Nuclear Medicine Usage Grows, Led by PET

An estimated 1,129,900 clinical PET studies were performed in the United States in 2005, according to a report released in August by IMV Medical Information Division, a market research and consulting firm in Des Plains, IL. These studies were performed in 1,725 hospital and nonhospital sites, using dedicated PET/CT or PET units, mobile units, or nuclear medicine cameras with coincidence detection. “PET/CT scanners have become the preferred technology for PET imaging, as the integration of functional PET images with anatomical visualization of CT has allowed more accurate and faster diagnosis,” said Lorna Young, senior director, Market Research at IMV. “While the proportion of PET/CT scanners (vs. PET scanners) installed to date is about 55%, over 90% of the units installed in 2005 were PET/CT scanners.” The study indicated that the PET imaging market is experiencing double-digit growth, with the number of patient studies increasing more than 60% since 2003, for an average annual growth rate of 26.5% over the 2-year period.

The researchers noted, however, that because PET is still relatively new, many sites are only beginning to use the technology. Although 1,725 sites offer PET imaging, nearly 1,000 of these use mobile service providers, typically for 1 or 2 days per week. A total of 735 sites own 1 or more fixed PET or PET/CT scanners.

The IMV report describes trends in PET and PET/CT patient studies by procedure type, apparatus type, manufacturer and year of installation, planned purchases, radiopharmaceutical utilization and expenditures by supplier, and site operations characteristics. Among the findings included in the report are:

- Ninety-three percent of patient studies performed on PET or PET/CT scanners are for oncologic indications and 7% are for cardiac and neurologic indications;
- Sixty percent of fixed PET and PET/CT scanners are installed in nonhospital locations, with 40% installed in hospitals; and
- The 5 states with the highest PET and PET/CT patient study volume are California, Florida, Texas, New York, and Pennsylvania.

Overall Nuclear Medicine Growth

These results were part of a larger IMV report and accompanying database on nuclear medicine utilization that pointed to significant differences in utilization between hospital and nonhospital sites. According to the report, an estimated 19.7 million nuclear medicine procedures were performed during 17.2 million patient visits in the United States in 2005 in more than 7,200 hospital and nonhospital sites. This represents a 15% increase from 2002 to 2005, from 14.9 to 17.2 million patient visits, for an average annualized rate of 5% per year over the period.

More than half (57%) of non-PET imaging patient visits were for cardiovascular studies, including cardiac perfusion. “Nuclear medicine utilization (not including PET procedures) has been driven by cardiovascular applications, which have grown from 35% of 1992 procedures to 57% in 2005,” said Young. “Although both hospitals and nonhospitals are equally likely to perform cardiovascular procedures, hospital sites are more likely to perform tumor localizations, radionuclide therapy, bone scans, and liver, respiratory and renal studies.”

The report describes trends in nuclear medicine patient visits by procedure type, radiopharmaceutical and pharmacologic stress agent utilization, planned purchases, networking, site operations characteristics, and apparatus, including manufacturer and year of installation. The report also covers adoption trends in new technologies, including SPECT/CT. Among the findings included are:

- An average of 1.8 nuclear imaging cameras are installed per site;
- Two-thirds of the cameras in nonhospital locations were installed during or after 2000, compared with only 45% of those installed in hospital sites;
- Replacement is rapid, with more than two-thirds of purchase activity at nuclear medicine sites targeted at replacement units; and
- Nuclear medicine sites are expanding their network capability to transmit images for both cardiology and radiology applications, such as images from catheterization labs, CT, MR imaging, echocardiography, and general ultrasound.


IMV Medical Information Division, Inc.
InfoSNM to Debut at SNM 2007 Annual Meeting

InfoSNM is coming to the 54th Annual Meeting of the SNM to be held in Washington, DC, June 2–6, 2007. I am extremely excited about the introduction of this new information technology component of the annual meeting, and I hope it will address an aspect of our field—the use of computers and information science—that has been missing.

The use of computers and information science continues to grow in all aspects of nuclear medicine, including clinical data processing, image data management, and education, as well as science. Computers have been an essential part of every nuclear medicine clinic since the introduction of the multigated radionuclide ventriculogram in the late 1970s. Today, computers seem to be everywhere, and our reading rooms are starting to look like NASA’s Mission Control center. We are all trying to figure out how best to push nuclear medicine studies to picture archiving and communication systems (PACS) in a manner that best represents the excellent work we do. This is not always easy. Our images are routinely displayed at about the size of postage stamps, without color or fusion and with no ability to display gated tomographic studies.

The use of information technology in education is also growing at an unbelievable pace, from developing sophisticated Web-based learning modules to tasks as simple as developing effective PowerPoint presentations for our lectures. We are also trying to develop more efficient ways to take advantage of distance learning opportunities without taking the human side of education totally out of the picture. We use computers for almost every aspect of biomedical research, particularly in the field of molecular imaging. Such efforts may begin with performing more efficient literature searches on the Web, leading to better automation of data acquisition and analysis. The development of graphic user interfaces to the processing tools we routinely use (e.g., kinetic modeling using compartmental analysis) can greatly simplify the process, particularly for the less sophisticated user. The use of computer-based models can be valuable in determining which animal or physics experiments are most likely to yield pertinent results. Sometimes we lose sight of the ways in which computers and information science touch so many aspects of what we do every day in nuclear medicine.

However, the SNM Annual Meeting has not previously provided an appropriate venue for demonstrating newer and better ways to apply information science and technology to our field. Scientific presentations and posters appropriately focus on the underlying science and less on the tools essential for performing that science. Every year, a few abstracts are submitted that focus on the presentation of a new computer application for data analysis. It is often difficult to grade these abstracts relative to their science and to determine where in the scientific program they belong. For example, someone may develop a really nice graphic user interface for kinetic modeling that many would find informative, interesting, and helpful, but where is the appropriate forum to present this excellent work? A few continuing education sessions each year touch on the use of computers, but these are often scattered throughout the educational program and are difficult to locate.

When I became chair of the Scientific Program Committee, I tried to think of ways to address the incorporation of presentations on the use of computers and information science into our annual meeting. Over the past few years, I have had several opportunities to attend the Radiological Society of North America Annual Meeting and have been impressed by the infoRAD component of their meeting. This is both an exhibit area and a continuous series of presentations that include computer demonstrations by vendors, computer classrooms used for commercial presentations as well as general computer education, and computer-based presentations by attendees on information science and technology developed in their own laboratories. I wondered if we could have something like this—perhaps beginning on a much smaller scale—at our own meeting.

We have established the InfoSNM program, which will be introduced at the SNM Annual Meeting next June in Washington, DC. The Scientific Program Committee, the Computer and Instrumentation Council, and the SNM Education Department have developed a program that will initially consist of 2 components.

