

**DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH**

**NATIONAL ADVISORY COUNCIL FOR
BIOMEDICAL IMAGING AND BIOENGINEERING**

**Summary of Meeting¹
May 18, 2015**

The National Advisory Council for Biomedical Imaging and Bioengineering (NACBIB) was convened for its 38th meeting on May 18, 2015, at the Bolger Center in Potomac, Maryland. Dr. Roderic I. Pettigrew, Director of the National Institute of Biomedical Imaging and Bioengineering (NIBIB), presided as Council Chairperson. In accordance with Public Law 92-463, the meeting was open to the public from 8:30 a.m. to 12:50 p.m. for review and discussion of program development, needs, and policy. The meeting was closed to the public from 2:00 p.m. to 2:45 p.m. for the consideration of grant applications.

Council members present:

Dr. Kristi Anseth, University of Colorado, Boulder, Boulder, CO
Dr. Carol Espy-Wilson, University of Maryland, College Park, MD
Dr. Karen Hirschi, Yale University, New Haven, CT
Dr. Cato T. Laurencin, University of Connecticut, Farmington, CT
Dr. Raphael Lee, University of Chicago, Chicago, IL
Dr. Mark Musen, Stanford University, Stanford, CA
Dr. Daniel Sullivan, Duke University Medical Center, Durham, NC
Dr. Bruce Tromberg, University of California, Irvine, CA
Dr. Sheldon Weinbaum, City College of New York, New York, NY

Ex officio members present:

Dr. Anne Plant, National Institute of Standards and Technology, Gaithersburg, MD
Dr. Sohi Rastegar, National Science Foundation, Arlington, VA
Dr. James G. Smirniotopoulos, Uniformed Services University of the Health Sciences, Bethesda, MD

Council members attending by telephone:

Dr. John C. Gore, Vanderbilt University Medical Center, Nashville, TN
Dr. James Thrall, Massachusetts General Hospital, Harvard Medical School, Boston, MA

Council members absent:

Dr. A. Gregory Sorensen, Siemens Healthcare North America, Malvern, PA

Ex officio members absent:

Ms. Sylvia Burwell, U.S. Department of Health and Human Services, Washington, DC
Dr. Francis Collins, National Institutes of Health, Bethesda, MD
Dr. P. Hunter Peckham, U.S. Department of Veterans Affairs, Cleveland, OH

Chairperson:

Dr. Roderic I. Pettigrew

Executive Secretary:

Dr. Jill Heemsker

¹ For the record, it is noted that members absent themselves from the meeting when the Council is discussing applications (a) from their respective institutions or (b) in which a conflict of interest may occur. This procedure only applies to applications that are discussed individually, not to "en bloc" actions.

Also present:

NIBIB staff present for portions of the meeting:

Ms. Holly Atherton	Dr. Chris Kelley
Mr. Angelos Bacas	Dr. Steven Krosnick
Dr. L. Michelle Bennett	Ms. Kai Lakeman
Ms. Shirley Coney-Johnson	Dr. Tiffani Bailey Lash
Dr. Richard Conroy	Dr. Richard Leapman
Ms. Desi Conway	Dr. Guoying Liu
Ms. Christine Cooper	Dr. Raymond MacDougall
Ms. Zoe Ann Copeland	Dr. Michael Marge
Ms. Monique Day	Dr. Rishi Mathura
Dr. Anthony Demsey	Mr. Todd Merchak
Dr. Henry Eden	Dr. Peter Moy
Ms. Kate Egan	Dr. Grace Peng
Ms. Angela Eldridge	Dr. Karen Peterson
Dr. Zeynep Erim	Dr. Edward Ramos
Mr. Anthony Fransella	Ms. Mew Rattanawatkul
Dr. David George	Ms. Vicki Rein
Ms. Pam Glikman	Dr. Mary Rodgers
Dr. John Hayes	Dr. Antonio Sastre
Ms. Eunica Haynes	Dr. Behrouz Shabestari
Dr. William Heetderks	Mr. Shaun Sims
Dr. Dennis Hlasta	Mr. Russell Songco
Ms. Alisha Hopkins	Dr. Manana Sukhareva
Mr. James Huff	Dr. Jessica Tucker
Dr. Rosemarie Hunziker	Ms. Florence Turska
Mr. Tom Izzard	Mr. Kwesi Wright
Dr. Tom Johnson	Dr. Ruixia Zhou
Mr. William Kane	Dr. Steven Zullo

