Early Results from Alzheimer's Neuroimaging Biomarker Project

Alzheimer's disease (AD) researchers soon may be able to reduce the time and expense associated with clinical trials, according to early results from the AD Neuroimaging Initiative (ADNI), a public–private research partnership organized by the National Institutes of Health (NIH). Preliminary results from the ADNI, presented at the Alzheimer's Association International Conference on the Prevention of Dementia (June 9–12; Washington, DC), outlined ways in which the results of the study may yield improved methods and uniform standards for imaging and biomarker analysis.

The ADNI study observes and tracks changes in healthy individuals, in those with mild cognitive impairment (MCI), and in those with AD. PET and MR results are correlated with laboratory analyses and clinical interviews to track cognitive performance over time. The $60-million, 5-year study began recruiting in early 2006 and has enrolled about 800 older individuals at 58 sites in the United States and Canada. The project is supported primarily by the NIH National Institute on Aging (NIA), with private sector support from pharmaceutical companies, other organizations, and the Alzheimer's Association through the Foundation for NIH. In addition to NIA, other federal partners are the NIH National Institute of Biomedical Imaging and Bioengineering and the Food and Drug Administration.

At the conference in Washington, ADNI principal investigator Michael Weiner, MD, of the Department of Veterans Affairs Medical Center and the University of California, San Francisco, gave a progress report and described the new ADNI database. Nine other ADNI researchers also reported on early results and preliminary findings from various studies, several of which focused on the results of early imaging efforts. A University of California, San Diego study found that MR and PET data could detect early cerebral cortex changes over a 6-month period in individuals with MCI. Additional studies will be needed to see whether these changes can predict timing and severity of progression to AD. A study reported by researchers at the Banner Alzheimer's Institute (Phoenix, AZ) compared PET changes over time in individuals with normal cognition, MCI, and AD and found that symptoms and images associated with each of these statuses were comparable and consistent across different clinical sites, a prerequisite for proceeding with multisite clinical trials using these imaging techniques in AD. A Mayo Clinic (Rochester, MN) study found that a single anatomic model of a brain may be used successfully to monitor performance of MR scanners at many different clinical sites, setting a valuable standard to ensure accuracy across the 80 MR devices that will be used over the study period.

A significant achievement of the ADNI is the creation of a publicly accessible database available to qualified researchers worldwide. The database already contains thousands of MR and PET brain images and clinical data and will include biomarker data obtained through blood and cerebrospinal fluid analyses. The database currently includes samples and brain images from 200 individuals with AD, 400 individuals with MCI, and 200 healthy adults. All are between 55 and 90 years of age.

"The database gives ADNI researchers easy access to a huge body of data. But its added value is its design as an international research resource, available worldwide to other researchers interested in neurodegenerative disease," said Susan Molchan, MD, NIA program director for ADNI. To date, more than 200 researchers have signed up for database access. Investigators may apply for access to ADNI data through the Web site at www.loni.ucla.edu/ADNI. In addition, qualified scientists may also ask for access to cerebrospinal fluid and blood samples. An application form is available under the "Scientist Home Page" link at www.adni-info.org.

Alzheimer's Disease Neuroimaging Initiative

Imaging and NIH High-End Instrumentation Grants

The National Center for Research Resources (NCRR), a part of the National Institutes of Health (NIH), announced announced on June 12 that it will provide $20.65 million for 14 high-end instrumentation (HEI) grants to fund cutting-edge equipment required in biomedical research. Of these projects, 9 will focus on advanced imaging techniques. Awarded to research institutions around the country, the grants support the purchase of sophisticated instruments costing more than $750,000.

"These high-performance imaging instruments and other advanced technologies enable both basic discoveries that shed light on the underlying causes of disease and the development of novel therapies to treat them," said Barbara Alving, MD, NCRR director. "The value of this investment in advanced equipment is greatly leveraged because each of these rare tools is used by a number of investigators, advancing a broad range of research projects." To qualify for an HEI award, institutions must identify 3 or more NIH-funded investigators whose research requires the requested instrument.