(1) We will institute a new abstract category: InfoSNM Computer Presentations. Abstracts for these presentations will be due at the same time as other scientific abstracts but will be reviewed by an entirely different set of reviewers using different criteria. Abstracts submitted for InfoSNM will be reviewed for the novelty of their use of computers rather than the novelty of their science. This use can be in education, data management, or science and can present the use of computers in the clinic and/or in the research lab. Each presentation will include both a poster that describes the work and a computer-based demonstration. Participants whose abstracts are chosen for presentation will have the option of using their own computers or sharing an SNM-provided computer with another presenter. Times will be designated at which presenters will describe their work,

(Continued on page 36N)
SNM Responds to Proposed USP <797> Revisions

On August 15 the SNM submitted comments to the U.S. Pharmacopeia (USP) regarding the proposed revisions of USP General Chapter <797> Pharmaceutical Compounding—Sterile Preparations. The proposed revisions of <797> appeared in the USP Pharmacopeial Forum (PF), Journal of Standards Development and Official Compendia Revision, 2006(May–June);32. The SNM document was supplemented by 2 reference attachments. One attachment was a set of comments by James A. Ponto, MS, a member of the SNM Committee on Pharmacopeia. The second was a PDF of an article by Mark Thomas, MS; Michael D. Sanborn, MS; and Rick Couldry, MS; on “IV admixture contamination rates: traditional practice sites vs. a class 1000 cleanroom” (Am J Health-Syst Pharm. 2005;62:2386–2392). The full texts of both attachments are available at: http://interactive.snm.org/index.cfm?PageID=5466. The full text of the proposed revisions is available at: www.usp.org/USPNF/pf/generalChapter797.html. Included here is the text of the main comment document submitted by the SNM.

Comments on Proposed Revisions USP General Chapter <797> Pharmaceutical Compounding—Sterile Preparations
Radiopharmaceutical Sciences Council Committee on Pharmacopeia
Society of Nuclear Medicine

The Society of Nuclear Medicine (SNM)—an international scientific and professional organization of more than 16,000 members dedicated to promoting the science, technology and practical applications of molecular imaging/nuclear medicine—appreciates the opportunity to submit comments regarding the concerns of the nuclear medicine community with the proposed revisions of USP General Chapter <797> Pharmaceutical Compounding—Sterile Preparations. The following comments were developed by the members of the Radiopharmaceutical Sciences Council (RPSC) Committee on Pharmacopeia, with the collaboration of representatives from the RPSC Committee on Radiopharmaceuticals, SNM and SNM/Technologist Section leadership.

GENERAL COMMENTS

Radiopharmaceuticals as CSPs

We are in general agreement with the establishment of a separate section titled “Radiopharmaceutical as CSPs” within the proposed revisions of <797>. We propose, however, that the SCC consider creation of an entirely new category for short-lived radiopharmaceuticals, an intermediate category between “Immediate Use” and “Low-Risk,” designated “Same-Day CSPs.” This proposal is in agreement with a suggestion made previously by James Ponto (Attachment 1).

As suggested by Mr. Ponto, the requirements for Same-Day CSPs would be:

• Personnel training and media fill challenge testing.
• Handling in a properly functioning ISO 5 hood (in a limited access room but not necessarily in a clean room).
• Good aseptic technique, especially no contact contamination on the critical surfaces (but not necessarily donning clean room garments and following other clean room procedures).

Mr. Ponto’s proposal is supported by a recent article (Attachment 2) that demonstrates that proper training in aseptic technique is more important than the physical environment when preparing admixtures for i.v. administration (Attachment 2).

Perhaps most importantly, we feel that the creation of a new category better reflects the unique nature of short-lived radiopharmaceuticals.

Definitions of Compounding, Dispensing, and Preparation

The SNM encourages the USP to refine the definitions of compounding, dispensing, and preparation of radiopharmaceuticals within <797> such that these definitions are consistent with existing USP monographs and FDA regulations. Furthermore, the Society believes that the preparation of a radiopharmaceutical by combining sterile components as described on the package insert should be excluded from the definition of compounding.

Personnel Training and Competency in Aseptic Manipulation Skills

The SNM strongly believes the most important safety measure in the preparation of sterile drugs is the proper training of competent personnel in aseptic technique. Therefore, we support the development of competencies and outcomes for personnel, activities, and facilities. However, we request that <797> refrain from overly prescriptive requirements regarding the means by which these competencies and outcomes are achieved.

Performance-based Compounding Guidelines

As with Personnel Training, the SNM feels that compounding guidelines should be performance-based, not prescriptive, thus allowing for more or less stringent controls depending on the specific compounding activity. Therefore, we support the use of the word “should,” but object to the word “must” throughout <797>.
Impact Evaluation on Enforcement and/or Compliance of <797>

As indicated above, the proposed revisions of <797> contain several references to activities that “must” be performed, rather than “should” be performed. This prescriptive language, combined with the fact that USP chapters numbered less than 1000 are enforceable, creates an environment in which <797> standards are essentially a set of de-facto regulations.

With this in mind, the SNM firmly believe <797> should be evaluated by the Office of Management and Budget (OMB) for its impact on enforcement or compliance of compounding practice standards by the FDA, Centers for Medicare & Medicaid Services, State Boards of Pharmacy, as well as various healthcare institutions and practitioners (e.g., individual pharmacies, hospitals, and clinics, etc.).

Patient Care & Patient Safety

The SNM is deeply concerned that implementation of <797> in its present form will have a significant (negative) impact on both patients and the health care system. The costs of renovating existing facilities to bring them into compliance with <797> will significantly increase the costs of drugs, including radiopharmaceuticals, and these increased costs will necessarily be passed on to patients. In some cases, nuclear medicine departments may not be able to absorb these costs and will be forced to close, resulting in delays in diagnosis or reliance on less effective but more readily available technologies.

SPECIFIC COMMENTS

1. As the term “ante-area” is not defined in the “Definitions” section and is indistinguishable from the defined term “anteroom” used throughout <797>, the SNM suggests only one term be used to avoid confusion.
2. Add a definition for the term “Biological Safety Cabinet, Class III [BSC].” This term appears on line #554, but is not explained within the “Definitions” section (the definition of “Biological Safety Cabinet, Class II [BSC] can be found on lines #125-128.)
3. Consolidate the names in lines #129-130 (i.e., Buffer Area, Buffer or Core Room, Buffer or Cleanroom Areas, Buffer Room Area, Buffer or Clean Area).
4. The name and definition for the term “Cleanroom” as listed in lines #133-137 seem to be perplexing. If the meaning of term “Cleanroom” is different from those for the terms (i.e., Buffer Area, Buffer or Core Room, Buffer or Cleanroom Areas, Buffer Room Area, Buffer or Clean Area), what should the classification be of the room air in a “Cleanroom”? If it should be ISO Class 7, what are the differences between the definitions of “Cleanroom” and “Buffer Area, Buffer or Core Room, Buffer or Cleanroom Areas, Buffer Room Area, Buffer or Clean Area”?
5. Add a definition for the term “Compounding” that is consistent with the FDA.
6. Add a definition for the term “Dispensing.”
7. The term “expiration date” appears numerous times (e.g., line #256, lines #659-660, line #1337); however it is not defined in the “Definitions” section.
8. Add a definition for the term “Hazardous Drug.”
9. Line #625—please define the term “Type B2 BSC.”
10. The statement in line #626 (i.e., “[CAI] located in an ISO Class 8 . . .”) is inconsistent with the stipulation in line #914 (i.e., “CAIs must be placed in an ISO Class 7 . . .”).
11. What risk level should be assigned to the compounding process for radiolabeling of autologous leukocytes (white blood cells) given that the blood from which the leukocytes are isolated is not sterile and cannot be sterilized without destroying the leukocytes?
12. Figure 1—Define the term “Buffer Zone” as it appears in the upper floor plan of Figure 1?