Non-NIBIB National Institutes of Health (NIH) employees:

Dr. Jon Lorsch, Director, National Institute of General Medical Sciences

Members of the public present for portions of the meeting:

Dr. Raag D. Airan, Johns Hopkins University, Baltimore, MD
Dr. Bradley D. Allen, Northwestern University, Evanston, IL
Dr. Costas Arvanitis, Harvard Medical School, Boston, MA
Mr. Milton Berrios, Bolger Center
Dr. Joseph E. Burns, University of California, Irvine, Irvine, CA
Ms. Erin Cadwalader, Lewis-Burke Associates, Washington, DC
Dr. James Scot Cordova, Emory University, Atlanta, GA
Dr. Seena Dehkhargani, Emory University, Atlanta, GA
Ms. Stephanie DeLuca, American Chemical Society
Dr. Ryne Didier, Oregon Health and Science University, Portland, OR
Dr. Vinay Duddalwar, University of Southern California, Los Angeles, CA
Dr. Michael E. Hahn, University of California, San Diego, San Diego, CA
Mr. Michael Kalutkiewicz, Academy of Radiology Research, Washington, DC
Mr. Andrew Menard, Brigham and Women's Hospital, Boston, MA
Dr. Emilia Olson, University of California, San Diego, San Diego, CA
Dr. Rebecca Rakow-Penner, University of California, San Diego, San Diego, CA
Dr. Bruce Rosen, Massachusetts General Hospital, Charlestown, MA
Ms. Kathy Sedgwick, NOVA Research Company, Silver Spring, MD
Dr. Steven Seltzer, Brigham and Women's Hospital, Boston, MA
Mr. William Shaw, Massachusetts General Hospital, Charlestown, MA

Dr. Jadranka Stojanovska, University of Michigan, Ann Arbor, MI
Dr. Valentina Taviani, Stanford University, Stanford, California
Dr. Lawrence Wald, Massachusetts General Hospital, Charlestown, MA
Dr. Shandong Wu, University of Pittsburgh, Pittsburgh, PA

I. Call to Order: Dr. Jill Heemskerk

Dr. Heemskerk called to order the 38th meeting of the National Advisory Council for Biomedical Imaging and Bioengineering. She reminded attendees that the morning session of the meeting was open to the public and welcomed attendees.

II. Director's Remarks: Dr. Roderic I. Pettigrew

A. Welcome

Dr. Pettigrew welcomed guests to the meeting, including leadership of the Academy of Radiology Research (ARR) and 13 recipients of Medical Technology Showcase Travel Awards from ARR and the Coalition for Imaging and Bioengineering Research.

B. NIBIB Awards and Honors

Several members of the NIBIB community recently received distinguished honors and awards. These include NIBIB grantees Dr. Daniel Sodickson, who was named Vice President-Elect of the International Society for Magnetic Resonance in Medicine, and Dr. Sangeeta Bhatia, who received the 2015 Heinz Prize for her work with humanized "micro-livers" in mice. Another NIBIB grantee, Dr. George Em Karniadakis, received the Wiederhielm Award for his highly cited original article in *Microcirculation*. Ex-officio Council Member Dr. Hunter Peckham received the American Spinal Injury Association's Lifetime Achievement Award, and Council Member Dr. Bruce Tromberg received the Michael S. Feld Biophotonics Award from the Optical Society of America.

C. New NIBIB Staff

Dr. Pettigrew welcomed five new members of NIBIB staff: Dr. L. Michelle Bennett, Chief Science Officer, Office of the Director; Dr. Edward Ramos, Program Director, Extramural Science Program; Dr. Behrouz Shabestari, Program Director, Division of Applied Science and Technology; Dr. Raymond MacDougall, Office of Science Policy and Communications; and Dr. Dennis Hlasta, Scientific Review Officer, Office of Scientific Review.

