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

NATIONAL ADVISORY COUNCIL FOR BIOMEDICAL IMAGING AND BIOENGINEERING Summary of Meeting¹ September 12, 2013

The National Advisory Council for Biomedical Imaging and Bioengineering (NACBIB) was convened for its 33rd meeting on September 12, 2013, 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 9:15 a.m. to 12:00 p.m. for review and discussion of program development, needs, and policy. The meeting was closed to the public from 1:00 p.m. to 2:30 p.m. for the report of the Board of Scientific Counselors and the consideration of grant applications.

Council members present:

Dr. John C. Gore, Vanderbilt University, Nashville, TN

Dr. W. Eric L. Grimson, Massachusetts Institute of Technology, Cambridge, MA

Dr. Nola M. Hylton, University of California, San Francisco, CA

Dr. Cato T. Laurencin, University of Connecticut, Farmington, CT

Dr. Raphael Lee, The University of Chicago, Chicago, IL

Dr. Mark Musen, Stanford University, Stanford, CA

Dr. Bruce J. Tromberg, University of California, Irvine, CA

Dr. Sheldon Weinbaum, The City College of New York, New York, NY

Dr. Michael Yaszemski, Mayo Clinic College of Medicine, Rochester, MN

Council member attending by telephone:

Dr. Etta D. Pisano, Medical University of South Carolina, Charleston, SC

Ex officio members present:

Dr. Anne Plant, National Institute of Standards and Technology, Gaithersburg, MD Dr. Sohi Rastegar, National Science Foundation, Arlington, VA

Council member absent:

Dr. James H. Thrall, Harvard Medical School, Boston, MA

Ex officio members absent:

Dr. Francis Collins, National Institutes of Health, Bethesda, MDDr. P. Hunter Peckham, U.S. Department of Veterans Affairs, Cleveland, OHMs. Kathleen Sebelius, U.S. Department.of Health and Human Services, Washington, DCDr. James G. Smirniotopoulos, Uniformed Services University of the Health Sciences, Bethesda, MD

Chairperson: Dr. Roderic I. Pettigrew

Executive Secretary: Dr. Anthony Demsey

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 applications that are discussed individually, not to "en bloc" actions.

Also present:

NIBIB staff present for portions of the meeting: Mr. Angelos Bacas Dr. Richard A. Baird Ms. Barbara Cantilena Ms. Shirley Coney-Johnson Dr. Richard Conroy Ms. Christine Cooper Ms. Zoe Ann Copeland Ms. Nancy Curling Ms. Monique Day Mr. Jeff Domanski Mr. Anthony Dorion Dr. Henry Eden Ms. Kate Egan Ms. Angela Eldridge Ms. Kathryn Ellis Dr. Zeynep Erim Dr. David George Ms. Marie Gill Ms. Pam Glikman Dr. Ruth Grossman Dr. John Hayes Ms. Eunica Havnes Dr. William Heetderks Ms. Alisha Hopkins Mr. James Huff Dr. Rosemarie Hunziker Mr. Tom Izzard Dr. Thomas Johnson Dr. Chris Kelley

Dr. Brenda Korte Dr. Steven Krosnick Dr. Richard Leapman Ms. Karin Lee Dr. Christina Liu Dr. Guoying Liu Dr. Hector Lopez Dr. Xiao-Zhong (James) Luo Dr. Shadi Mamaghani Ms. Jessica Meade Mr. Todd Merchak Mr. Joe Mosimann Dr. Peter May Dr. Vinay Pai Dr. Grace Peng Dr. Karen Peterson Ms. Christine Rogers Mr. Rolaudo Romero Ms. Stephanie Sabourin Dr. Antonio Sastre Dr. Belinda P. Seta Dr. Hari Shroff Mr. Shaun Sims Ms. Jessica Tucker Ms. Florence Turska Ms. Keisha Whitaker-Duncan Mr. Kwesi Wright Dr. Ruixia Zhou Dr. Steven Zullo

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

Dr. Yvonne Bennett, Center for Scientific Review

Non-NIH Federal employees: None

Ms. Margot Kern

Members of the public present for portions of the meeting:

Mr. William Portobanco, Bolger Center Mr. Michael Peters, American College of Radiology Ms. Kathy Sedgwick, NOVA Research Company Ms. Shawn Willis, National Capitol Captioning, LLC

I. Call to Order: Dr. Anthony Demsey

Dr. Anthony Demsey called to order the 33rd meeting of the National Advisory Council for Biomedical Imaging and Bioengineering. He reminded attendees that the morning session of the meeting would be open to the public, welcomed attendees, and introduced Dr. Roderic Pettigrew, who formally welcomed all participants.