In summary, the Society of Nuclear Medicine applauds and supports reasonable regulation(s) that improve patient safety. Radiopharmaceuticals, however, provide unique challenges in their preparation and dispensing, and the proposed document is confusing regarding these challenges. Because Nuclear Medicine/Pharmacy has a documented safety record and the short-lived radiopharmaceuticals do not fit well within the proposed revision of <797>, we propose the creation of a new category, Same-Day CSPs, as per the suggestion of James Ponto. We also urge that the SCC seriously consider the potential impact of the proposed changes in <797> both in terms of increased patient costs and very real potential of discontinued service in some areas of the United States.

Thank you for offering us an opportunity to express our concerns and comments with regard to the proposed revisions to <797>. We sincerely hope that you and the members of SCC would consider the above comments and suggestions. Thank you for your time and consideration.

Jeffrey A. Clanton, MS
President, Radiopharmaceutical Sciences Council

Joseph C. Hung, PhD
Chair, Committee on Pharmacopeia
Future Focus Highlights Molecular Imaging Summit

The SNM joined with industry partners to host a collaborative summit on “Molecular Imaging: Shaping the Future,” July 27–30 in Key Biscayne, FL. The purpose of the summit was to bring nuclear medicine academic and practice innovators together with industry leaders to discuss, explore, and expand on topics raised in last year’s Joint SNM/Radiological Society of North America Molecular Imaging Summit (see Newsline coverage, J Nucl Med. 2005;46[9]:11N–14N,42N). This year’s summit was sponsored solely by SNM, with support and participation from Biogen Idec; Bioperspectives; Bracco Diagnostics, Inc.; Bristol–Myers Squibb Medical Imaging; Capintec, Inc.; Cardinal Health: GE Healthcare; IBA Molecular; Mallinckrodt, Inc.; MDS Nordion; Merck & Co., Inc.; Philips; Siemens Medical Solutions, USA; and Spectrum Dynamics.

Martin Sandler, MD, SNM president, and Mathew L. Thakur, PhD, a past president of SNM and organizer of last year’s summit, cochaired the meeting and welcomed attendees to a reception on the evening of July 27 at the Ritz-Carlton Hotel. The next morning, Steven Gutman, MD, director of the Office of In Vitro Diagnostic Device Evaluation and Safety in the U.S. Food and Drug Administration Center for Devices and Radiological Health, delivered a keynote presentation on “In Vivo Biomarkers in Diagnosis: FDA Regulations and Industry/Academia Partnership.”

Newsline looks briefly this month at the topics, presenters, and some of the challenges and conclusions outlined in breakout sessions at the summit. The complete proceedings of the summit, with individual presentations, reference materials, summary statements, and breakout session white papers will be published by SNM later in the fall.

Drug Discovery

The first session on July 28 focused on drug discovery and was chaired by Chaitanya Divgi, MD, with cochair Alexander McEwan, MD. Panel members and topics discussed included: Steven Bodovitz, PhD, Trends in Innovation in Drug Discovery; Richard Pestell, MD, PhD, Light-Activated Gene Therapy, New Selective Therapies for Disease; Eric D. Agleppa, PhD, Rational Design for Peptide Drugs; Chaitanya Divgi, MD, Therapeutic Applications of Antibodies; and Juri Gelovani, MD, PhD, Recent Advances in Biomarkers for Diagnosis and Treatment.

These presenters and participants in subsequent discussion sessions focused on modern drug discovery as a prolonged and expensive process that carries a high risk of failure. Time elapsed between identification of a new chemical entity and regulatory approval may be more than 10 years, and total costs may reach $500–$750 million. The appropriate application of molecular imaging in drug discovery and drug development, however, promises to significantly speed up this development process while reducing the associated costs. Molecular imaging techniques are already being used in receptor occupancy studies that underpin dosage and toxicity research and with transgenic animal models to validate drug development. New methodologies using radio-labeled drugs in pharmacokinetic and pharmacodynamic studies are enhancing understanding of the ways in which molecular imaging techniques can augment and enhance traditional routes to drug development. As preclinical instrumentation becomes more quantitative, molecular imaging will become a routine and significant part of pharmaceutical research. Imaging gene and epigenetic expression will be important for the future, as researchers look to understand and characterize tumor biology in vivo. In clinical trials, molecular imaging probes also will play an increasingly important role in assessing the effectiveness of novel therapies. The result will be safer and more effective drugs that reach clinical usage more quickly.

Clinical Issues

The second session focused on clinical issues and was chaired by Steven M. Larson, MD, and cochaired by Martin P. Sandler, MD. Larson opened the session with topic summaries on Molecular Imaging in the Clinical Area and 18F-FDG Imaging: Molecular or Functional?, followed by P. David Mozley, MD, Molecular Imaging: A Tool for Developing Central Nervous System Drugs; Albert Sinusas, MD, What is the Role of Molecular Imaging in the Management of Cardiac Disorders?; and Adrian Nunn, MD, From Clinical Trials to Prescriptions.

Participants agreed that it is clear that in the short term work will continue to focus on examining and validating future clinical applications for 18F-FDG PET/CT for oncology (diagnosis and staging, treatment planning and response, detection of recurrent or residual disease, restaging), for myocardial perfusion (coronary artery disease, myocardial viability), and for neurology and neurosurgery (brain tumors, medically intractable epilepsy, stroke, movement disorders, Alzheimer’s disease, and other dementias). Clinically approved indications for 18F-FDG PET imaging are likely to continue to expand from areas of current research, including therapy monitoring and assessing the effectiveness of cardiac and other interventions. At the same time, researchers are exploring a large number of other radio-labeled tracers, with particularly promising results in genetic markers, DNA synthesis, hypoxia studies, and monitoring of anti-angiogenesis therapies. Bioluminescence imaging is also a growing part of the molecular imaging armamentarium.

Basic Research

On July 29, the summit’s third session, on basic research, was chaired by Michael Welch, PhD, and cochaired by Mathew L. Thakur, PhD. Panel members and topics included: David Geho, MD, PhD, Oncogene Cell Differentiation/Cell Transduction; Michael J. Welch, PhD, Recent Trends in Radionuclide-Based Molecular Imaging; John C. Gore, PhD, Role of MR in Molecular Imaging; Lihong V. Wang, PhD, Optical Imaging: Progress and Perspectives; and Malcolm J. Avison, PhD, Radiologic Approaches to Molecular Imaging.
The breakout session on basic and translational research focused on the importance of interdisciplinary teams of molecular imaging scientists, molecular biologists, imaging physicians, oncologists, pathologists, bioinformaticists, epidemiologists, and other scientists in advancing molecular imaging and associated sciences. Such efforts currently include profiling tissue specimens; identifying, characterizing, and classifying biomarkers; developing and characterizing imaging probes and biomarkers; and generating consensus lists of biomarkers relevant to targeted diseases. The group made a number of specific predictions about near- and longer-term results of such collaborations. Among these were:

- The evolution toward the practice of molecular medicine will blur traditional boundaries between medical disciplines;
- Chemists and molecular biologists will expand the focus of the field, bringing the knowledge to develop site-specific probes and new reporter-probe systems;
- More research will be performed on developing signal amplification techniques, which eventually will lead to techniques to image the genome and downstream proteomic outcomes;
- The development of information technology systems that fully integrate all facets of a patient’s history and clinical picture with information gained from molecular profiling will be required;
- Novel probes will be used across the spectrum of molecular imaging modalities to identify new targets within cells and receptors and to quantify treatment effects on the expression of these markers; and
- Traditional tracer-based nuclear medicine research will be expanded within the molecular imaging arena to include optical imaging and magnetic resonance spectroscopy.