D. NIBIB Fiscal Year (FY) 2015 Budget

The NIBIB 2015 R01/R21 payline was increased from the 9th to the 10th percentile, with the Expanded Opportunity Zone (EOZ) to include from the 11th to the 20th percentile. Overall, 13 percent of NIBIB research project grant applications were funded in FY14; the National Institutes of Health (NIH) average was approximately 17 percent.

E. NIH Activities

Precision Medicine Initiative

Precision medicine is an approach to disease prevention and treatment that takes into account individual differences in genes, environment, and lifestyle. In January 2015, President Obama unveiled the Precision Medicine Initiative (PMI) to generate scientific evidence necessary to move the precision medicine concept into everyday clinical practice. Some \$215 million in funding is split among the NIH, the National Cancer Institute, the U.S. Food and Drug Administration (FDA), and the Office of the National Coordinator for Health IT. NIH is planning the formation of a 1-million-person national research cohort to collect genetic data, biological samples, and diet/lifestyle information. As part of the planning effort, a series of public workshops is being held this year. Dr. Pettigrew is co-chair of the NIH team which is planning a workshop to be held on July 27-28: Mobile and Personal Technologies in Precision

Medicine, to consider the scientific, methodological and practical implications of incorporating mobile or personal technologies into the national cohort study.

Pediatric Research using Integrated Sensor Monitoring Systems

The *Pediatric Research using Integrated Sensor Monitoring Systems* (PRISMS) program is intended to develop noninvasive health monitoring systems to study pediatric asthma. NIBIB is the lead Institute on three related Funding Opportunity Announcements (FOAs) released in April.

Common Fund Activities

The *Single Cell Analysis Challenge* attempts to identify new ways to track the high resolution molecular state of a single cell in complex tissue over time. Five prizes were awarded for Phase 1 applications, which focused on theoretical written approaches to this problem. Dr. Paul Blainey at MIT received a \$40,000 first prize for his proposal entitled “Single-cell time lapse gene expression profiling via an engineered self-reporting pathway.” Sixteen Phase 1 prize winners and finalists are eligible to compete for two Phase 2 awards, which emphasize implementation of approaches proposed in Phase 1.

Stimulating Peripheral Activity to Relieve Conditions (SPARC) issued a U18 FOA entitled “Exploratory Technologies to Understand the Control of Organ Function by the Peripheral Nervous System for SPARC.”

Congressional Hearing and Staff Briefings

Senate staff from the Appropriations Subcommittee on Labor, Health and Human Services, Education and Related Agencies visited NIH in March. In April, Dr. Pettigrew and others presented testimony on biomedical innovation before the Senate Health Education, Labor and Pensions (HELP) Committee. In May, Dr. Pettigrew met with staffers of members of the House of Representatives Energy and Commerce, Budget, Ways and Means and other Committees

F. NIBIB Activities

Reverse Paralysis Consortium

NIBIB is leading a stakeholder consortium on spinal stimulation to address paralysis. An epidural spinal stimulation treatment developed by NIBIB grantee Dr. Reggie Edgerton and colleagues has improved bladder, bowel and sexual function in seven patients with complete motor paralysis, resulting in substantial improvement in their quality of life. Following a November 2014 workshop to discuss future research needs, NIBIB continues to explore collaboration with the Reeve Foundation to accelerate research in this important area.

Human Placenta Project

The Human Placenta Project is focused on generating an individualized fingerprint of placental well-being. This work requires development and optimization of new tools, with bioinformatics and imaging playing a key role. Some \$41 million is available for this research activity in FY15.

NIBIB-Coulter College Commercializing Innovation (C3i) Partnerships

The NIBIB-Coulter partnership program supports the Small Business Innovation Research (SBIR) community and helps investigators develop skills to become successful entrepreneurs. SBIR principal investigators (PIs) are paired with successful industry mentors to develop strategies for making their discoveries more rapidly available to the public.

Engineering-Focused Medical School Program

The University of Illinois at Urbana-Champaign recently announced a unique engineering-focused medical school program that could begin enrolling students as early as Fall 2017.