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

A. New Council Members

Dr. Pettigrew introduced Dr. Raphael Lee and welcomed him to the Council.

B. Awards

Dr. Pettigrew reported that NIBIB investigator Dr. Lihong Wang, Washington University in St. Louis, MO, received the 2014 Institute of Electrical and Electronics Engineers (IEEE) Biomedical Engineering Award "for pioneering photoacoustic tomography." Dr. Wang was recognized for his outstanding contributions to biomedical engineering.

C. FY 2013 Budget

Dr. Pettigrew described the impact of sequestration and other budget cuts that amounted to a \$1.6 million reduction in the NIH budget during Fiscal Year 2013. As a result, approximately 700 fewer grants were awarded and about 700 fewer patients were admitted into clinical protocols being conducted at the NIH Clinical Center.

These reductions present a particular challenge to NIBIB because, as the budget has been shrinking, the number of meritorious applications NIBIB receives has expanded. For example, the number of applications under consideration at the September 2013 Council is more than twice the number that were considered at the Council meeting five years ago, when the NIBIB budget was roughly about the same. NIBIB and the Council will continue to discuss and explore ways to fund as much meritorious research as possible.

D. NIH Activities Update

Initiative to Enhance Reproducibility and Transparency of Research Findings

Dr. Pettigrew described a new NIH initiative designed to address significant concerns about a lack of reproducibility and transparency of critical findings, particularly in preclinical research. The problem is evidenced by the increased number of drug trials that fail based on inadequate, unsubstantiated, or errant data. Examples include the failure of an amyotrophic lateral sclerosis (ALS) drug trial and a 2011 report indicating that pharmaceutical firm Bayer HealthCare could not validate the relevant preclinical research for nearly two-thirds of 67 in-house projects. These concerns about bias and a lack of overall statistical and scientific rigor point to the need for reform in the way that research is reviewed.

Specific underlying issues include poor training and evaluation as well as perverse reward incentives such as the push to publish quickly. Principles for resolving these issues include raising awareness, enhancing training, improving evaluation of applications, protecting the integrity of science by adopting more systematic review processes, and increasing stability for investigators. NIH Institutes and Centers are conducting pilot studies to evaluate the process of the "scientific premise" of grant applications; developing a checklist to systematically evaluate grant applications; altering the biosketch format; reducing "perverse incentives" by enhancing support to experienced investigators; and supporting replication studies.

Big Data

Dr. Pettigrew provided an update on NIH efforts to address the challenge of maintaining, analyzing, and sharing massive datasets. The Big Data 2 Knowledge website (bd2k@nih.gov) was launched recently, and the first funding opportunity announcement (FOA) has been released. These awards will fund centers of excellence to develop approaches and methods aimed at sharing, analyzing, and evaluating large datasets. The plan is to fund six to eight investigator-initiated Centers at a level of \$3 to \$4 million each.

Increasing Diversity of the NIH-Funded Workforce

The NIH Common Fund has launched a program designed to support development of transformative approaches toward increasing recruitment and retention of people from backgrounds that are underrepresented in biomedical research across the lifespan of research or research-related careers. The program comprises three integrated initiatives: Building Infrastructure Leading to Diversity (BUILD), the National Research Mentoring Network (NRMN), and the Coordinating and Evaluation Center.

BUILD will provide research experiences for undergraduates and resources for faculty at underresourced institutions with high concentrations of students from disadvantaged backgrounds. NRMN will coordinate nationwide pairings of students and faculty for robust mentoring relationships, develop best practices for mentoring, and provide training for mentors. The Coordinating and Evaluation Center will assess BUILD and NRMN initiatives and coordinate resource sharing among BUILD, NRMN, and other diversity programs.