One of the greatest challenges in this rapidly evolving research environment was identified as finding ways to translate new discoveries and techniques effectively and rapidly to the clinical setting.

**Instrumentation and Animal Models**

Session 4, which focused on instrumentation and animal models, was chaired by Cheryl Marks, PhD, and cochaired by Peter Conti, MD, PhD. Marks opened the session with Animal Models for Human Diseases: Is There a Future Without Them? She was followed by Paul Acton, PhD, who summarized Animal Imaging Equipment: Recent Advances.

Nuclear medicine practitioners and industry representatives who participated in this breakout session predicted a continuing and rapid evolution in imaging technologies, driven by innovative hybrid modalities and approaches. The accompanying expansion of imaging capabilities will allow identification of imaging probes specific for molecular processes, and new multimodality imaging technologies will be developed to appropriately apply these new probes. The group cited recent advances in dynamic SPECT for cardiac imaging as an example of an application that will bring molecular imaging into daily practice. Other predictions included:

- Routine use of nanoparticle delivery vehicles for both imaging and therapy agents, including gene therapy;
- Molecular profiling of individual cancers;
- Development of therapeutic antibodies;
- Refinement and introduction of novel peptide imaging probes; and
- Exploration of tissue-specific, light-activated gene expression markers.

**Standardization and Education**

The final session, on standardization and education, was chaired by Lalitha Shankar, MD, PhD, and cochaired by Virginia Pappas, CAE. Shankar opened the meeting with PET Standardization: NIH Findings. She was followed by William Heetderks, MD, PhD, who spoke on Education and Training Activities at the National Institute of Biomedical Imaging and Bioengineering.

Discussants in this breakout sessionconcurred that devising and maintaining adequate standards and effective means of continuing education and re-education are the central challenges in an environment of rapid technologic and scientific change. As new probes and imaging technologies enter mainstream clinical practice and as the field of molecular imaging becomes integrated into daily nuclear medicine, novel educational approaches must be introduced for all nuclear medicine professionals. Moreover, this challenge is compounded by the growing diversity of the field. Innovative tools must be developed to prepare current and future generations of graduates to be molecular imagers and clinical scientists in molecular imaging. At the same time, standardized imaging protocols must be developed and validated, along with quantitative imaging methodologies, and standardized outcome measures for molecular imaging techniques in all phases of clinical trials. The participants in this discussion endorsed the development and awarding of pilot research grants for young investigators and bridge funding to investigators entering the field, as well as identification of new funding opportunities by soliciting funding from agencies not traditionally associated with imaging research. At the same time, as a result of new Accreditation Council for Graduate Medical Education requirements, the length of nuclear medicine training will be expanded. Led by the SNM, an effort is underway to ensure that training in molecular imaging science and technique can be successfully integrated into enhanced curricula.
Critical Questions

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ometimes the questions are more important than answers. This was the rationale behind SNM’s recent groundbreaking molecular imaging summit, which brought together forward-thinking researchers, commercial sector representatives, and officials from national government/regulatory agencies to explore “Shaping the Future.”

This first-of-its-kind forum allowed nearly 70 senior-level participants over 3 days to interact and explore questions about drug discovery, clinical issues, basic research, instrumentation/animal models, and standardization/education as they relate to molecular imaging and therapy.

In Search of Answers

Who are the most likely researchers to bridge the translational gap from molecular science to clinical practice? If targeting agents are used to determine or optimize biologically effective doses, what are the costs, safety issues, and other potential problems? What are the advantages and disadvantages of nuclear imaging in terms of clinical applications, and what other types of imaging will be seen as “molecular”? What is there “beyond FDG”? What are the barriers to the translation of new agents to the clinic? With the ability to detect and molecularly classify tumors less than a centimeter in size, which patients should be evaluated? Is there a future without animal models for human diseases? Will imaging enable quantifying known—or discovering new—parameters that are surrogate markers of response? What are the essential elements for an environment for training in molecular imaging science? How should chemists and others from the physical sciences be trained clinically? How can one best interest and recruit bright chemists and clinicians to molecular medicine?

With these and multiple other questions, panel presenters and attendees who are leaders in their fields addressed the future of molecular imaging. Panel presenters are developing statement papers on the various subjects—and questions—that were discussed; these statements will be published in future months.

As summit organizer, SNM recognizes the critical role for molecular imaging in future patient care and is working actively with the commercial sector to facilitate the movement of molecular discoveries from bench to bedside and with officials from the government and federal agencies to identify the needs and resources for advancing the nation’s health care. Mathew Thakur, PhD, as the summit chair, assembled an exceptional molecular imaging think tank with assistance from SNM President Martin Sandler, MD; Alexander (Sandy) McEwan, MD, and Peter Conti, MD, PhD.

The participant list was impressive. Industry representatives came from Biogen Idec, Bioperspectives, Bracco Diagnostics Inc., Bristol-Myers Squibb Medical Imaging, Capintec Inc., Cardinal Health, GE Healthcare, IBA Molecular, Mallinckrodt Inc., MDS Nordion, Merck & Company Inc., Philips, Siemens Medical Solutions USA, and Spectrum Dynamics. Also attending the end-of-July session in Key Biscayne, FL, were representatives from the FDA’s Office for In Vitro Diagnostic Device Evaluation and Safety, the Los Alamos National Laboratory, the National Cancer Institute, and the National Institutes of Health’s National Institute of Biomedical Imaging and Bioengineering.

Individuals attended from Cross Cancer Institute; Kimmel, M.D. Anderson, and Memorial Sloan-Kettering cancer centers; and George Mason, Texas A&M, Thomas Jefferson, Vanderbilt, and Yale universities, as well as the University of Southern California and the University of Pennsylvania.

SNM appreciates the participation and work of the individuals who served on the summit’s panels: Eric D. Agdeppa, PhD; Steven Bodovitz; Chaitanya Divgi, MD, PhD (chair); Juri Gelovani, MD, PhD; and Richard Pestell, MD, PhD, drug discovery; Steve Larson, MD (chair); P. David Mozley; Adrian Nunn, PhD; and Albert Sinusas, MD, clinical issues; Malcolm Avison, PhD; David Geho, MD, PhD; John Gore, PhD; LiHong Wang, PhD; and Michael Welch, PhD (chair), basic research; Paul Acton, PhD, and Cheryl Marks, PhD (chair), instrumentation/animal model; and William Heetderks, MD, PhD, and Lalitha Shankar, MD, PhD (chair), standardization/education.