G. Science Highlights

Platelets in Health and Disease

Dr. Pettigrew described how researchers have created a functional model of the bone marrow system that produces platelets. Platelets are critical for clotting and wound healing, and their production is subject to mediation by infection, disease, and chemotherapy drugs. PI Dr. David Kaplan used silk scaffolds that mimic vasculature and allow platelet flow and hemodynamics in combination with a silk sponge material that mimics three-dimensional bone marrow and supports platelet formation. This system will facilitate further study of platelet production and function.

Predicting Sports-Related Concussions with an Instrumented Mouthguard

NIBIB grantee Dr. David Camarillo and NIBIB Diversity Supplement Awardee Fidel Hernandez at Stanford University recently published findings from their unique study on predicting sports-related concussions. Thirty-one subjects—collegiate football players, professional boxers, and a professional mixed martial artist—wore instrumented mouthguards that enable researchers to characterize the forces responsible for concussion in six degrees-of-freedom measures in three planes. Study findings show that peak principal strain in the corpus callosum was the strongest predictor of concussion, followed by two criteria that included rotation measurements—peak rotational acceleration magnitude and Head Impact Power.

Circulating Tumor Cell Clusters: Metastatic Prostate Cancer Patients

Dr. Pettigrew reported that Dr. Mehmet Toner is developing a chip to capture circulating cancer cell clusters from blood samples. These clusters are considerably rarer than individual cancer cells and thought to be more potent in causing metastatic disease. The study found that 30 to 40 percent of patients with breast and prostate cancers and melanoma had tumor clusters. The chip will be valuable for studying the biology of the cell clusters and has potential for biomarker and diagnostic studies.

III. Review of Council Procedures and Regulations: Dr. Jill Heemsker

Dr. Heemsker welcomed visitors and members of the science press and scientific society constituencies. She noted for the record that a quorum was present for this Council meeting. She acknowledged Ms. Pam Glikman and Ms. Alisha Hopkins for expert handling of meeting logistics. She noted that Council member A. Gregory Sorensen was absent.

Review of Council regulations, policies, and procedures, as well as conflict-of-interest, confidentiality, and lobbying guidelines, was deferred to the closed session.

A. Approval of the January 23, 2015, NACBIB Meeting Minutes

A motion to approve minutes of the January 23, 2015 NACBIB meeting was forwarded, seconded, and approved unanimously.

IV. Exploring Alternative Funding Models: Dr. Jon Lorsch

Dr. Lorsch presented an overview of the efforts of the National Institute of General Medical Sciences (NIGMS) to develop a more productive, efficient, and sustainable biomedical research enterprise.

One of NIGMS's strategic goals is to refocus its portfolio on investigator-initiated research. In FY 2014, these efforts contributed to a 5 percent jump in the success rate of investigator-initiated research applications.

Dr. Lorsch noted that 20 percent of scientists receive 50 percent of NIH funding, and it is generally thought that these highly-funded investigators are the most productive.. Yet, an increasing body of evidence from other NIH Institutes and other funders suggests that this assumption is incorrect. A 2010 analysis of publications and impact factors showed that awarding an R01 to a researcher who already has obtained \$400,000 in direct costs-funding produces one additional paper; awarding an R01 to someone who has no additional funding yields five papers, a four-paper difference in yield. An analysis conducted by the National Heart, Lung, and Blood Institute (NHLBI) reached similar conclusions. Using citations as the measure of impact, the NHLBI data show that productivity does not scale in proportion to funding levels.

NIGMS is using a new metric to guide its funding strategy: the number of investigators supported. By funding research programs instead of individual projects, NIGMS aims to increase funding stability that will enhance investigator willingness to take on ambitious scientific projects and to approach problems creatively; increase flexibility for investigators to follow new research directions as opportunities arise; improve distribution of funding among investigators to increase overall scientific productivity and maximize discovery; reduce time researchers spend writing grant applications so that they can spend more time conducting research; and reduce time spent reviewing grant applications.