E. NIBIB Activities Update

New NIBIB Website

Dr. Pettigrew described the new look and improved functionality of the NIBIB website. The site now offers quick access to funding opportunities, science news and highlights, and multimedia content. A new science education section includes fact sheets, videos, and other classroom-friendly content. The site has improved search technology and site navigation, and is now optimized for mobile devices. Dr. Pettigrew displayed some of NIBIB's activities on social media channels and presented a sample video, "Science in 60 Seconds."

Dr. Pettigrew showed a second video that featured scientific advances supported by NIBID. "Six Awesome Technologies That Your Tax Dollars Paid to Create" highlighted the following technologies: organ transplants for mice; dissolving stents; the world's smallest magnetic resonance imaging (MRI) machine; a handheld ultrasound machine; a polymer that curls when exposed to water; and electrode implants in paraplegics.

NIBIB Partnership with India: Unobtrusive Technologies to Measure Blood Pressure

NIBIB is supporting a \$2 million Request for Applications (RFA), for which India is offering a parallel opportunity, to transform detection and management of hypertension, the leading contributor to deaths worldwide. Many people with high blood pressure are unaware they have it, and treatment is often ineffective due to poor compliance and inadequate monitoring. Therefore, the goal is to develop technologies that would provide feedback to patients and clinicians in low-resource settings.

NIBIB DEBUT Challenge 2013 Winners

Dr. Pettigrew announced the winners of the 2013 NIBIB Design by Undergraduate Teams (DEBUT) Challenge. This year, there were 31 entries from 19 universities in 14 states.

The Diagnostic Devices category winners were from the University of California, Los Angeles. They designed a high-throughput, microfluidic device to monitor enzymatic activity as a means to assess efficacy of a drug on a patient-by-patient basis prior to its administration.

A Dartmouth University team won the Therapeutic Devices category. They developed a novel microflora refinement system for fecal microbiota transplantation. The automated, hands-off system uses fecal microbiota transplantation to restore a healthy gut bacterial ecosystem after infection by Clostridium difficiles, a pathogen that typically is unresponsive to antibiotics.

In the Technology to Aid Underserved Populations and Individuals with Disabilities category, a team from Rice University developed an accurate, low-cost mechanical device to regulate intravenous fluid delivery for children in the developing world. The device employs a counterbalance weight system that does not

require electricity or electronic components. Dr. Pettigrew presented a brief video of a demonstration of this device. Dr. Pettigrew commented that last year's winners in this category have created a company to manufacture the \$10 spirometer they developed.

F. Upcoming Events

The Multi-Scale Modeling Consortium is scheduled to meet in early October at the Interagency Modeling and Analysis Group annual meeting. This meeting will focus on drug discovery and development and multicellular tissue models.

The National Cancer Institute (NCI)-NIBIB Point of Care Technologies for Cancer conference also is scheduled to take place next month. A number of NIBIB grantees will make presentations.

G. Grantees

Dr. Pettigrew highlighted recent developments from NIBIB grantees.

NIBIB grantee Dr. Yuni Dewaraja at the University of Michigan has developed a technological approach to predicting success of specific therapeutic doses in non-Hodgkin lymphoma (NHL) patients. A large number of NHL patients relapse and die after standard treatment, and new radioimmunotherapy treatment options have not been adopted due to the inability to determine the delivered dose to the tumor on a tumor-by-tumor and patient-by-patient basis. Dr. Dewaraja's approach combines modeling techniques and conventional nuclear imaging using SPECT/CT to determine tumor- and patient-specific effective doses prior to delivery and implementation of therapy.

NIBIB grantees at the Massachusetts Institute of Technology (MIT)—Klavs Jensen and Bob Langer—have advanced the somewhat challenging technology of delivering target macromolecules (e.g., genes, proteins, quantum dots) into the cell, a promising technology with potential value in laboratory investigations as well as therapeutic applications. Other techniques such as electroporation and chemical poration can destroy the cell. The MIT approach passes cells and fluid through a constricted channel, temporarily deforming the cells and creating pores in the lipid bilayer membrane that allow macromolecules to penetrate the cell. Broadly applicable to a variety of cells, including those that previously have been difficult to transfect, the technique has a transfection efficiency ten times greater than that of electroporation.