Among the imaging systems to be funded in this round of HEI grants are: (1) PET tracer development and production equipment at the University of Wisconsin School of Medicine and Public Health (Madison); (2) a 7T

human MR imaging and spectroscopy system at Vanderbilt University (Nashville, TN); (3) a high-field 9.4T MR small animal scanner at the University of Texas Health Sciences Center (San Antonio); (4) a 3T MR scanner at the Brigham and Women's Hospital (Boston, MA) for research on image-guided interventions; (5) a similar unit at the Nathan S. Kline Institute for Psychiatric Research (Orangeburg, NY) for neurologic studies; (6) a nuclear MR spectrometer to study intermolecular interactions at the Burnham Institute for Medical Research (La Jolla, CA); (7) another nuclear MR spectrometer to research protein structure, function, and folding at the University of Connecticut School of Medicine and Dentistry (Farmington); (8) a high-performance, electron microscope to enable 3D imaging of sections of cells and biological tissues at the University of California, San Diego; and (9) a confocal hybrid imaging system at the University of Maryland Biotechnology Institute (Baltimore, MD). Other funding will go to mass and hybrid spectrometers and DNA sequencing instrumentation at Johns Hopkins University (Baltimore, MD); the University of Arizona (Tucson); the University of Colorado Health Sciences Center (Denver); the University of Washington (Seattle); and Yale University (New Haven, CT).

More information about the program, including application guidelines, is available at: http://www.ncrr.nih.gov/biomedical_technology/high-end_instrumentation.

National Center for Research Resources

Mobile PET/CT Staff More Exposed To Radiation, Study Shows

On June 13 Researchers from Surrey University (Guildford, UK) reported on a study suggesting additional precautions and radiation dose awareness for those staffing mobile PET/CT units. The results of the study were presented at the United Kingdom Radiological Congress (Manchester) by Khalid Alsafi and colleagues. The research team observed 118 PET/CT image acquisitions (56 in mobile units and 62 in installed units) and recorded radiation levels with electronic personal dosimeters. Each acquisition period was divided into 6 phases to more carefully identify the timing of radiation exposure to staff. The results indicated that the average staff dose per patient during the injection phase was similar in mobile and fixed units (2.3 and 2.79 mSv, respectively). However, overall the staff dose in the mobile units was as much as 20% higher than that in fixed units, a surprising figure that was linked to staff accompanying patients to onboard bathroom facilities in mobile units.

Fewer than 20 mobile PET/CT units are operative in the UK, and the authors cited substantial waiting lists for imaging as a compelling reason to consider implementation of more units. They cautioned, however, that unit design, workload, and staffing patterns for these units must be revised from those in place at fixed instrumentation sites. Among the remedies they suggested were the use of health aides to escort patients to the bathroom and redesign of units so that technologists are not stationed near the bathroom.

Surrey University

Pennsylvania Requests Agreement State Status

The Nuclear Regulatory Commission (NRC) announced on June 15 that it is considering a request from Governor Edward G. Rendell of Pennsylvania to assume part of the NRC's regulatory authority over certain nuclear materials in the state. If the request is accepted, Pennsylvania will become the 35th state to sign such an agreement with the NRC. Under the proposed agreement, the NRC would transfer to Pennsylvania the responsibility for licensing, rulemaking, inspection, and enforcement activities for: (1) radioactive materials produced as a byproduct of processes related to the production or utilization of special nuclear material (enriched uranium or plutonium); (2) naturally occurring or accelerator-produced byproduct material (NARM); (3) source material (uranium and thorium); and (4) special nuclear material in quantities not sufficient to support a nuclear chain reaction.

If the agreement is approved, approximately 690 NRC licenses, many of them for medical and industrial uses, would be transferred to Pennsylvania's jurisdiction. In addition, Pennsylvania would retain regulatory authority for approximately 460 NARM licenses. The NRC would retain jurisdiction over regulation of commercial nuclear power plants and federal agencies using certain nuclear material in the state, as well as a number of other activities identified in 10 *Code of Federal Regulations* Part 150. In addition, NRC would retain authority for the review, evaluation, and approval of sealed sources and devices containing certain nuclear materials within the state.