NIGMS is piloting the Maximizing Investigators' Research Award (MIRA R35), which awards one NIGMS R35 per PI. The award is longer than current R01 averages (5 years instead of 4) and is not tied to specific aims. PIs will be reviewed based on their track records and overall research ideas moving forward, including consideration of their contributions to workforce development. Because constant funding fluctuation creates enormous inefficiencies with startup costs, budgets can be modulated during competing review in order to prevent abrupt termination of research groups. MIRA will have separate FOAs, review panels, and distinct review criteria for established PIs versus new investigators. If the pilot is successful, NIGMS will expand the approach to include all PIs who are working on questions relevant to the NIGMS mission.

Discussion

Dr. Rosen noted that the NIGMS approach is similar to the NIH intramural programs at many Institutes and asked whether the intramural model works for where NIGMS wants to go. Dr. Lorsch agreed that the intramural model is similar and intramural productivity is high..

V. Task Force Report: Dr. Bruce Tromberg

Dr. Tromberg reported for the Task Force on Strategies for Efficient Use of Research Dollars that was formed in May 2014. The Task Force was charged with assessing the needs of the biomedical imaging and bioengineering research community in the context of the NIBIB mission; initiating a broader discussion on the challenges associated with funding the technology-oriented mission of NIBIB; and developing recommendations for how NIBIB can most effectively use its limited resources.

The Task force has reached three key areas of agreement: (1) the issues surrounding the impact of peer review require more scholarly analysis; (2) NIBIB paylines (at 9th percentile) and success rates (at 13 percent) are much too low; and (3) the research community and society are suffering the consequences. Promising, potentially impactful ideas, technologies, and people are not being funded. This has led to erosion of the number of NIBIB investigators and their morale, lost scientific opportunities, disappearance or marginalization of fields and subfields, and too much of researchers' time being spent writing grant proposals.

Dr. Tromberg outlined six key strategies:

1. Establish target goals for increasing the NIBIB payline and marshal the financial resources needed to reach these targets.
2. Enhance NIBIB impact by increasing the number of investigators and diversity of NIBIB awards.

3. Develop new concepts to support investigators at crucial moments in their careers.
4. Assess whether the current structure has created funding inequities for underrepresented investigators and new applicants.
5. Build morale within the NIBIB research community perception and foster a spirit of inclusiveness and a desire to contribute to the NIBIB mission.
6. Advocate on behalf of NIH by highlighting the importance of biomedical research to society.

Dr. Tromberg described possible ways to implement each strategy. The Task Force Report outlining these recommendations will be made available on the NIBIB website.

VI. Funding Strategies Discussion

Dr. Sullivan asked whether the Task Force has considered using the Foundation for the National Institutes of Health to build partnerships. Dr. Tromberg responded that the task of bringing in substantial resources to NIBIB requires someone with a role similar to a university development director who is focused on this work full time.

Dr. Plant commented on how funding issues push investigators to publish too quickly. The recommended changes could reduce this pressure and stimulate opportunities for more careful research that addresses reproducibility concerns. Dr. Lorsch agreed that improved funding stability could ameliorate pressure to publish in a short timeframe.

Dr. Laurencin expressed concern about looking at the number of publications and citations per grant as an endpoint. Investigators funded via R03s and R21s must demonstrate meaningful results in a shorter timeframe than those with R01s, which accounts for variation in the numbers of publications. Dr. Lorsch explained that the NIGMS analysis looked at R01 equivalents, which mitigates concern about large versus small projects. In addition, these metrics were aggregated over a large number of investigators to look at the entire NIGMS research portfolio. Dr. Lorsch added that he would not use this metric to evaluate an individual investigator, although promotion and tenure committees are known to do so.

Dr. Laurencin asked whether the Task Force has considered crowdsourcing approaches that would involve the public in funding research. Dr. Tromberg noted that the Task Force has focused on identifying opportunities such as partnering with agencies that are aligned with the NIBIB mission. An ongoing advisory committee would be useful to investigate additional approaches.

Dr. Rastegar commented that the National Science Foundation (NSF) develops private/public partnerships on an ad hoc basis and is viewing this strategy with interest.