Discussion

Dr. Grimson complimented the NIBIB team on the website features, especially in light of current budgetary restrictions. Dr. Hylton concurred and asked about availability of videos for use in high school science classes. NIBIB staff member Kate Egan responded that the videos are available on YouTube and Facebook, and NIBIB staff are working to broaden distribution to science teachers.

Dr. Laurencin commented that as fund levels are dropping, investigators are submitting more applications. With biomedical engineering being the fastest growing engineering discipline, numerous new faculty members are entering the workforce. Dr. Pettigrew clarified that the number of high-scoring applications is disproportionate to the increase in number of applications; submissions have increased 17 to 20 percent, while the proportion of high-scoring applications has increased 80 percent in the last four years.

Dr. Weinbaum asked about the small number of submissions to DEBUT. With all undergraduate biomedical engineers required to do senior design projects, there is great potential to increase the number of applications. Dr. Heetderks indicated that NIBIB staff are looking for ways to increase that number.

Dr. Lee expressed his delight that NIBIB is involved in the Big Data initiatives. Creating models to understand these data is critical, and NIBIB participation in these efforts is key.

III. Review of Council Procedures and Regulations: Dr. Anthony Demsey

Dr. Demsey noted for the record that a quorum was present for this Council meeting. Council members Drs. Etta Pisano and James Thrall were unable to attend. Dr. Pisano would join the afternoon session via telephone. Ex officio members Peckham and Smirniotopoulos also were unable to attend. Dr. Demsey welcomed visitors and members of the science press and scientific society constituencies. He thanked Ms. Pam Glikman for her efforts in planning the meeting.

A. Council Regulations, Policies, and Procedures

Dr. Demsey summarized elements of the Government in the Sunshine Act and the Federal Advisory Committee Act that govern all Advisory Council meetings. These Acts require the U.S. Department of Health and Human Services to open Advisory Council meetings to the public except when proprietary or personal information is discussed. To comply with these regulations, NACBIB meetings are open to the public except during review of individual grant applications. Dr. Demsey reviewed conflict of interest, confidentiality, and lobbying guidelines.

B. Future NACBIB Meeting Dates

The next NACBIB meeting is scheduled for Thursday, January 23, 2014. Dr. Demsey asked Council members to inform him about conflicts with any of the upcoming meeting dates listed at the bottom of the agenda.

C. Approval of the May 17, 2013, NACBIB Meeting Minutes

A motion to approve minutes of the May 17, 2013, NACBIB meeting was forwarded, seconded, and approved unanimously.

IV. Working Group Report: Dr. William Heetderks

Dr. Heetderks summarized working group discussions, most notably about joint activities with NCI and translational science. One idea under consideration is a program director exchange to increase interaction and encourage NCI and NIBIB staff to work together. Working group members also emphasized the potential for adding imaging studies to ongoing NCI trial designs.

The working group discussed program progress reviews and the recent molecular imaging meeting in the context of accelerating translation of molecular imaging technologies and devices from bench to bedside. Available data support a strong case that these technologies not only work but also are cost-effective. Members of the working group agreed that NIBIB should be more assertive in its efforts to collaborate with the Center for Medicare and Medicaid Services.

In addition, the working group considered ways to fund translational work using new kinds of awards such as TR01s and Pioneer Awards. These mechanisms are a better fit for "impactful risk" activities—high-risk efforts that have potential to be extremely useful—that are not a good fit for traditional mechanisms like R01s.

Dr. Tromberg added that NIBIB is uniquely positioned to translate technology and devices to the clinic. He remarked that development of probes in the absence of technology to deliver them is an area where NIBIB could provide a push.

V. Imaging Biology at High Spatiotemporal Resolution: Dr. Hari Shroff

Dr. Shroff outlined his efforts to develop novel microscopy techniques for use in studying biological processes of unprecedented temporal and spatial resolution. His primary focus has been fluorescence microscopy, which offers the advantages of excellent contrast and specificity, multiple colors, and high-speed live imaging. The diffraction limit presents a challenge in fluorescence microscopy. When the

fluorescence emitted from a protein is visualized in an optical microscope, the image is 100 times larger than the actual molecule. A great deal of detail is lost due to the blurring of the fluorescence emission.

