cooperative clinical research | 0 | 0 | 0 | 0 | 0 | 0 |
| Biomedical research support | 0 | 5,000 | 0 | 7,000 | 0 | 8,000 |
| Minority biomedical research support | 0 | 0 | 0 | 0 | 0 | 0 |
| Other | 18 | 1,808,000 | 16 | 1,233,000 | 15 | 1,233,000 |
| Subtotal, Other Research | 35 | 3,985,000 | 34 | 3,593,000 | 33 | 3,594,000 |
| Total Research Grants | 741 | 255,862,000 | 691 | 257,278,000 | 676 | 257,166,000 |
| Research Training: | FTTPs | | FTTPs | | FTTPs | |
| Individual awards | 11 | 475,000 | 16 | 701,000 | 16 | 703,000 |
| Institutional awards | 119 | 5,383,000 | 156 | 7,138,000 | 155 | 7,138,000 |
| Total, Training | 130 | 5,858,000 | 172 | 7,839,000 | 171 | 7,841,000 |
| Research & development contracts | 15 | 8,875,000 | 10 | 11,985,000 | 9 | 11,545,000 |
| (SBIR/STTR) | (2) | (15) | (2) | (15) | (2) | (17) |
| | FTEs | | FTEs | | FTEs | |
| Intramural research | 7 | 3,326,000 | 7 | 5,669,000 | 7 | 7,737,000 |
| Research management and support | 43 | 14,909,000 | 47 | 15,438,000 | 47 | 15,519,000 |
| Total, NIBIB | 50 | 288,830,000 | 54 | 298,209,000 | 54 | 299,808,000 |
| (RoadMap Support) | | (986,000) | | (1,885,000) | | (2,681,000) |
| (Clinical Trials) | | (0) | | (0) | | (0) |

## NATIONAL INSTITUTES OF HEALTH
## National Institute of Biomedical Imaging and Bioengineering

### Budget Authority by Activity
### (dollars in thousands)

| ACTIVITY | FY 2004 Actual | | FY 2005 Appropriation | | FY 2006 Estimate | | Change | |
|---|---|---|---|---|---|---|---|---|
| | FTEs | Amount | FTEs | Amount | FTEs | Amount | FTEs | Amount |
| Extramural Research: | | | | | | | | |
| Biomedical Imaging and Bioengineering | | $271,336 | | $277,102 | | $276,552 | | ($550) |
| Subtotal, Extramural research | | 271,336 | | 277,102 | | 276,552 | | (550) |
| Intramural research | 7 | 3,326 | 7 | 5,669 | 7 | 7,737 | --- | 2,068 |
| Res. management & support | 43 | 14,168 | 47 | 15,438 | 47 | 15,519 | --- | 81 |
| Total | 50 | 288,830 | 54 | 298,209 | 54 | 299,808 | --- | 1,599 |

**NATIONAL INSTITUTES OF HEALTH**
**National Institute of Biomedical Imaging and Bioengineering**

**Summary of Changes**

| | | | | |
|---|---|---|---|---|
| FY 2005 Estimate | | | | $298,209,000 |
| FY 2006 Estimated Budget Authority | | | | 299,808,000 |
| Net change | | | | 1,599,000 |
| | FY 2005 Appropriaton | | Change from Base | |
| CHANGES | FTEs | Budget Authority | FTEs | Budget Authority |
| A. Built-in: | | | | |
| 1. Intramural research: | | | | |
| a. Within grade increase | | $1,066,000 | | $15,000 |
| b. Annualization of January 2005 pay increase | | 1,066,000 | | 10,000 |
| c. January 2006 pay increase | | 1,066,000 | | 18,000 |
| d. One less day of pay | | 1,066,000 | | (4,000) |
| e. Payment for centrally furnished services | | 975,000 | | 5,000 |
| f. Increased cost of laboratory supplies, materials, and other expenses | | 3,628,000 | | 79,000 |
| Subtotal | | | | 123,000 |
| 2. Research Management and Support: | | | | |
| a. Within grade increase | | 5,759,000 | | 91,000 |
| b. Annualization of January 2005 pay increase | | 5,759,000 | | 52,000 |
| c. January 2006 pay increase | | 5,759,000 | | 100,000 |
| d. One less day of pay | | 5,759,000 | | (22,000) |
| e. Payment for centrally furnished services | | 4,061,000 | | 20,000 |
| f. Increased cost of laboratory supplies, materials, and other expenses | | 5,618,000 | | 100,000 |
| Subtotal | | | | 341,000 |
| Subtotal, Built-in | | | | 464,000 |