Dr. Weinbaum asked how other Institutes are achieving a higher success rate than NIBIB. Dr. Pettigrew explained that NIBIB's lower-than-average success rate is due to an imbalance between the NIBIB budget and the number of applications the Institute receives: NIBIB's budget is 1 percent of the total NIH budget, but NIBIB receives nearly 3 percent of applications submitted to NIH.

Noting that only investigators who have two or more NIGMS R01s are eligible to apply for the MIRA awards, Dr. Pettigrew asked why NIGMS did not include investigators with two NIH R01s. Dr. Lorsch answered that NIGMS wanted to define the applicant pool.

Dr. Lee remarked on the discrepancy between growth in the bioengineering field and national leading economic indicators. For the United States to be a leading economic influence in the world, we must continue to create new ideas and make fundamental discoveries. NIBIB must make the case to the general public that it is a good idea to support the work being done by the Institute.

Dr. Rosen remarked on the potential challenges of a hybrid model that combines smaller grants and investigator-specific grants.

Dr. Lorsch noted that longer-term awards—though desirable—have drawbacks. For example, regular scientific reviews occur less frequently. In addition, the longer the term of an award, the smaller the budget turnover; this could be problematic if there is a decrease in the overall budget.

Dr. Weinbaum suggested creating a prestigious yet modest young investigator award similar to the highly competitive NSF career award, which is investigator-oriented. Dr. Rastegar added that NSF recently increased their career award from \$400,000 to \$500,000 over five years.

Dr. Tromberg concluded that despite rigorous boundary conditions, there are options that could improve NIBIB's overall portfolio and increase optimism in the community. New NIBIB committees and task forces will need to focus on implementation of these options and continue to survey community response.

A motion to accept the Task Force Report and forward its recommendations to the Director was made, seconded, and approved.

VII. BRAIN Initiative Working Group Report: Dr. Bruce Rosen

Dr. Rosen reported on activities of the Brain Research through Advancing Innovative Neurotechnologies (BRAIN) initiative. NIH is focusing on brain circuits and networks and how their interaction creates humans' unique cognitive and behavioral capabilities. He noted that funding for BRAIN has slipped below projections. For example, the FY 2015 budget called for \$60 million in new money, but only \$25 million was received; contributions from various Institutes raised the total budget to \$81.4 million.

Current BRAIN goals include identifying the diversity of brain cell types and tracking their function throughout development; tracking movements of neurotransmitters in real time; developing a human brain imaging device 100 times more sensitive than magnetic resonance imaging (MRI); and developing a wearable positron emission tomography (PET) scanner to measure brain activity in daily life.

Future activities will focus on understanding links between circuits and behavior; measuring and modulating neural activity; partnering with manufacturers to facilitate access to novel stimulating or recording devices for clinical studies; engaging small business in development of tools and technology; and creating a culture of worldwide neuroscience research collaboration.

VIII. Expanding the Scope and Power of MR Instrumentation: Dr. Lawrence Wald

Dr. Wald presented an overview of recent advances in MRI hardware and acquisition. He noted that, as a noninvasive, flexible modality, MRI is perfectly positioned to bridge science with individualized healthcare. We have barely scratched the surface of MRI's potential.

Dr. Wald displayed a standard MRI image showing a gross anatomical picture of the brain in which the lobular structure and the cortex are visible, although barely resolved. More spatial resolution is needed to produce images at the next level of brain architecture—the laminar architecture of the cortex and the columnar architecture of neuronal units—and, eventually, to the neuron and synapse level. Fundamentally, there is no limit to what MRI can do, and with improved technology, MRI eventually may be used to look at the scale of pathology.

Dr. Wald offered an example of how improved MRI technology benefitted a patient, a 14-year-old girl with intractable epilepsy (i.e., 20 seizures per day, uncontrolled by medication). Standard MRIs showed no problems. An improved detector with higher sensitivity made it possible to produce a higher-resolution image showing improper formation of a small portion of the patient's cortex. After a surgeon removed the malformation, the patient became and continues to live seizure-free.

Since this case, MRI has been useful in identifying pathologies underlying epilepsy in other patients. Dr. Wald noted that he envisions expanding the use of MRI to identify the underlying pathologies of psychiatric spectrum disorders, thereby transforming their diagnosis and treatment.

