Multiagency Effort to Focus on PET as Biomarker

On February 14, the National Cancer Institute (NCI), the Food and Drug Administration (FDA), and the Centers for Medicare and Medicaid Services (CMS) announced the formation of the Oncology Biomarker Qualification Initiative (OBQI), an agreement among the 3 agencies to collaborate on improving the development of therapies and outcomes for cancer patients through biomarker development and evaluation. To the surprise of many in research and industry, the first collaborative project will focus not on biologic samples but on the validation and standardization of 18F-FDG PET in the identification and characterization of biochemical changes in cancer. Details of the mechanisms by which this research will be funded and completed were not included in the original agreement announcement, although insiders point to initial funding of PET assessments of radioimmunotherapy in patients with non-Hodgkin’s lymphoma.

The OBQI is the first time the 3 U.S. Department of Health and Human Services (HHS) agencies have focused together on biomarkers as a way to accelerate the development and evaluation of cancer therapies. “We are excited about this effort to speed the development and delivery of new cancer treatments for patients,” said HHS Secretary Mike Leavitt. “By bringing together the scientific, regulatory, and delivery expertise of these 3 agencies, we can bring targeted, more personalized cancer diagnostics, treatments, and preventions to patients more rapidly.”

Under the OBQI, biomarker research will focus on: (1) standardizing and evaluating imaging technologies to assess treatments; (2) developing scientific bases for diagnostic assays to enable personalized therapeutic approaches; (3) instituting new trial designs to utilize biomarkers; and (4) aggregating trial data in an accessible format to ensure that key findings are shared. A joint press release accompanying the announcement indicated that OBQI will address questions about ways in which specific biomarkers can be used to:

- Provide early assessments of response to treatment;
- Determine more definitively whether apoptosis is occurring, regardless of tumor size;
- Identify which patients are at high risk of recurrence after therapy;
- Predict response in specific patients to specific therapies; and
- Efficiently and effectively evaluate investigational therapies.

The FDA and NCI formed an Interagency Oncology Task Force (IOTF) in 2003 that served as the source for the current interagency Memorandum of Understanding, which, among its goals includes “standardization of approaches for evaluating biomarkers and tools in diagnosing, staging, and assessing therapeutic response in cancer clinical trials.” The agencies have agreed to “collaborate through working groups and steering committees to develop strategic plans, set priorities, and leverage resources and expertise from multiple sources, including the private sector, toward the goal of improving the clinical utility of biomarker technologies as diagnostic and assessment tools that facilitate the development of safer and more effective cancer therapies.”

“By identifying biomarkers for specific cancers and clinically evaluating them, researchers will have an evidence base for their use in targeted drug development and to determine which therapies are likely to work for patients before treatment selection,” said NCI Deputy Director and Deputy Director for Advanced Technologies and Strategic Scientific Initiatives Dr. Anna Barker. “Rather than waiting weeks to months to determine if a specific drug works for a patient, biomarkers could be used to monitor real-time treatment responses.”

The OBQI team will design a number of initiatives to identify and clinically qualify other cancer biomarkers in 2006 and 2007, and these and the PET imaging initiative will be funded as separate projects through the participating agencies. It is anticipated that one of the participating agencies will host a central OBQI Web site through which news of the individual initiatives can be accessed. Language included in the initial press release indicated that the OBQI will bring together scientists already at work on FDA Critical Path and NIH Roadmap Initiatives and will also represent the work of the NCI/FDA IOTF.

The full text of the interagency Memorandum of Understanding is available at www.fda.gov/oc/mous/domestic/FDA-NCI-CMS.html. Newsline will follow closely upcoming announcements of specific programs and requests for funding applications related to this initiative.
A Memoir of Pediatric Nuclear Medicine: Part 1. Pioneers and Early Advances

Dr. Conrad Nagle, Newsline editor, has requested that I provide an essay on the history of pediatric nuclear medicine. I recognize that the development of a complex medical discipline results from a series of introductory innovations and contributions by many individual practitioners and by industry. These innovations and contributions, small and large, evolve over time and build one upon the other. Any attempt to define notable events may overlook earlier works or contributions that preceded it. Therefore, I have decided to include both seminal events and a personal memoir of my years in practice.