An Expanded Purpose, Name

For more than 50 years, the society has successfully educated the world about the potential of nuclear medicine. With SNM setting a new core purpose “to improve health care by advancing molecular imaging and therapy,” you can see the importance of holding the “Shaping the Future” industry molecular imaging summit. More and more—in big and small ways—you will continue to see the society emphasizing its new strategic direction. By now, you may have noticed the increased use of the SNM acronym—as opposed to the “Society of Nuclear Medicine”—in our communications with members and the public. Prominently using “SNM” and the society’s new tagline “Advancing Molecular Imaging and Therapy” maintains the society’s core identity and moves it forward with the evolving molecular imaging and therapy field in a much more inclusive way. In the near future, the society will debut a number of other initiatives—including creating messages for marketing materials, developing a visual identity, and redesigning the Web site—as SNM continues its strategic course to become the recognized leader of molecular imaging and therapy and nuclear medicine.
Niederhuber to Head NCI

President Bush announced on August 18 his intention to formally appoint John E. Niederhuber, MD, as the 13th director of the National Cancer Institute (NCI). Niederhuber has been a professor, cancer center director, National Cancer Advisory Board chair, external advisor to the NCI, grant reviewer, and laboratory investigator supported by NCI and the National Institutes of Health (NIH). Since June he has served as NCI’s acting director. “Dr. Niederhuber is a nationally renowned surgeon and researcher and has dedicated his entire academic career to the treatment and study of cancer, thus making him an excellent choice to be the next director of NCI,” said National Institutes of Health (NIH) director Elias A. Zerhouni, MD. NCI is the only NIH institute or center with a leader directly appointed by the U.S. president.

In addition to his management of NCI, Niederhuber remains involved in research through a laboratory on the NIH campus. Under his leadership, the Laboratory of Tumor and Stem Cell Biology (part of the Cell and Cancer Biology Branch of the NCI Center for Cancer Research) is studying adult tissue stem cells as the cell of origin for cancer. Niederhuber also holds an appointment on the NIH Clinical Center medical staff.

Before joining NCI in a full-time capacity, Niederhuber was a professor of surgery and oncology at the University of Wisconsin School of Medicine in Madison. He also served as director of the University of Wisconsin Comprehensive Cancer Center, one of 61 NCI-designated cancer centers. Earlier in his career, he chaired the Department of Surgery at Stanford University in Palo Alto, CA, and has held professorships at the Johns Hopkins University School of Medicine (Baltimore, MD) and at the University of Michigan in Ann Arbor.

The lab, National Cancer Institute Newsline

Nuclear Medicine Week, October 1–7

Each year, the SNM and SNMTS join forces with the nuclear medicine and molecular imaging community to gain recognition and support for the field. Celebrated during the first week of October, Nuclear Medicine Week encourages community members to take pride in their profession—recognizing their colleagues for their hard work and promoting nuclear medicine to the entire medical community as well as to the public. The theme of this year’s celebration, to be held October 1–7, is “Tomorrow’s Technology: Today’s Images.”

Nuclear Medicine Week allows physicians, technologists, scientists, and others involved in nuclear medicine and molecular imaging to take a proactive role in the advancement of the field. Each practice and institution takes its own approach to marking the annual event, but popular activities include distribution of informational pamphlets on nuclear medicine to hospital staff, referring physicians, patients, and local schools; holding staff appreciation events; creating public or school programs where information about nuclear medicine procedures and advances are discussed; opening facilities for tours by hospital staff and educators; and contacting local media outlets to encourage coverage of the benefits of nuclear medicine.

The SNM makes support materials available each year to help in Nuclear Medicine Week activities. In addition to informational pamphlets and posters, this year’s supplementary materials include Nuclear Medicine Week–labeled lunch coolers, USB memory sticks, sports bottles, pens, and patches. Society of Nuclear Medicine Topic of Security Detector Triggers Resurfaces

Concern about patients triggering radiation-sensitive security alarms after undergoing nuclear medicine procedures came again to the attention of the public this summer with a border security incident and a widely publicized British report and recommendations. An 83-year-old Canadian man who had undergone nuclear cardiac imaging on the previous day set off radiation detectors at the U.S.–Canadian border. The Vancouver Sun reported on Aug. 16 that border guards stopped Stanley Smith on August 11 when he attempted to enter the United States at the Peace Arch. Alarms were set off during a routine security screening. Smith was surrounded by heavily armed security guards, who took his passport and medical documents and questioned him for more than a half hour. Smith said, “It was a nightmare, believe me. All I heard was buzz, buzz, buzz, and I thought, ‘What in the hell is that for?’ I had no idea I was radioactive. I got the injection in the hospital, but I didn’t know what it was. There must be a lot of people who get these injections, and don’t know. Today’s security is so tough. And those security people, they have no sense of humor whatsoever.”

Only days earlier, the British Medical Journal (2006;333:293–294) published an article reinforcing previous advice about informing patients that they might trigger alarms. Their research was sparked by reports of a patient who activated an airport radiation detector more than 6 weeks after receiving ¹³¹I therapy. After a literature search, the authors identified 4 additional cases that highlight the length of time necessary before a patient can be assured of passing through security checkpoints without incident. They noted that their own nuclear medicine department had amended the advice given to patients after radiiodine treatment to indicate that airport alarms may be triggered up to 12 weeks after therapy. “Airports... (“Continued on page 26N)
(Continued from page 22N) worldwide are deploying more sensitive radiation detection systems and hence one would expect more such cases unless we take responsibility of forewarning our patients,” they wrote.

The Washington Post recently reported that in the last 6 years U.S. customs officers have responded to 318,000 radiation detection alarms, but that none of these alarms have resulted in the identification of illegal materials. SNM provides information for clinicians on this issue online at www.snm.org/security.

Vancouver Sun
British Medical Journal

Neagley to Edit JNMT

Frances L. Neagley of San Francisco, CA, has been named editor in chief of the SNM Technologist Section’s Journal of Nuclear Medicine Technology. The peer-reviewed quarterly journal, published by SNM since 1972, focuses on technology, quality assurance, radiation safety, and clinical applications of nuclear medicine. Neagley recently retired as a senior nuclear medicine technologist from the Davies campus of the California Pacific Medical Center in San Francisco. She succeeds Beth A. Harkness, a physicist in the radiology department of the Henry Ford Health System in Detroit, MI. Harkness will leave the editor in chief post on December 31, after 2 terms (6 years) of service.

“I believe Fran Neagley will make an excellent editor in chief,” noted SNMTS President D. Scott Holbrook, speaking for the Technologist Section’s 8,000 members. “Fran brings nearly 35 years of clinical experience, along with a passion for excellence, to the top editorial position. I’m confident Fran—like her predecessor Beth Harkness—will add new and exciting dimensions to the journal.”

“The Journal of Nuclear Medicine Technology is the primary SNMTS member benefit,” said Neagley, who began transitioning into the editor position on July 1. “While keeping the high scientific content of JNMT, I intend to increase its relevancy to all technologists—beginning with some state-of-the-art articles.” Neagley, who will assume full editorial responsibility for the journal on January 1, also wants to increase the number of continuing education articles. She is currently identifying associate and consulting editors and wants “to increase input, variety, and topicality” in the journal.

Neagley served as nuclear medicine supervisor with the Davies Medical Center, 1980–1998; as chief technologist with the San Diego Nuclear Medical Group, 1975–1980; and as staff technologist with Stanford University Hospital in Palo Alto, CA, 1970–1973. She holds a bachelor’s degree in biology and is certified by the Nuclear Medicine Technology Certification Board and the American Registry of Radiologic Technologists.