**NATIONAL INSTITUTES OF HEALTH**
**National Institute of Biomedical Imaging and Bioengineering**

**Summary of Changes --continued**

| CHANGES | 2005 Current Estimate Base | | Change from Base | |
|---|---|---|---|---|
| | No. | Amount | No. | Amount |
| B. Program: | | | | |
| 1. Research project grants: | | | | |
| a. Noncompeting | 448 | $172,311,000 | (20) | ($1,889,000) |
| b. Competing | 148 | 47,601,000 | 6 | 1,812,000 |
| c. SBIR/STTR | 37 | 8,930,000 | 0 | (36,000) |
| Total | 633 | 228,842,000 | (14) | (113,000) |
| 2. Research centers | 24 | 24,843,000 | 0 | 0 |
| 3. Other research | 34 | 3,593,000 | (1) | 1,000 |
| 4. Research training | 172 | 7,839,000 | (1) | 2,000 |
| 5. Research and development contracts | 10 | 11,985,000 | 9 | (440,000) |
| Subtotal, extramural | | | | (550,000) |
| | FTEs | | FTEs | |
| 6. Intramural research | 7 | 5,669,000 | 0 | 1,945,000 |
| 7. Research management and support | 47 | 15,438,000 | 0 | (260,000) |
| Subtotal, program | | 298,209,000 | | 1,135,000 |
| Total changes | 54 | | 0 | 1,599,000 |

**NATIONAL INSTITUTES OF HEALTH**
**National Institute of Biomedical Imaging and Bioengineering**

**Budget Authority by Object**

| | FY 2005 Appropriation | FY 2006 Estimate | Increase or Decrease |
|---|---|---|---|
| Total compensable workyears: | | | |
| Full-time employment | 54 | 54 | 0 |
| Full-time equivalent of overtime & holiday hours | 0 | 0 | 0 |
| Average ES salary | | | $0 |
| Average GM/GS grade | 13.0 | 13.0 | 0.0 |
| Average GM/GS salary | $88,551 | $91,208 | $2,657 |
| Average salary, grade established by act of July 1, 1944 (42 U.S.C. 207) | $0 | $0 | $0 |
| Average salary of ungraded positions | 115,894 | 119,371 | 3,477 |

| OBJECT CLASSES | | FY 2005 Appropriation | FY 2006 Estimate | Increase or Decrease |
|---|---|---|---|---|
| | Personnel Compensation: | | | |
| 11.1 | Full-Time Permanent | $3,565,000 | $3,768,000 | $203,000 |
| 11.3 | Other than Full-Time Permanent | 1,538,000 | 1,570,000 | 32,000 |
| 11.5 | Other Personnel Compensation | 200,000 | 210,000 | 10,000 |
| 11.7 | Military Personnel | 0 | 0 | 0 |
| 11.8 | Special Personnel Services Payments | 198,000 | 250,000 | 52,000 |
| | **Total, Personnel Compensation** | 5,501,000 | 5,798,000 | 297,000 |
| 12.0 | Personnel Benefits | 1,324,000 | 1,360,000 | 36,000 |
| 12.1 | Military Personnel Benefits | 0 | 0 | 0 |
| 13.0 | Benefits for Former Personnel | 0 | 0 | 0 |
| | **Subtotal, Pay Costs** | **6,825,000** | **7,158,000** | **333,000** |
| 21.0 | Travel & Transportation of Persons | 495,000 | 556,000 | 61,000 |
| 22.0 | Transportation of Things | 71,000 | 78,000 | 7,000 |
| 23.1 | Rental Payments to GSA | 0 | 0 | 0 |
| 23.2 | Rental Payments to Others | 19,000 | 19,000 | 0 |
| 23.3 | Communications, Utilities & Miscellaneous Charges | 142,000 | 150,000 | 8,000 |
| 24.0 | Printing & Reproduction | 184,000 | 193,000 | 9,000 |
| 25.1 | Consulting Services | 75,000 | 75,000 | 0 |
| 25.2 | Other Services | 1,300,000 | 1,929,000 | 629,000 |
| 25.3 | Purchase of Goods & Services from Government Accounts | 17,123,000 | 15,737,000 | (1,386,000) |
| 25.4 | Operation & Maintenance of Facilities | 5,000 | 6,000 | 1,000 |
| 25.5 | Research & Development Contracts | 5,002,000 | 6,894,000 | 1,892,000 |
| 25.6 | Medical Care | 0 | 0 | 0 |
| 25.7 | Operation & Maintenance of Equipment | 108,000 | 110,000 | 2,000 |
| 25.8 | Subsistence & Support of Persons | 0 | 0 | 0 |
| **25.0** | **Subtotal, Other Contractual Services** | **23,613,000** | **24,751,000** | **1,138,000** |
| 26.0 | Supplies & Materials | 455,000 | 608,000 | 153,000 |
| 31.0 | Equipment | 1,288,000 | 1,288,000 | 0 |
| 32.0 | Land and Structures | 0 | 0 | 0 |
| 33.0 | Investments & Loans | 0 | 0 | 0 |
| 41.0 | Grants, Subsidies & Contributions | 265,117,000 | 265,007,000 | (110,000) |
| 42.0 | Insurance Claims & Indemnities | 0 | 0 | 0 |
| 43.0 | Interest & Dividends | 0 | 0 | 0 |
| 44.0 | Refunds | 0 | 0 | 0 |
| | **Subtotal, Non-Pay Costs** | **291,384,000** | **292,650,000** | **1,266,000** |
| | **Total Budget Authority by Object** | **298,209,000** | **299,808,000** | **1,599,000** |