Super-resolution microscopy attempts to circumvent the diffraction limit by triggering only a few, wellseparated molecules to glow at one time. Turning these molecules off and on through many cycles builds a super-resolution image of the molecule centers and creates a picture that is closer to reality. This "pointillist" method employs various switchable dyes to enable isolation of fluorescence.

Dr. Shroff's postdoctoral work focused on making photoactivated localization microscopy (PALM) more applicable to cell biology. Upon joining NIBIB's newly formed intramural program in 2009, he began working with PALM in three dimensions and quickly recognized the challenge presented by the time required to acquire and build three-dimensional images. Two-dimensional acquisition took one to ten seconds, whereas three-dimensional acquisition can take hours. Many phenomena inside cells or tissues (e.g., microtubules moving inside a cell, cell division, or calcium waves) occur at fast timescales. Dr. Shroff realized he needed to develop techniques that are more appropriate for imaging these faster phenomena inside living cells. This led to his work in structured illumination microscopy (SIM).

Shining sharply patterned light on a fluorescent specimen creates interference, which allows higher resolution information in the specimen to be encoded into lower resolution information observable in the microscope. Encoding higher resolution information and using mathematics to mix the frequencies can increase resolution. This technique is relatively fast, and the mathematical processing rejects computationally out-of-focus light so that samples appear very crisp on a dark background.

Unfortunately, mathematics alone cannot remove out-of-focus light in thicker samples. Solving this problem requires depth penetration. Sweeping the illumination source throughout the sample and recording the fluorescence one point at a time enables microscopers to build the whole volume of a specimen in thicker samples.

Dr. Shroff's next challenge was increasing the resolution of a confocal microscope. He discovered that a team of scientists in Germany (Müller and Enderlein) had published a paper describing a mathematical approach that doubles the resolution; their image scanning microscopy (ISM) combines the resolving power of conventional confocal-laser scanning microscopy with a fast, wide-field microscope, and doubles lateral optical resolution in fluorescence imaging.

Although SIM is much gentler than PALM on living samples, unfortunately, SIM implementation is very slow. Thus, Dr. Shroff's team developed a concept for dramatically increasing the speed of this technique called multifocal SIM (MSIM). This method uses a parallelized approach with many excitation foci and permits super-resolution imaging up to approximately 2 Hz. MSIM provides resolution doubling in three dimensions and the ability to look at thicker specimens. In addition, its simple design and implementation makes it five to ten times cheaper than commercially available confocal microscopes. The MSIM code is open source and is available via the web so that other laboratories can use it.

Producing one super-resolution SIM image requires capturing many raw images (i.e., from 10 to 100). This constrains speed and increases data storage and processing needs. The key to solving this complication became clear when Andrew York, Dr. Shroff's postdoctoral fellow, noted that every digital processing step in MSIM has an optical analog. Some of these steps can be accomplished with hardware; for example, a mask can be built to reject the out-of-focus light. This new "instant SIM" (iSIM) approach offers super-resolution as fast as the camera frame rate will allow. Using multiple colors makes it possible to image the interaction between two components. Dr. Shroff expects that the technology can be used in single cells and whole embryos. At present, the microscope at NIH is the only one of its kind in the world that can perform at this level. Dr. Shroff's team is working to commercialize the microscope so that others can do this kind of work.

Although iSIM is less damaging to live samples, it is not appropriate for studying biological phenomena that occur over the course of hours or days, such as neurodevelopment. Researchers have identified the transparent C. elegans worm as a model that can be used to identify general principles of neural

development. Dr. Shroff and a team of scientists from Yale, Sloan Kettering, and the University of Connecticut are building a four-dimensional atlas of neural development in C. elegans; that is, they are optically reconstructing neurodevelopment decisions of all 222 neurons in the worm embryo. A first draft of the digital model of the worm's adult nerve ring is available via a website (wormguides.org), with links to crucial information about each cell's function, gene expression profile, and network of synapses and cell-cell interactions.