A memoir is a report or record of events based on the writer’s personal observation or special knowledge. It is often corrupted by personal bias and a paucity of knowledge of the true facts surrounding the events. However, without embarking upon a major research project, the memoir can often provide insight into the history of a discipline. The significant events included in this memoir are those that most affected my practice. It is important to remember that it is the popularization of procedures or techniques by individuals that is most easily recalled, not necessarily the first report or original innovator.

The Beginnings

In 1946, notable military men and scientists, including H.H. Arnold, Albert Einstein, Harold Urey, and J.R. Oppenheimer, published a booklet titled One World or None. They were concerned about the future uses of atomic energy and spoke up for applications outside of the military. To my knowledge the first postwar symposium on the use of radioisotopes in biology and medicine was presented at the University of Wisconsin in 1948. Among the nuclear medicine pioneers participating in that symposium were Paul C. Aebersold, MD, Glenn T. Seaborg, PhD, and Joseph G. Hamilton, MD.

Pediatric nuclear medicine had its clinical beginnings in 1946. According to a Nuclear Regulatory Commission report, more than 1,000 radioisotope studies of the thyroid gland in children and adolescents were performed at 21 institutions in the United States between 1946 and 1948. Thus, early on, many practitioners identified the utility of nuclear medicine in children. Among these researchers was Hamilton at the University of California, Berkeley, who studied the thyroid gland of a child using $^{131}I$ and a Geiger–Muller tube. This image of a child undergoing a thyroid radioisotope study has been reproduced many times in texts and presentations as an early example not only of the use of radioisotopes in children but of the introduction of clinical nuclear medicine.

In 1955, George V. Taplin, MD, at the University of California at Los Angeles reported on the use of $^{131}I$-labeled rose bengal to study liver function. With C.C. Winter, MD, a urologist, Taplin in 1956 reported on the use of $^{131}I$-labeled diodrast to study renal function with scintillation probes. These procedures further laid the foundation for pediatric nuclear medicine.
foundation for the beginnings of routine pediatric nuclear medicine.

In 1954, medical student David Kuhl introduced the photorecorder that allowed the transfer of scintillation events in a crystal into a visual plot or image. This would prove to be an important element in the development of the rectilinear scanner. Benedict Cassen, MD, invented the rectilinear scanner, which “painted” a picture of radioisotope distribution in the patient’s body (7).

One of the first pediatric practitioners to routinely use radioisotopes in children for imaging was Mel Tefft, MD, a radiotherapist at the Boston Children’s Hospital (MA). In the early 1960s, he imaged the brain and other organs with a rectilinear scanner and 197Hg (8). For lack of space, his scanner was set up in a corridor outside the radiotherapy department.

Two signal events accelerated the development of the subspecialty of pediatric nuclear medicine. The first was the invention of the gamma camera by Hal Anger, who developed his prototype cameras at the Donner Laboratory in California between 1952 and 1958 (9,10). Alex Gottschalk, MD, joined Anger at the Donner Laboratory in 1962 and studied a few children with the prototypes. The gamma camera was especially suited for pediatric imaging because of its dynamic capabilities and an 8-inch field of view that was large enough to encompass most organs in the child. Images could be obtained in a matter of seconds to minutes rather than an hour or more with the rectilinear scanner.

John Kuranz, a founder of the Nuclear–Chicago Corporation in Chicago, IL, recognized the potential of the gamma camera for medical imaging. His company supported the development of the first commercially available 8-inch scintillation crystal, 19-photomultiplier tube gamma camera, installed in 1962 for William Myers, MD, at the Ohio State University Hospital at Columbus. The gamma camera allowed dynamic imaging of renal function, a major impetus to the use of radioisotopes in children. Pioneers such as Taplin, Winter, Keith Britton, MD, Gerald Burke, MD, Arlene Halko, MD, and John Harbert, MD, reported on the use of dynamic renal scintigraphy and renography with the gamma camera in the early to mid 1960s.