**NATIONAL INSTITUTES OF HEALTH**
**National Institute of Biomedical Imaging and Bioengineering**

**Salaries and Expenses**

| OBJECT CLASSES | FY 2005 Appropriation | FY 2006 Estimate | Increase or Decrease |
|---|---|---|---|
| **Personnel Compensation:** | | | |
| Full-Time Permanent (11.1) | $3,565,000 | $3,768,000 | $203,000 |
| Other Than Full-Time Permanent (11.3) | 1,538,000 | 1,570,000 | 32,000 |
| Other Personnel Compensation (11.5) | 200,000 | 210,000 | 10,000 |
| Military Personnel (11.7) | 0 | 0 | 0 |
| Special Personnel Services Payments (11.8) | 198,000 | 250,000 | 52,000 |
| **Total Personnel Compensation (11.9)** | **5,501,000** | **5,798,000** | **297,000** |
| Civilian Personnel Benefits (12.1) | 1,324,000 | 1,360,000 | 36,000 |
| Military Personnel Benefits (12.2) | 0 | 0 | |
| Benefits to Former Personnel (13.0) | 0 | 0 | 0 |
| **Subtotal, Pay Costs** | **6,825,000** | **7,158,000** | **333,000** |
| Travel (21.0) | 495,000 | 556,000 | 61,000 |
| Transportation of Things (22.0) | 71,000 | 78,000 | 7,000 |
| Rental Payments to Others (23.2) | 19,000 | 19,000 | 0 |
| Communications, Utilities and Miscellaneous Charges (23.3) | 142,000 | 150,000 | 8,000 |
| Printing and Reproduction (24.0) | 184,000 | 193,000 | 9,000 |
| **Other Contractual Services:** | | | |
| Advisory and Assistance Services (25.1) | 75,000 | 75,000 | 0 |
| Other Services (25.2) | 1,300,000 | 1,929,000 | 629,000 |
| Purchases from Govt. Accounts (25.3) | 8,842,000 | 8,357,000 | (485,000) |
| Operation & Maintenance of Facilities (25.4) | 5,000 | 6,000 | 1,000 |
| Operation & Maintenance of Equipment (25.7) | 108,000 | 110,000 | 2,000 |
| Subsistence & Support of Persons (25.8) | 0 | 0 | 0 |
| **Subtotal Other Contractual Services** | **10,330,000** | **10,477,000** | **147,000** |
| Supplies and Materials (26.0) | 455,000 | 608,000 | 153,000 |
| **Subtotal, Non-Pay Costs** | 11,696,000 | 12,081,000 | 385,000 |
| **Total, Administrative Costs** | **18,521,000** | **19,239,000** | **718,000** |

**NATIONAL INSTITUTES OF HEALTH**
**National Institute of Biomedical Imaging and Bioengineering**

SIGNIFICAN ITEMS IN HOUSE, SENATE, AND CONFERENCE APPROPRIATIONS COMMITTEE REPORTS

FY 2005 House Appropriations Committee Report Language (H. Rpt. 108-636)