Copies of the proposed agreement, the governor's request, and supporting documents, as well as the NRC staff's assessment are available through the NRC Agency-wide Documents Access and Management System (ADAMS) at www.nrc.gov. More information about the Agreement State program is available at http://nrc-stp.ornl.gov.

Nuclear Regulatory Commission

HHS Advisory Board to be Appointed

U.S. Department of Health and Human Services (HHS) Secretary Mike Leavitt announced on June 19 the establishment of a public health advisory panel on chemical, biological, nuclear, and radiological agents. To be called the National Biodefense Science Board, the group will advise the secretary on preventing, preparing for, and responding to release of such agents, whether such releases are naturally occurring, accidental, or deliberate. The board, which was authorized by the Pandemic and All-Hazards Preparedness Act, also will advise the secretary about trends, challenges, and opportunities in the field and provide recommendations for research and development.

"Planning responses to incidents involving chemical, biological, nuclear, or radiological agents requires state-of-the-art science," Leavitt said. "This new advisory board will add a wide range of expertise and viewpoints from outside of government to help inform HHS decision-making processes." The board will include 13 members appointed by the secretary from science, public health, and medicine. Four will be from the pharmaceutical, biotechnology, and device industries; 4 will be from academic institutions; and of the remaining 5, 1 must be from an organization representing health care consumers and 1 must be a practicing health care professional. The secretary also will appoint federal officials to support the board's functions. The board's charter and additional information are available at www.hhs.gov/aspr/omsph/nbsb.

Department of Health and Human Services

U.S./European Pharmaceutical Cooperation

The U.S. Food and Drug Administration (FDA), the European Commission (EC), and the European Medicines Agency (EMEA) announced on June 18 their agreement to expand current cooperative activities in several areas. At a meeting held June 14–15, the FDA and the EU reviewed the past year's activities under the existing plan and noted that the ultimate goal of continued cooperation is "to promote and protect public health, reducing regulatory burden and costs and bringing innovative products to patients in a timely manner." Building on past achievements in cooperation on vaccines, oncology, and pharmacogenomics, it was agreed to expand interactions in the areas of pediatrics and medicinal products for rare diseases ("orphan drugs"). In addition, the cooperative plan's scientific dialogue has been widened to include extensions of therapeutic indications and risk management plans. A new Principles of Interaction document (www.fda.gov/oia/pediatricsIP.htm) was released to define the cooperative efforts and facilitate the timely exchange of information on scientific and ethical issues for pediatric therapeutics. An Implementation Plan for Medicinal Products for Human Use (www.fda.gov/oia/impplan.htm), covering transatlantic medicine regulatory cooperation, was revised to describe under what circumstances information will be shared among the parties.

Following the guidelines of the Framework for Advancing Transatlantic Economic Integration between the EU and the FDA, new areas of transatlantic regulatory cooperation were discussed, notably regulatory cooperation on medical devices and cosmetics. In an "effort to avoid future disharmony," regulatory cooperation on new medicines legislation was discussed. In addition, planning progressed on a Transatlantic Workshop on Administrative Simplification in Medicines Regulation, to be held on November 28 in Brussels, Belgium.

U.S. Food and Drug Administration

NIH Funds Knockout Mouse Repository

The National Institutes of Health (NIH) announced on June 26 $4.8 million in funding to establish and support a repository for its Knockout Mouse Project (KOMP). This award is the final component of a more than $50-million trans-NIH initiative to increase the availability of genetically altered mice and related materials. The University of California, Davis and Children's Hospital Oakland Research Institute (CHORI; CA) will collaborate to preserve, protect, and make available about 8,500 types of knockout mice and related products.

Knockout mice are lines of mice in which specific genes have been completely disrupted, or knocked out. Systematic disruption of each of the 20,000 genes in the mouse genome will allow researchers to determine the role of each gene in normal physiology and development. Researchers can use knockout mice to develop better models of many inherited human diseases. The repository will archive, maintain, and distribute up to 8,500 strains of embryonic stem cell clones, live mouse lines, frozen embryos and sperm, and vectors, while assuring product quality and availability for all materials. The 4-year grant funds establishment and operation of the repository.