Society of Nuclear Medicine

FDA Seeks UDI Comments

The U.S. Food and Drug Administration (FDA) announced on August 9 that it is seeking information on how the use of a unique identifier system could improve the delivery and monitoring of medical care. The complete notice appeared in the August 11 Federal Register (www.fda.gov/OHRMS/DOCKETS/98fr/06-6870.htm). A public meeting is planned in the fall, and comments received before November 9 will be used to help the agency determine what next steps to take in developing a unique device identifier (UDI) system.

“Much like the bar code rule for drugs and biological products, unique identifiers for medical devices could have many potential benefits for improving the quality of care for patients,” said Daniel Schultz, MD, director of the FDA Center for Devices and Radiological Health. “A UDI system could have broad applications in reducing medical errors, facilitating device recalls, improving medical device adverse event reporting, and encouraging cost effectiveness by improving delivery and supply chain efficiency.” As the number and complexity of medical devices grow, the FDA is looking at new technologies that may help to identify and manage risk. According to a press release announcing the opening of the comment period, the FDA believes that a UDI system could provide information that would be associated with a specific device throughout its lifetime. For example, a UDI could identify which devices are compatible, such as implanted devices that can be used safely with MR imaging systems.

FDA representatives have already met with groups of stakeholders and found that most supported the development of a UDI system as a way to improve patient safety. Another potential benefit cited was better management of the purchase, distribution, and use of medical devices. The FDA also commissioned 2 reports from outside experts on automatic and unique identification of medical devices. The reports identified several potential benefits, including identifying incompatibility with devices or potential allergic reactions. In addition, FDA has been working with the Agency for Healthcare Research and Quality and with other federal partners to better understand issues associated with the development, implementation, and use of a UDI system.

“It is essential that we monitor the performance of medical products after they are approved and make sure that we quickly discover any potential problems that might arise,” said Andrew C. von Eschenbach, MD, Acting Commissioner, FDA. “To improve our post-market data collection at FDA, we are using a total product lifecycle approach to how we look at medical devices and focusing more attention on the kinds of systems and processes we need to have in place to monitor products after they are approved.”

During the comment period, FDA wants to learn about the feasibility, utility, benefits, and costs associated with developing and implementing a UDI system for medical devices. In addition, the agency wants to hear about various automatic identification technologies, such as bar code and radiofrequency, that could be used with a UDI system. A list of questions

(Continued on page 36N)
Each month the editor of Newsline selects articles on diagnostic, therapeutic, research, and practice issues from a range of international publications. Many selections come from outside the standard canon of nuclear medicine and radiology journals. Note that although we have divided the articles into therapeutic and diagnostic categories, these lines are increasingly blurred as nuclear medicine capabilities rapidly expand. Many diagnostic capabilities are now enlisted in direct support of and, often, in real-time conjunction with therapies. These briefs are offered as a monthly window on the broad arena of medical and scientific endeavor in which nuclear medicine now plays an essential role.

**Diagnosis**

**SPECT and MR in Nanof ormulated Drug Delivery**

In an article e-published ahead of print on August 14 in the *Journal of Leukocyte Biology*, Gorantla and researchers from the University of Nebraska Medical Center (Omaha), Creighton University (Omaha, NE), and Baxter Healthcare Corp. (Round Lake, IL) reported on the potential for quantitative MR and SPECT imaging of macrophage tissue migration in nanoparticle-formulated drug delivery. This work is part of continued interest by this group in the development of a macrophage-based nanoparticle system for antiretroviral (ART) drug delivery. Taking as their hypothesis that the same mononuclear phagocytes, bone marrow and blood monocytes, tissue macrophages, microglia, and dendritic cells that serve as targets, reservoirs, and vehicles for HIV dissemination can be used as vehicles for ART, the authors reported on blood marrow macrophages as carriers for nanoparticle-formulated indinavir. SPECT, T2-weighted MR imaging, gamma scintillation spectrometry, and histology provided quantitative metrics. The study was conducted in a drug-naïve mouse model, in which bone marrow macrophages labeled with super paramagnetic iron oxide and/or $^{111}$In-oxine were injected. Kinetics were observed over 14 days. SPECT and MR imaging indicated that bone marrow macrophage densities were significantly greater in the liver and spleen than in other tissues or organs. Transfer of bone marrow macrophages loaded with nanoparticle-formulated indinavir produced drug levels in lymphoid and nonlymphoid tissues that exceeded reported therapeutic concentrations by 200- to 350-fold on day 1 and remained in excess of 100- to 300-fold on day 14. The authors concluded that “these data show real-time kinetics and destinations of macrophage trafficking and demonstrate the feasibility of monitoring macrophage-based, nanoparticle-formulated ART.”

*Journal of Leukocyte Biology*

**$^{99m}$Tc-GSA SPECT in Acute Hepatic Damage**

Togashi et al. from the Yamagata University (Japan) reported on August 18 ahead of print in *Hepatology Research* on a study designed to clarify the clinical significance of the asialoglycoprotein receptor (ASGPR) in the human liver in acute hepatitis and fulminant hepatic failure. The study included 18 healthy individuals, 42 patients with acute hepatitis, and 10 patients with fulminant hepatic failure. All underwent $^{99m}$Tc-galactosyl human serum albumin SPECT imaging, with ASGPR expression analyzed separately in the right and left hepatic lobes using indices developed by the authors for this and similar studies. Mean uptake ratio and uptake density values for the whole liver and each lobe decreased in accordance with the severity of acute hepatic damage. In patients with fulminant hepatic failure, reduction in these values was greater in right than left lobes. Overall, these values for the whole liver correlated well with hepatic functional reserve and total bilirubin levels, and a smaller time-course study indicated that expression of ASGPRs in the right lobe recovered faster than in the left. The authors concluded that this technique “is a clinically useful and reliable indicator for assessing the severity of regional hepatic damage and evaluating regional liver regeneration.”

*Hepatology Research*

**PET Models of Brain Drug Concentrations**

In an article e-published on August 8 ahead of print in the *European Journal of Clinical Pharmacology*, Syvanen et al. from Uppsala Imanet (Sweden) reported on a study designed to use PET in combination with venous blood sampling and an arteriovenous transform to predict and model brain drug kinetics. They applied their modeling procedure to data from a clinical PET study in which both arterial and plasma sampling had been performed in parallel with PET measurement of radio-labeled pharmaceutical kinetics in the brain. Predictions of kinetics based on an arterial input were compared with those based on a venous input, each calculated with and without an arteriovenous transform. The authors found that venous-based models for brain distribution using the arteriovenous transform performed as well as models based on arterial data and better than venous-based models without the transform. In addition, the kinetics of 3 different brain regions could be adequately modeled with a common arteriovenous transform and an individual brain distribution model. The (Continued on page 30N)
PET and Islet Graft Survival

Lu et al. from the University of California, Los Angeles, reported in the July 25 issue of the Proceedings of the National Academy of Sciences USA (2006;103:11294–11299) on the use of PET in the noninvasive quantitative assessment of islet graft survival. Although islet transplantation is a promising therapeutic approach in patients with type 1 diabetes, both continuing graft function and graft rejection are difficult to monitor. The authors engineered a recombinant adenovirus that targeted isolated islets to express a PET-positive reporter gene. These engineered islets were then transplanted into a mouse model and imaged using microPET. They found that the magnitude of signal on PET was directly related to the transplanted islet mass. In addition, studies in which transplanted islets were dispersed throughout the liver found that clear signals from the liver region of PET reporter-expressing islets were detectable for several weeks. Additional studies indicated that transduction, PET reporter expression, and repeated microPET imaging had no apparent deleterious effects on islet function after implantation. These studies show promise in providing a foundation for exploring noninvasive imaging in patients with type 1 diabetes who undergo islet transplantation to restore glucose homeostasis.