Item

***Bone Imaging*** - The Committee encourages NIBIB to make new bone imaging techniques a primary focus, speeding the development of new imaging modalities that better capture bone quality, including bone micro- and macro-architecture, quantification of bone mass and crystalline composition, which are necessary to develop diagnostic and treatment therapies for patients with metabolic bone diseases. The Committee encourages NIBIB to participate actively in trans-NIH initiatives that address these priorities (p. 99)

Action taken or to be taken

Improvements in imaging technologies supported by the NIBIB have the potential to significantly affect the diagnosis and treatment of bone disease. For example, increased image resolution will enable the detection and measurement of bone loss associated with many bone diseases. Specifically, improvements in technologies such as computed tomography (CT) and other techniques that incorporate x-ray imaging will enable better understanding of the pathogenesis and treatment of bone disease. Work currently supported by the NIBIB will facilitate improved imaging techniques that better capture bone quality, including bone micro- and macro-architecture, quantification of bone mass and crystalline composition, enabling earlier disease detection. Improved technologies will also provide a means to monitor the efficacy novel pharmaceuticals. In addition, NIBIB, in collaboration with the National Institute of Arthritis and Musculoskeletal and Skin Disease (NIAMS), is planning a conference for 2005 that will provide recommendations from the scientific community to identify future research directions for NIBIB and NIAMS.

Item

***Organ Imaging*** - The Committee encourages the Institute to focus on improved tissue and organ imaging technologies and on the growth of artificial tissues. Progress in these fields will have multiple benefits, including addressing issues such as invasive diagnostic tests now required for liver diseases and the need to address the shortage (p.99)

Action taken or to be taken

In the past century, radiologists relied on morphologic information obtained with various imaging techniques for disease detection and diagnosis, and for monitoring therapeutic responses. The techniques most commonly used for imaging human organ diseases include computerized tomography (CT), magnetic resonance imaging (MRI) and ultrasound (US). With

advances in molecular techniques, and the successful mapping of the human genome, the era of personalized medicine has clearly arrived, bringing with it important advances in clinical organ imaging. The integration of techniques from molecular biology, immunology, genetics, chemistry, and tissue engineering with imaging techniques will give unprecedented capabilities to study biochemistry and physiology in intact human organs, and should lead to the development of new diagnostic and therapeutic methods.

Over the last year, the NIBIB has been actively involved in developing an Inter-Agency "Action Plan for Liver Disease Research." Also, the NIBIB—in collaboration with NCI and NIDDK—sponsored a workshop entitled "Hepatocellular Carcinoma: Screening, Diagnosis, and Management." Both activities emphasized the need for developing novel molecular imaging approaches that could detect and characterize liver disease in the early stages, when it can be treated successfully.

The NIBIB also serves as the lead NIH Institute on a Roadmap initiative entitled "Innovation in Molecular Imaging Probes." This initiative will support the "high-risk" development of novel molecular imaging probes for human studies. In addition, the NIBIB supports a grant portfolio related to the development of novel imaging techniques. Together, these two major areas will enhance the development of molecular imaging of internal organs for clinical studies.

Item

***Diabetic Retinopathy*** - The Committee encourages NIBIB to collaborate with NEI on the development and application of scanning technologies that will be affordable and accessible to allow for early detection of diabetic retinopathy (p.99)

Action taken or to be taken

The NIBIB maintains a focused portfolio in the development and application of scanning/imaging technologies for early detection of diabetic retinopathy. Topics covered include the development of low-cost devices for digital retinal imaging, the application of retinal blood flow imaging for improved understanding and treatment of diabetic retinopathy, the development of intrinsic signal optical imaging and applications toward noninvasive functional imaging of the retina, and the development of retinal imaging/treatment instrument that combines a scanning laser ophthalmoscope and eye tracking to achieve diffraction limited retinal imaging.

In addition to these on going efforts, the NIBIB also collaborates with the NEI on an initiative entitled "Non-Invasive Imaging for Diabetic Retinopathy." This initiative solicits research applications to develop, apply, and evaluate noninvasive technology that is practical, affordable, and accessible so that patients with diabetes can benefit from remote site disease screening. The NIBIB will continue these efforts and will collaborate with the NEI on the development and application of scanning technologies that will be affordable and accessible to allow for early detection of diabetic retinopathy.