Bigger Magnets and New Arrays

Expanding MRI capability has required bigger magnets and new technology. With 7 tesla (7T) technology, it is possible to produce very high-resolution images from the top of the brain to the bottom. Mastering the engineering aspects of 7T technology took about ten years, with much of that time focused on detector arrays, which are critical to determining scanner sensitivity and play an important role in encoding the image.

With new arrays, it is now possible to get high-resolution images of the corticospinal (C-Spine) tract. Dr. Wald showed MRI images of an amyotrophic lateral sclerosis patient that revealed inflammation around the C-Spine, pathology made visible for the first time.

Dr. Wald's work produced an exciting new tool that was useful to researchers at Massachusetts General Hospital (MGH). Yet, for these improvements to have a real impact, the tool must be translated for widespread clinical use. To accomplish this, Dr. Wald has partnered with Siemens Healthcare. The team produced a 32-channel array prototype, which Siemens evaluated and redesigned. The 64-channel head/neck array went through the same process. Today, these coil arrays are being used in thousands of labs and clinical MRI facilities around the world.

New methods and high-channel-count coils have made it possible to obtain tenfold and higher accelerations in the time required to obtain images. For example, the simultaneous multislice method introduced in 2001 was not widely accepted because it was difficult to disambiguate the pixels from three "pancaked" images; 32-channel coils were not readily available at the time. Using 32-channel coils made it possible to shift the middle image by one-half field of view, dramatically simplifying the problem; three clean images can be pulled apart without loss of sensitivity. With high-channel-count coils, diffusion imaging can be done three times faster with no penalty in signal to noise.

With fMRI, 12 slices can be acquired simultaneously; 170 slices per second are reconstructed on a scanner. This is an unprecedented increase in temporal resolution of fMRI.

Extending this approach to anatomical imaging, a three-dimensional (3D) volume scan can be taken ten times faster than with traditional methods at a loss in sensitivity of 10 percent, which is barely noticeable to the eye. Obtaining a half-millimeter, isotropic-resolution, whole-brain 3D image at 7T would normally take an hour to encode but now takes about five minutes.

"Garden variety" clinical imaging also can benefit from these advances. For example, turbo spin echo implementations of the RARE (Rapid Acquisition with Refocused Echoes) technique can be completed ten times faster.

New technology also has transformed functional brain imaging—moving from lobes and the cortex to laminar and columnar resolution and, equally important, from group averages to individual subject results. Driven by acceleration and improved detectors, these advances have resulted in a huge increase in voxel volume. Dr. Wald described several fMRI applications, from simple topographic maps of the visual field to deeper areas of the brain that are more difficult to image.

Targeted Contrast Agents

The introduction of targeted contrast agents shows great promise for highlighting disease. Challenges include (1) obtaining approval to use relatively high doses of the agent in humans and (2) picking out small changes against a complex image background.

To address these challenges, Dr. Wald's team used a sort of "spot the difference" approach, similar to the blink comparators that astronomers use to spot a nova in a star field. To make this method work, the pre/post interval must be very short to eliminate patient movement. Dr. Wald's team introduced an external excitation step to modulate the contrast agent—turning it on and 10 milliseconds later turning it off. The team has tested several excitation methods, including external acoustic waves and magnetic particles.

Modulating the contrast agent in this way has produced a 100-fold increase in the ability to see contrast changes. This huge effect could allow scientists to cut the contrast agent dose in half.

Portable Units

Portable imaging units can be used in the field to answer simple but important questions. In Berlin, an ambulance equipped with a computerized tomography scanner is sent in response to suspected stroke emergencies; the scan is used to rule out hemorrhage so that paramedics know whether it is safe to use a blood thinner. The image quality may not be optimal, but the special-purpose device can answer a specific clinical question. Why not do this with MRI?

Challenges to portable MRI units include the cryogenics, heavy magnets, high electrical demands, and high cooling demands. The device must plug into a standard outlet in an oncologists' office without special shielding. It must be lightweight and portable, and the image quality must be good enough to answer specific clinical questions (e.g., detecting bleeds, monitoring hydrocephalus treatment, monitoring edema in brain tumor treatment).