Dr. Shroff described a conceptual approach for studying the embryo without damaging or killing it—tailoring the light to illuminate only the plane that is seen by the camera. By shaping the illumination into a sheet and rapidly scanning this through the volume, one can quickly acquire a three-dimensional volume without dosing the embryo unacceptably. Although the light sheet concept dates back over 100 years, when the technique was used to investigate colloidal properties of gold, the complexity of device requirements made its application impractical. About 10 years ago, Ernst Stelzer published a paper about using light sheets to study whole fish embryos without killing them. The technique was called Selective Plane Illumination Microscopy (SPIM). Dr. Shroff's team developed inverted microscope-based SPIM (iSPIM) as a module that can be added to a conventional microscope base. The module includes two objectives positioned at 90 degrees with respect to one another; one brings in a light sheet that is scanned rapidly through the volume while the other objective collects the fluorescence at 90 degrees.

The most recent technical innovation on this microscope is the dual-view iSPIM system (diSPIM), which allows imaging of multiple planes in less than one second. This system is about 30 times faster than any other four-dimensional imaging technology of comparable signal-to-noise ratio. The diSPIM enables qualitative inspection of features that otherwise would be invisible, as well as qualitative characterization of the growth and the velocity of these neurons as they move through the embryo.

The Shroff lab team is writing a program to virtually untwist twitching embryos. This will make it easier to align multiple datasets. Dr. Shroff indicated that this same scheme might be applied to other, more complicated animals that also move a great deal during the embryogenesis phase of development.

Questions and Discussion

Dr. Pettigrew remarked that Dr. Shroff is investigating how to achieve the optimal temporal resolution necessary to understand biological processes; that is, the speed at which communication signals are transmitted within biological systems. He asked Dr. Shroff to define his goal in terms of increasing temporal resolution. Dr. Shroff responded that measuring volume in a behaving organism would require improving volumetric speed at least two orders of magnitude. The necessary instrumentation is available today, but dyes that are proportionally brighter do not yet exist.

Dr. Pettigrew commented that the neurodevelopment project is inspiring, with its focus on discovering how neurons make the appropriate connections and how that occurs in space and time. He asked

Dr. Shroff how he is addressing the logistical and practical problems of working with different groups and, particularly, how they are matching multiple datasets in space and time. Dr. Shroff indicated that all four groups of collaborators were together over the summer, which provided an unprecedented opportunity to troubleshoot the project. All data are uploaded to a server farm. Once the team has solved the embryo-twisting problem, they will tackle how to combine data from multiple embryos.

Dr. Gore inquired about the possible role for compressed sensing techniques. Dr. Shroff replied that investigators are just beginning to use those methods in terahertz imaging but not so much in fluorescence.

Dr. Tromberg commented that molecular interactions also are embedded in the images Dr. Shroff is capturing. He asked whether the team has looked at fluctuation correlation techniques to try to understand those interactions. Dr. Shroff agreed that this is a good idea; he needs the right person to analyze the data.

Dr. Lee asked Dr. Shroff what point-spread function he is using. Dr. Shroff explained that the investigators modeled the point-spread function from a bead they collected on a gel. This becomes more complicated in thicker specimens, but the worm embryos are relatively small. The microscopy research

community deals with this issue by using adaptive optics, a technique borrowed from astronomy; they adjust the illumination or emission such that they achieve an ideal point-spread function.

Dr. Weinbaum described his interest in imaging dendritic cells that have a 20- to 30-micron-long process and asked whether this could be done with the new microscopy techniques. Dr. Shroff responded that, in principle, this is within the realm of possibility. Indeed, looking at just a few molecules relaxes some of the constraints on the types of dyes that can be used.

Dr. Seto asked whether it is possible to track proteins going through the endoplasmic reticulum Dr. Shroff had shown. Dr. Shroff indicated that it could be done, if an appropriate fluorescent label could be identified.

VI. Adjournment

The open session of the NACBIB meeting was adjourned at 12:00 p.m.

VII. Closed Session

The grant application review portion of the meeting was closed to the public in accordance with provisions set forth in Section 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 2:30 p.m.

Certification:

We certify that, to the best of our knowledge, the foregoing minutes are accurate and complete.²

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Anthony Demsey, 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

 $^{^{2}}$ These minutes will be approved formally by the Council at the next meeting on January 25, 2014, and corrections or notations will be stated in the minutes of that meeting.