FY 2005 Senate Appropriations Committee Report Language (S. Rpt. 108-345)

Item

***Artificial Tissues*** - The Committee encourages the Institute to focus on improved tissue and organ imaging technologies and on the growth of artificial tissues. Progress in these fields will have multiple benefits including addressing issues such as invasive diagnostics tests now required for liver diseases and the need to address the shortage of livers and other organs available for transplantation (p.155)

Action taken or to be taken

Work in the growth of artificial tissues is being supported by the tissue engineering and advanced biomaterials science programs at the NIBIB. Research addresses both the basic sciences—understanding the biological processes that control the directed growth of new engineered tissues from cells, as well as the clinical sciences—the development of new biomaterials that act as scaffolds for engineered tissues. Scaffold materials help to shape and guide the growth of engineered tissues for augmentation or replacement procedures in which the native tissue is lost through disease, injury, or surgery. The NIBIB is addressing the shortage of organs that are available for transplantation by supporting the research and development of totally artificial organs as well as tissue engineered organs. Artificial organs utilize materials and engineering principles to produce biologically functional structures that are capable of replacing or augmenting organs that are diseased or insufficient. Examples of relevant technologies are artificial filtration systems that can perform dialysis, encapsulated cells that can produce insulin for the treatment of diabetes, and new materials and pumping technologies that can improve ventricular assist devices.

Item

***Imaging Techniques*** - The Committee urges NIBIB to make new bone imaging techniques a primary focus, speeding the development of new imaging modalities that better capture bone quality, including bone micro- and macro-architecture, quantification of bone mass and crystalline composition. This is necessary to develop diagnostic and treatment therapies for patients with metabolic bone diseases. The Committee urges NIBIB to participate actively in trans-NIH initiatives that address these priorities (p.155)

Action taken or to be taken

Improvements in imaging technologies supported by the NIBIB have the potential to significantly affect the diagnosis and treatment of bone disease. For example, increased image resolution will enable the detection and measurement of bone loss associated with many bone diseases. Specifically, improvements in technologies such as computed tomography (CT) and other techniques that incorporate x-ray imaging will enable better understanding of the pathogenesis and treatment of bone disease. Work currently supported by the NIBIB will facilitate improved imaging techniques that better capture bone quality, including bone micro- and macro-architecture, quantification of bone mass and crystalline composition, enabling earlier

disease detection. Improved imaging techniques will also provide a means to monitor the efficacy novel pharmaceuticals. In addition, NIBIB, in collaboration with the National Institute of Arthritis and Musculoskeletal and Skin Disease (NIAMS), is planning a conference for 2005 that will provide recommendations from the scientific community to identify future research directions for NIBIB and NIAMS.

Item

***Pet MicroPET Scans*** -The Committee continues to encourage this new Institute to devote significant resources to molecular imaging technologies such as positron emission tomography [PET] and microPET to take advantage of the capacities of molecular imaging to detect disease process at the molecular level and to monitor the effectiveness of targeted gene therapies now under development. The Committee also encourages the new Institute to develop its research agenda in close collaboration with other, disease-specific Institutes at NIH, so that new imaging technologies are closely tied to the research projects being undertaken by the various other Institutes of NIH (p.155)

Action taken or to be taken

It is understood by the NIBIB that one of the most promising, and rapidly evolving, areas of diagnostic medicine is that of molecular imaging, which includes positron emission tomography (PET), functional magnetic resonance imaging (fMRI), and a range of optically-based technologies. Along with these are corresponding approaches devised for the study of small laboratory animals, such as mircoPET, microCT, and microMRI. The NIBIB continues to give these efforts high priority by supporting grants and major symposia and conferences. For example, in FY 2004 the NIBIB co-sponsored with other NIH Institutes the third annual meeting of the Society of Molecular Imaging and the fourth Inter-Institute Workshop on Diagnostic Optical Imaging and Spectroscopy. In addition, components of the recently established NIBIB intramural PET Radiochemistry and Imaging Physics program focus on the development of new molecular probes, and tools developed in this laboratory serve also to support research in other NIH institutes. Likewise, the NIBIB and the Center for Devices and Radiological Health (CDRH) at the Food and Drug Administration have signed an interagency agreement establishing a joint Laboratory for the Assessment of Medical Imaging Systems (LAMIS); an important aspect of this joint effort is to assess and optimize molecular and other medical imaging systems.