Proceedings of the National Academy of Sciences USA

SPECT and Coronary Atherosclerosis in Hemodialysis

Hase et al. from Toho University Ohashi Hospital (Tokyo, Japan) reported in the August issue of Therapeutic Apheresis and Dialysis (2006; 10:321–327) on a study using 201TI SPECT to determine possible risk factors for progression of coronary atherosclerosis in patients undergoing hemodialysis. The study included 77 patients on hemodialysis who underwent pharmacologic challenge myocardial perfusion imaging with 201TI SPECT with high-dose adenosine triphosphate. Myocardial perfusion effects were found in 36 patients. Participants were followed for 2 years. Seventy-eight percent of patients with perfusion defects experienced cardiac events during the follow-up period, whereas only 15% of those without such defects experienced events. Cutoff values of plasma concentrations of C-reactive protein were devised to yield positive and negative values for the prediction of coronary events of 65% and 74%, respectively. The authors concluded that both myocardial perfusion SPECT and routine measurement of plasma concentration of C-reactive protein might be useful for prediction of coronary atherosclerosis progression in patients undergoing hemodialysis.

Therapeutic Apheresis and Dialysis

Dopamine Receptor Binding in Epilepsy

In a study published in the August issue of Epilepsia (2006;47:1392–1399), Werhahn et al. from the Johannes Gutenberg University (Rhineland-Palatinate, Germany) reported on an 18F-fallypride PET study of dopamine D2/D3 receptor binding in human focal epilepsy. The study included 7 patients with temporal lobe epilepsy and 9 age-matched volunteers. All patients underwent MR imaging, interictal and ictal video electroencephalography, and 18F-FDG, and epilepsy was determined on histology to be the result of hippocampal sclerosis in all. All participants then underwent 18F-fallypride imaging. The authors calculated binding potentials using a simplified reference tissue and compared epileptogenic regions of interest with those in the unaffected hemisphere in each patient and with binding in healthy participants. They found that 18F-fallypride binding was significantly decreased in the epileptogenic temporal lobe in all patients, a decrease that was especially evident in areas surrounding the seizure-onset zone at the pole and lateral aspects of the temporal lobe. Although the hippocampus uptake of 18F-FDG and hippocampal MR volumes were also significantly reduced, no significant decrease of 18F-FP binding was found in these areas. The authors concluded that these results indicate that the epileptogenic temporal lobe might correspond to “the ‘irritative zone,’ indicating that D2/D3 receptors might play a specific role in the pathophysiology of mesial temporal lobe epilepsy.”

Epilepsia

PET Aids in AD Gene Identification

Theuns et al. from the Flanders Interuniversity Institute for Biotechnology and the University of Antwerp (Belgium) reported in the September issue of Human Mutation (2006; 27:888–896) on the identification of a novel mutation in the amyloid precursor protein (APP) gene associated with early onset of Alzheimer’s disease (AD). The group has reported in previous publications on genetic variability in the APP promoter and have expanded perspectives on the various missense mutations that have been described. In this study, in addition to identifying and locating the mutation in a patient with familial early onset AD, they verified in vitro expression of increased Aβ42 and decreased Aβ40 levels, resulting in a nearly 3-fold increase in the normal Aβ42/Aβ40 ratio. The patient then underwent PET imaging which revealed “significantly increased cortical
amyloid deposits, supporting that in humans this novel APP mutation is likely causing disease.”

The same research group, this time with Brouwers as first author, also reported on August 24 ahead of print in Brain on a study of APP variability in 750 patients with AD (mean age at onset, 75.0 ± 8.6 years). Three different APP promoter mutations were identified in 7 patients, and the authors explored the relationship of these mutations to age of onset and to familial history of dementia. They concluded that their evidence suggests that “mutations in APP regulatory sequences are more frequent than APP coding mutations in APP regulatory sequences leading to providing in vivo evidence of single-gene mutations causing human epilepsy. The authors tested the hypothesis that individuals affected by the GABRG2(R43Q) mutation associated with familial generalized epilepsy have reduced binding to the GABA(A) receptor complex as assessed by 11C-flumazenil PET. The study included 14 individuals with the targeted mutation and 20 healthy individuals, each of whom underwent PET imaging. Receptor binding in individuals with the mutation was reduced compared with that in controls. The greatest reductions were found to be in the insular and anterior cingulate cortices. In addition to providing in vivo evidence of reduced benzodiazepine receptor binding in individuals with this mutation, the authors concluded that these findings “are likely to represent an important clue to the mechanisms linking this gene defect and the epilepsy phenotype.”

PET Reveals Receptor “Saturation” in Smokers

In the same month that a widely publicized study reported that the amount of nicotine in cigarettes had risen by 10%–30% in the past decade, researchers from the University of California, Los Angeles, described results indicating that cigarette smoking saturation brain α4β2 nicotinic acetylcholine receptors (nAChRs) in individuals who are tobacco dependent. Brody et al, published their report in the August issue of the Archives of General Psychiatry (2006;63:907–915). The study included 11 tobacco-dependent smokers who underwent 2-[18F]-fluoro-3-2S-azetidinylmethoxy pyridine (18F-2FA) PET imaging in 14 sessions, each with varying tobacco use, from none to satiety (2.5–3 cigarettes). The authors found that smoking only 1–2 puffs of a cigarette resulted in 50% occupancy of α4β2 nAChRs for >3 hours. Smoking 1 or more cigarettes resulted in >88% receptor occupancy. The authors concluded that “cigarette smoking in amounts used by typical daily smokers leads to nearly complete occupancy of α4β2 nAChRs,” indicating that tobacco-dependent smokers maintain this saturation throughout the day. They added that because α4β2 nAChRs are desensitized after prolonged binding to nicotine, the extent of receptor occupancy found in this study “suggests that smoking may lead to withdrawal alleviation by maintaining nAChRs in the desensitized state.”

Archives of General Psychiatry

Panic Disorder Treatment Imaged

In an article e-published ahead of print on August 2 in Neuroimage, Sakai and colleagues from a consortium of Japanese hospitals and universities reported on 18F-FDG PET imaging to elucidate the mechanisms by which cognitive-behavioral therapy improves symptoms in individuals with panic disorder. The study included 12 patients who showed improvement in panic disorder after cognitive-behavioral therapy and who underwent 18F-FDG PET brain imaging both before and after therapy. In 11 of these 12 patients, decreased glucose utilization was seen in the right hippocampus, left anterior cingulate, left cerebellum, and pons, and increased glucose utilization was seen in the bilateral medial prefrontal cortices. The authors noted significant correlations between these findings and scores on the Panic Disorder Severity Scale and numbers of panic attacks preceding each scan. They concluded that “the completion of successful cognitive-behavioral therapy involved not only reduction of the baseline hyperactivity in several brain areas but also adaptive metabolic changes of the bilateral medial prefrontal cortices in panic disorder patients.”