Previously funded portions of the KOMP include 2 awards totaling $47.2 million for the creation of mouse embryonic stem cell lines in which 8,500 different genes have been knocked out. Recipients were Regeneron Pharmaceuticals, Inc. (Tarrytown, NY) and a collaborative team from the University of California at Davis, CHORI, and the Wellcome Trust Sanger Institute (Hinxton, UK). NIH also supported the establishment of a data coordination center by the Jackson Laboratory (Bar Harbor, ME) to track the scheduling and progress of knockout production. In addition, NIH issued smaller awards to the University of Pennsylvania (Philadelphia) and the Samuel Lunenfeld Research Institute of Mount Sinai Hospital (Toronto, Canada) to improve the efficiency of methods for creating knockout lines.

More information about KOMP resources is available at www.komp.org. To request information or products, researchers can e-mail service@komp.org.

National Institutes of Health

NCI Launches Community Cancer Centers Program

The National Cancer Institute (NCI), part of the National Institutes of Health (NIH), announced on June 14 the launch of a 3-year pilot phase of a new program designed to bring state-of-the-art cancer care to patients in community hospitals across the United States. The NCI Community Cancer Centers Program (NCCCP) will encourage collaboration among private–practice medical, surgical, and radiation oncology physicians, with close links to NCI research and to the network of 63 NCI-designated Cancer Centers, most of which are based at large research universities. Building on this expanded network, the NCCCP sites will explore ways to share information via electronic medical records to enhance patient care.

"Improving access to cutting-edge therapies and providing simple and secure methods of exchanging medical information between health care consumers and providers are key issues," said Mike Leavitt, secretary of the Department of Health and Human Services. "The NCCCP pilot program holds great potential to inform us of the best ways to expand the reach of clinical research and further the important adoption of electronic medical records at the community level."

The pilot program will research new and enhanced ways to assist, educate, and better treat the needs of underserved populations, including elderly, rural, inner-city, and low-income patients as well as racial and ethnic groups with unusually high cancer rates. "A key component of the NCI Community Cancer Centers program will be education," said Elias A. Zerhouni, MD, director of NIH. "Studying new ways to help patients and members of the community better understand the lifestyle issues that affect cancer risk could pay dividends for many diseases by implementing approaches proven effective by NCI's research."

The pilot will begin at 8 free-standing community hospitals and 6 additional hospitals operated by health care systems in Montana, Connecticut, Georgia, Louisiana, South Dakota, California, Delaware, Missouri, Indiana, Wisconsin, Texas, Colorado, Maryland, and Nebraska. The sites will be funded for a collective total of $5 million per year. An NCI panel of experts and an independent group of outside experts will set milestones, monitor progress, and evaluate the success of the 3-year pilot and then issue recommendations for a full-fledged program.

NCCCP pilot sites will study how community hospitals nationwide could most effectively develop and implement a national database of voluntarily provided electronic medical records that would be accessible to cancer researchers. They will also study methods of expanding and standardizing the collection of blood and tissue specimens voluntarily obtained from patients for cancer research. The sharing of imaging results, including those from nuclear medicine techniques, is planned as an integral part of future assessments. For more information on the NCCCP pilot program and sites, visit: www.cancer.gov/newscenter/pressreleases/NCCCPpilotQ&A.

National Cancer Institute

NIH to Examine Peer Review

National Institutes of Health (NIH) Director Elias A. Zerhouni, MD, announced on June 8 the formation of 2 working groups to examine the NIH peer review process for funding scientific research. "Peer review is such a fundamental and critical part of the research process, that it requires our constant vigilance," said Zerhouni. "With the increasing breadth and complexity of science, along with the increased number of research grant applications, we need to take a comprehensive look at our review process and make the necessary changes to strengthen it for applicants and reviewers alike. Although our peer review system is outstanding and emulated throughout the world, we want to make it even better."

The 2 new NIH working groups, 1 internal and 1 external, will seek input from within NIH and from the scientific community, including investigators, scientific societies, grantee institutions, and voluntary health organizations. The groups will study the context, criteria, and culture of peer review to make sure the most talented individuals and reviewers are engaged in the process. Those named to serve on the external group were drawn almost entirely from academia, whereas the internal group represents a range of NIH institutes. Results from the external working group will be presented to the full Advisory Committee to the Director in December. The internal NIH working group will present its findings to the NIH Director's Steering Committee during the same month. Both working groups will meet in January 2008 to develop a set of integrated recommendations for next steps.