Burke and Halko at the Michael Reese Hospital in Chicago published the first report on the use of an 11-inch gamma camera to produce a 131I-iodohippurate renogram. They first localized the kidneys with an injection of 201Hg-chlormerodrin, and each kidney then was studied separately by positioning the kidney in the center of the field and administering separate injections of the radiiodinated hippuran (11).
In the late 1960s, Nuclear–Chicago modified the electronics of their 19-inch Pho Gamma III camera to “split the crystal,” so that both kidneys could be viewed simultaneously and the radioactivity counts from each kidney could be recorded separately on a graph chart recorder. The larger size of the Pho Gamma III camera was ideal for children. At Children’s Memorial in Chicago, we soon availed ourselves of the “split crystal technique” for renography (Figs. 3, 4). We improvised the technique of a 2-minute image with the Polaroid camera, which revealed any mispositioning so that we could easily adjust the child to recover the remainder of the renogram. Serendipitously, we recognized that the 2-minute image was a wonderful monitor for determining the glomerular function rate (GFR) of the kidneys. With experience, I could fairly accurately estimate the GFR by simply viewing the image. I believe that the results from this technique were about as accurate as all the later GFR techniques, many of which are still controversial. The later instrumentation advances of the tape recorder device and data recorder with region of interest instrumentation removed the need for special skills to position the child on the camera or to image kidneys not in their normal position.

The second major development in the early 1960s was the clinical introduction of $^{99m}$Tc-pertechnetate by Paul Harper, MD, a general surgeon, and his colleagues at the hospital of the University of Chicago (12). The 140-keV energy emission of $^{99m}$Tc allowed penetration of most body organs. The efficient energy absorption in the thinner crystal of the gamma camera increased the image resolution, and the short effective half-life of the radioisotope allowed its use in children.

The number of studies and innovative techniques in pediatric nuclear medicine increased significantly between 1963 and 1972. In 1971, the first dedicated pediatric nuclear medicine symposium was held at Johns Hopkins in Baltimore, MD. The presentations at the symposium resulted in the first pediatric nuclear medicine text, with contributions from 85 authors representing both pediatric and adult practice. Published in 1974, the book was edited by A. Everette James, MD, Henry N. Wagner, Jr., MD, and Robert E. Cooke, MD (17).

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In 1971, Gopal “Mani” Subramanian, PhD, and John McAfee, MD, developed 99mTc-polyphosphate for skeletal scintigraphy (18). Pediatric nuclear medicine took a giant step forward with the 99mTc-labeled phosphate radiopharmaceuticals. The lower total-body absorbed dose from this class of radiopharmaceuticals enabled the study of benign disorders of the skeletal system in children. The characteristics of 18F for bone scintigraphy had restricted its use in children to the study of bone cancer and metastases. The 99mTc-phosphate radiopharmaceuticals allowed additional studies of bone and soft tissue disorders, including infection, trauma, and sports injuries.

In October 1972 and January 1973, Seminars in Nuclear Medicine devoted issues to pediatric nuclear medicine. I was honored to serve as guest editor for those issues, which were combined in 1975 as a text published by Leonard Freeman, MD, and Donald Blaufox, MD (19).

In 1973, Hirsch Handmaker, MD, and Jerold Lowenstein, MD, hosted a pediatric nuclear medicine symposium at the Children’s Hospital of San Francisco (CA). A multiauthor book representing the proceedings of that conference followed in 1975 (20).

Many other advances have forwarded the cause of pediatric nuclear medicine. Among these are the works of Massoud Majd, MD, who publicized the importance of phenobarbital in preparation for hepatobiliary scintigraphy in children with persistent neonatal jaundice (21). He is also recognized for his research in a swine model documenting that defects visualized with renal cortical scintigraphy are localized in sites of pyelonephritis (22). Majd also was an early pioneer in the use of captopril for the diagnosis of renovascular hypertension in children (23). George Sfakianakis, MD, popularized this technique (24).