Dr. Wald's team undertook constructing a small MRI using a 45-kg magnet in a birdcage arrangement that creates a "uniform-ish" field. The magnet is rotated around the patient's head. The changing inhomogeneous field is used to encode the position of water in the head and compute an image. The next step is to place prototypes in the MGH emergency room and the CURE Uganda Children's Hospital.

Training Future Engineers

Dr. Wald described his association with a Massachusetts Institute of Technology sophomore-level course that uses medical devices to teach the principles of signal processing. The course required 20 fully programmable, tabletop MRI scanners. Dr. Wald's goal was to keep costs down while ensuring that the scanners produced quality images that would excite the students about MRI. He added that his graduate students learned a great deal during the process of building the tabletop MRI system; they were drawn to making them better.

Discussion

Dr. Lee asked how close the technology is to obtaining useful information about the folded states of proteins. Dr. Wald stated that there are methods to look at how a protein might perturb free water, but looking at actual protein structure is close to science fiction. Perhaps a contrast agent could be created to react in a particular way with one protein.

Dr. Tromberg asked about the scale of displacement sensitivity in the acoustic wave method Dr. Wald described. Could frequency dependence be used to map mechanical properties? Dr. Wald responded that it is plausible to sweep for hundreds of frequencies to try to observe the mechanical nature of whatever the contrast agent is bound to. A displacement of at least a couple of microns would be necessary to produce visible effect. Dr. Wald says he presents this very preliminary, speculative work to get other people thinking about how to "kick" the contrast agent to see that effect with MRI.

Dr. Heetderks asked Dr. Wald to describe his strategy for the nonlinear field MR using the next-generation magnet. Dr. Wald explained that his team is using a genetic algorithm to optimize magnet placement, which has proven much better than human placement. It would be better to design directly for that linear term, but this has been computationally excessive.

Dr. Pettigrew asked what challenges remain related to the portable units. Dr. Wald noted that the biggest challenges include radiofrequency shielding and determining how frequently the equipment must be calibrated. In terms of operational expertise, the equipment will have only four buttons (i.e., T1, T2, proton density, and diffusion), eliminating the need for user input that would require intensive training.

Dr. Pettigrew asked how Dr. Wald deconvolves the composite signal from an inhomogeneous magnetic field. Dr. Wald responded that he is intrinsically coding a 3D image, which is put into a model and inverted all at once.

Dr. Pettigrew commended Dr. Wald for his inventive approach that has led to so many new ways to use MRI technology, which has reached a substantial level of maturity.

IX. Adjournment

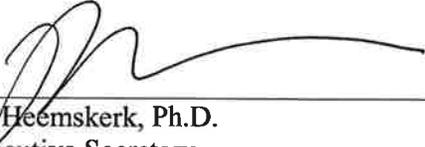
The open session of the NACBIB meeting was adjourned at 12:50 p.m.

X. Closed Session

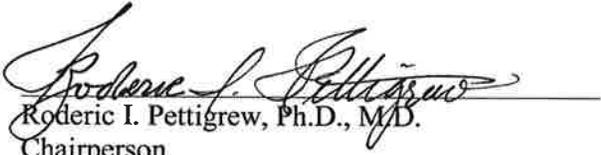
The grant application review portion of the meeting was closed to the public in accordance with provisions set forth in Sections 552b(c)(4) and 552b(c)(6), Title 5, U.S. Code, and 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. appendix 2). The closed session was adjourned at 2:45 p.m.

Certification:

We certify that, to the best of our knowledge, the foregoing minutes are accurate and complete.¹



Jill Heemskerk, Ph.D.
Executive Secretary
National Advisory Council for Biomedical Imaging and Bioengineering
Director, Office of Research Administration
National Institute of Biomedical Imaging and Bioengineering



Roderic I. Pettigrew, Ph.D., M.D.
Chairperson
National Advisory Council for Biomedical Imaging and Bioengineering
Director, National Institute of Biomedical Imaging and Bioengineering

¹ These minutes will be approved formally by the Council at the next meeting on September 18, 2015, and corrections or notations will be stated in the minutes of that meeting.