National Institutes of Health

Radiation Summer School

Students and scientists from around the world gathered at the U.S. Department of Energy Brookhaven National Laboratory (BNL; Upton, NY) to participate in the 4th annual National Aeronautics and Space Administration (NASA) Space Radiation Summer School. The group worked in BNL's Medical Department and NASA Space Radiation Laboratory (NSRL), a unique facility that simulates the harsh radiation environment of outer space, to study the possible risks astronauts may face during future long-term space flights. As NASA plans a mission to Mars, an outpost on the Moon, and exploration of near-Earth asteroids, many potential health risks remain unknown. Space radiobiology, a relatively new field that blends the disciplines of physics and biology, addresses questions about these risks.

"While there is a wealth of data describing the effects of conventional radiation like x-rays, the same is not true for the types of radiation present in space. It is essential to define the potential risks of exposure to space radiation and, if necessary, develop effective countermeasures to permit safe missions of longer durations than in the past," said Peter Guida, medical department liaison scientist for the program at BNL. Eleanor Blakely, the 2007 NASA Summer School director and a scientist from the Lawrence Berkeley National Laboratory (CA), added, "Our goal is to attract the highest quality students from diverse scientific backgrounds and help train them to be the next wave of space radiation researchers." The program has 3 scientific modules: physics, biology, and experimental methods.

Fifteen graduate students, postdoctoral fellows, and working scientists and 4 auditing professionals participated in this year's program. The intensive, 3-week course offers a unique physical and intellectual environment not duplicated in U.S. universities,

medical schools, or research institutes. Students participate in both classroom activities and scientific experiments, working side-by-side with space scientists from research organizations and universities. Experimental creativity and interdisciplinary approaches are emphasized. "This year's crop of students is the most internationally diverse yet, with 11 different countries represented," said Guida. "Even though the program is only in its 4th year, many of our graduates are already making contributions to the field."

Brookhaven National Laboratory

(Continued from page 43N)

2011 but will also need to demonstrate active participation in MOC activities over the entire 10-year period extending from 2007 until 2017.

The ABNM is providing an online service (MY PROFILE under MAINTENANCE OF CERTIFICATION at www.abnm.org) so that each diplomate may document the components for his or her MOC, including CME and self-assessment module CME credits. The ABNM initiated a $150 yearly administrative fee in 2006 for MOC documentation on its Web site as validation of candidates' participation in the MOC program. For individuals who delay paying the yearly fee, the past year's fee will be added to current charges when that diplomate requests participation in MOC.

A Tradition of Assuring Quality Care

Although this MOC program is new, organized medicine has long recognized the need to assure the public that physicians take active steps to provide quality care. In 1917, the general board certification program was first adopted in the United States. Today, 90% of practicing physicians are certified by 1 of the 24 boards accredited by the American Board of Medical Specialties (ABMS). It is the ABMS that has mandated that each discipline's specialty board adopt an MOC program. As a result, the ABNM introduced its program, with the requirement for participation from timed-certificate holders and the expectation of participation from lifetime certificate holders. If there is any doubt about the need for the program or the importance of reassuring the public, one has only to look at the frequent national news stories about medical errors and poor-quality practice. In 2004, the Institute of Medicine stated to Congress and the nation that: "44,000–98,000 Americans die each year as a result of preventable errors caused by faulty systems or processes used in their care. Health care systems fail to translate knowledge into practice."

Each month, Newsline features additional information to help physicians understand the options in fulfilling each part of the MOC program. Those who are diplomates of the American Board of Radiology (ABR) or have Special Competence in Nuclear Medicine certification by the ABR should refer to the specific requirements of the ABR MOC Program (www.theabr.org), which differs from the ABNM MOC program.

Conrad E. Nagle, MD
Chair, SNM Task Force on MOC
Editor, Newsline

J. Anthony Parker, MD, PhD
Chair, American Board of Nuclear Medicine