Neuroimage

11C-Flumazenil PET Gene Mutation Studies in Epilepsy

Fedi et al. from Austin Health Heidelberg (Victoria, Australia) reported on July 26 ahead of print in Neuroimage on a study using 11C-flumazenil PET to explore newly discovered single-gene mutations causing human epilepsy. The authors tested the hypothesis that individuals affected by the GABRG2(R43Q) mutation associated with familial generalized epilepsy have reduced binding to the GABA(A) receptor complex as assessed by 11C-flumazenil PET. The study included 14 individuals with the targeted mutation and 20 healthy individuals, each of whom underwent PET imaging. Receptor binding in individuals with the mutation was reduced compared with that in controls. The greatest reductions were found to be in the insular and anterior cingulate cortices. In addition to providing in vivo evidence of reduced benzodiazepine receptor binding in individuals with this mutation, the authors concluded that these findings “are likely to represent an important clue to the mechanisms linking this gene defect and the epilepsy phenotype.”

Neuroimage
“provide evidence for a predisposition to self-administer cocaine based on D2 receptor availability and demonstrate that the brain dopamine system responds rapidly following cocaine exposure.” Individual differences in the rate of recovery of D2 receptor function during abstinence were noted. They added that “The present findings also suggest that more vulnerable individuals are even more likely to continue using cocaine because of the cocaine-induced reductions in D2 receptor levels.” The article was covered in numerous media outlets.

*Nature Neurosciences*

**PET in Pediatric and Young Adult Bone Sarcoma**

Kneisel et al. from the Carolinas Medical Center (Charlotte, NC) reported on July 27 ahead of print in *Clinical Orthopaedics and Related Research* on the use of 18F-FDG PET to detect occult nonpulmonary metastases in young patients newly diagnosed with either Ewing’s sarcoma or osteosarcoma. The retrospective study included data from 55 patients who were younger than 30 years old at initial imaging. PET detected metastases in 12 (22%) of these patients, 8 of whom (67%) had disease outside the lung. Only 4 (7%; 3 [18% of] patients with Ewing’s sarcoma and 1 [3% of] patient with osteosarcoma) were upstaged to stage IV solely as a result of PET findings. In patients with Ewing’s sarcoma, the most important alteration in treatment decision was the substitution of radiation for surgery for local control.

*Clinical Orthopaedics and Related Research*

**PET vs. Scintigraphy in 131I-Negative Thyroid Cancer**

In an article e-published on August 8 ahead of print in the *Journal of Clinical Endocrinology and Metabolism*, Rodrigues et al. from the Hietzing Hospital and the Medical University of Vienna (Austria) reported on a comparison of 99mTc-depreotide scintigraphy and 18F-FDG PET in the diagnosis of radioiodine-negative thyroid cancer. The study included 10 radioiodine-negative patients with suspected recurrent or metastatic thyroid cancer who were imaged with both 99mTc-depreotide scintigraphy and 18F-FDG PET. Scintigraphy and PET provided true-positive results in 9 (90%) and 7 (70%) patients, respectively. In 3 patients, scintigraphy was better than PET in detecting recurrent or metastatic disease, whereas PET identified metastatic disease not seen on scintigraphy in only 1 patient. The authors concluded that these results indicate the potential value of 99mTc-depreotide scintigraphy “for the diagnosis of thyroid cancer in the setting of detectable thyroglobulin and negative radioiodine scan.” They added that scintigraphy in this setting “adds complementary information regarding the somatostatin receptor status of lesions, which may be helpful for individual therapy planning in this group of patients which are hard to manage clinically.”

*Journal of Clinical Endocrinology and Metabolism*

**Scintigraphy in 131I-Negative Thyroid Cancer**

Valsamaki et al. from the Alexandria University Hospital (Athens, Greece) reported in the August 15 issue of the *International Journal of Cancer* (2006; 119:968–970) on a case study evaluating 99mTc-depreotide scintigraphy in the restaging of papillary thyroid carcinoma with detectable serum thyroglobulin levels and negative 131I whole-body scan. The patient was a 68-year-old man with stage 3 papillary thyroid cancer, recent negative 131I whole-body scan, and a mild increase in serum thyroglobulin. The patient underwent 99mTc-depreotide whole-body planar and cervicothoracic scintigraphy, and results were compared with findings from ultrasound and CT studies and from nodal neck dissection and histopathology. 99mTc-depreotide scintigraphy identified cervical lymph node metastases that did not accumulate radioiodine, findings that were confirmed on ultrasound, CT, and histopathology. In addition, lymph node immunoreactivity was positive for somatostatin receptor subtypes 2, 5, and 3. The authors concluded that “scintigraphy with 99mTc-depreotide could prove a useful adjunct to the armamentarium for the follow-up of papillary thyroid cancer, especially in the setting of detectable serum thyroglobulin and negative 131I whole-body scan.”

*International Journal of Cancer*

**211At-Labeled mAb in CD25-Expressing Leukemias**

Zhang et al. from the National Institutes of Health reported in the August 15 issue of *Cancer Research* (2006;66:8227–8232) on the evaluation of a 211At-labeled anti-CD25 monoclonal antibody (mAb) as a potential radioimmunotherapy agent for CD25-expressing leukemias and lymphomas. Studies were performed in severe combined immunodeficient/nonobese diabetic mice bearing the karpas299 leukemia and in nude mice bearing the SUDHL-1 lymphoma. Pharmacokinetic investigations indicated that clearance and biodistribution of the 211At-labeled mAb were quite similar to those for the same mAb labeled with 125I (with the exception of higher stomach uptake of the 211At). Therapy using 15 µCi of the 211At-labeled mAb prolonged survival of the leukemia-bearing mice significantly when compared with untreated mice and with mice treated with a 211At-labeled nonspecific control antibody. By day 46 after initiation of the study, all of the mice in the control and control antibody groups had died, but >70% of mice in the 211At-labeled mAb–treated group were still alive. The authors conclude that these data point toward “an effective therapeutic agent for patients with CD25-expressing leukemias.”

*Cancer Research*

(Continued on page 36N)
**PET in Court**

The nuclear medicine community watched with interest in August as PET imaging was used as part of the defense strategy in an appeal on behalf of a convicted murderer in Georgetown County, SC. Lawyers for Stephen Stanko, an inmate on death row at Lieber Correctional Institution in Ridgeville, filed an appeal on August 21 indicating that PET imaging showed brain damage. The basis of the appeal, which will go to the South Carolina Supreme Court, is that Stanko’s execution would be unconstitutional because he has brain damage and could not control his actions. The filing came at the same time that state prosecutors announced their intention to seek a second death penalty for Stanko in another killing. The defendant’s lawyer told the press that the initial introduction of PET in the defendant’s first trial “was a precedent-setting case. . . . We’re opening our eyes to why people do these things. He [Stanko] has a brain defect from birth. He has 50%–80% loss of function in the frontal lobe and that translates into lack of character.” The appeal may take up to 1 year.

Prosecutors and most medical observers were skeptical of the attorney’s remarks and of the relevance of PET results in this case. However, the case—and the public interest generated—are reminders that as nuclear medicine procedures continue to explore verifiable measures of brain function in addiction, schizophrenia, and a range of dementias, nuclear medicine experts will be more frequently called upon to interpret the results of imaging in the legal setting.

*Myrtle Beach Online*