**NATIONAL INSTITUTES OF HEALTH**
**National Institute of Biomedical Imaging and Bioengineering**

**Authorizing Legislation**

| | PHS Act/ Other Citation | U.S. Code Citation | 2005 Amount Authorized | FY 2005 Appropriation | 2006 Amount Authorized | 2006 Budget Estimate |
|---|---|---|---|---|---|---|
| Research and Investigation | Section 301 | 42§241 | Indefinite | $290,370,000 | Indefinite | $291,967,000 |
| Imaging and Bioengineering | Section 41B | 42§285b | Indefinite | | Indefinite | |
| National Research Service Awards | Section 487(d) | 42§288 | a/ | 7,839,000 | b/ | 7,841,000 |
| Total, Budget Authority | | | | 298,209,000 | | 299,808,000 |

a/ Amounts authorized by Section 301 and Title IV of the Public Health Act.
b/ Reauthorizing legislation will be submitted.

**NATIONAL INSTITUTES OF HEALTH**
**National Institute of Biomedical Imaging and Bioengineering**

**Appropriations History**

| Fiscal Year | Budget Estimate to Congress | House Allowance | Senate Allowance | Appropriation 1/ |
|---|---|---|---|---|
| 2002 | 40,206,000 | 39,869,000 | 140,000,000 | 111,984,000 |
| Rescission | | | | (33,000) |
| 2003 | 120,502,000 | 270,494,000 | 283,100,000 | 280,100,000 |
| Rescission | | | | (1,821,000) |
| 2004 | 282,109,000 | 282,109,000 | 289,300,000 | 288,900,000 |
| Rescission | | | | (1,771,000) |
| 2005 | 297,647,000 | 297,647,000 | 300,800,000 | 300,647,000 |
| Rescission | | | | (2,438,000) |
| 2006 | 299,808,000 | | | |

1/ Reflects enacted supplementals, rescissions, and reappropriations.

**NATIONAL INSTITUTES OF HEALTH**

**National Institute of Biomedical Imaging and Bioengineering**

**Detail of Full-Time Equivalent Employment (FTEs)**

| OFFICE/DIVISION | FY 2004 Actual | FY 2005 Appropriation | FY 2006 Estimate |
|---|---|---|---|
| Office of the Director | 9 | 5 | 5 |
| Extramural Science Programs | 15 | 18 | 18 |
| DEAS | -3 | | |
| Office of Research Administration | 13 | 12 | 12 |
| Office of Administrative Management | 9 | 12 | 12 |
| Intramural Science Programs (Transfer) | 7 | 7 | 7 |
| Total | 50 | 54 | 54 |
| FTEs supported by funds from Cooperative Research and Development Agreements | (0) | (0) | (0) |

| FISCAL YEAR | Average GM/GS Grade |
|---|---|
| 2002 | 12.3 |
| 2003 | 11.9 |
| 2004 | 12.3 |
| 2005 | 13.0 |
| 2006 | 13.0 |

**NATIONAL INSTITUTES OF HEALTH**
**National Institute of Biomedical Imaging and Bioengineering**

**Detail of Positions**

| GRADE | FY 2004 Actual | FY 2005 Appropriation | FY 2006 Estimate |
|---|---|---|---|
| Total - ES Positions | | | |
| Total - ES Salary | | | |
| GM/GS-15 | 3 | 9 | 9 |
| GM/GS-14 | 13 | 16 | 16 |
| GM/GS-13 | 9 | 10 | 10 |
| GS-12 | 3 | 5 | 5 |
| GS-11 | 2 | 2 | 2 |
| GS-10 | | | |
| GS-9 | 4 | 2 | 2 |
| GS-8 | 1 | | |
| GS-7 | 3 | 3 | 3 |
| GS-6 | | | |
| GS-5 | | | |
| GS-4 | | | |
| GS-3 | | | |
| GS-2 | | | |
| GS-1 | | | |
| Subtotal | 38 | 47 | 47 |
| Grades established by Act of July 1, 1944 (42 U.S.C. 207): | | | |
| Assistant Surgeon General | | | |
| Director Grade | | | |
| Senior Grade | | | |
| Full Grade | | | |
| Senior Assistant Grade | | | |
| Assistant Grade | | | |
| Subtotal | | | |
| Ungraded | 18 | 27 | 27 |
| Total permanent positions | 38 | 47 | 47 |
| Total positions, end of year | 56 | 74 | 74 |
| Total full-time equivalent (FTE) employment,end of year | 50 | 54 | 54 |
| Average ES salary | | | |
| Average GM/GS grade | 12.3 | 13.0 | 13.0 |
| Average GM/GS salary | $78,374 | $88,551 | $91,208 |