Ted Harcke, MD, and Gerald Mandel, MD, published on a variety of subjects affecting the musculoskeletal system, drawing on their experience at the Alfred I. DuPont Institute for Children in Wilmington, DE. Harcke promoted intraoperative probe monitoring for surgical removal of osteoid osteoma and other tumors in difficult-to-reach but critical areas, such as the spine. He traveled at his own expense to many institutions, including our own, to assist practitioners in setting up the handheld scintillation probe detector to perform the procedure correctly (25).

In 1970, while attempting to image appendicitis with 99mTc-pertechnetate, T.C. Jewett, MD, a surgeon, and Diane Duszynski, MD, at Buffalo Children’s Hospital (NY), recognized this as a valuable approach for localizing Meckel’s diverticulum (26,27). T.H. Berquist, MD, would report in 1973 that this radiotracer localized in ectopic gastric mucosa in the “Barrett’s” lesion of the esophagus (28). In our own studies of several children with “Barrett’s esophagus,” we found that 99mTc-pertechnetate did not always localize in the lesion. Biopsy or surgical removal of the stricture lesions demonstrated a lack of mucosal cells in those lesions. These strictures were the result of metaplasia from gastroesophageal reflux and not a true ectopic gastric mucosa, as Barrett originally described. Tapan Chadhuri, MD, did excellent research on animals and proved that it was the mucous cell in the gastric mucosa that localized the 99mTc-pertechnetate. (29). The “mucous cells” in the colon do not localize the radioisotope, and I always used that as an example to teach the functional rather than the anatomic aspect of nuclear medicine. I published our experience with Meckel’s diverticulum in 1980, and Sfakianakis and I conducted a comprehensive 10-year revue of Meckel’s diverticular scintigraphy to point out the immense value of that technique for imaging of rectal bleeding in children (30–32).

Larry Holder, MD, in Baltimore, MD, and others published important works on scrotal scintigraphy (33). The test took less than 30 minutes and had a high degree of accuracy in differentiating the various disorders. The surest means of determining torsion of the testicle had previously been by surgery, with many nonsurgical conditions mimicking torsion and proceeding to unnecessary intervention. Today, scrotal scintigraphy has been replaced by techniques with color Doppler ultrasonography.

S. Ted Treves, MD, developed the method for accurately and noninvasively quantifying left-to-right cardiac shunts in children (34,35). This innovation provided cardiologists with a means of measuring and monitoring the severity of shunts within the heart.

David Gilday, MD, and Judith Ash, MD, in Toronto, Ontario, have published extensively on all aspects of pediatric nuclear medicine and have represented the field throughout the world in their lectures and presentations.

In 1983, Jack Sty, MD, and Robert Starshak, MD, at Milwaukee Children’s Hospital (WI) recognized the value of bone scintigraphy in detecting child abuse, an approach we reviewed in an article in Seminars in Nuclear Medicine (36,37). From a legal aspect, the number of lesions that are detected has a significant impact on the outcome of court trials. Bone scintigraphy is a much more sensitive detector of abuse lesions than is plain radiography. In fact, we demonstrated that anterior rib lesions are just as common as posterior rib lesions but are poorly recognized by X-rays. I was summoned to court in a number of abuse cases and found that demonstrating 5 or 10 lesions rather than 1 or 2 provided compelling evidence of child abuse.

Sty and I published a review article on the use of radionuclides in the evaluation of the spleen in children (38). R.G. Wells, MD, and Sty also published an excellent review of the role of nuclear medicine in the screening of neonates with thyroid disorders (39). Sty’s books on pediatric nuclear medicine imaging have set the standard for quality and offer an extensive bibliographic reference source for almost every procedure in pediatric nuclear medicine. His books in my library are worn and broken from use (40,41).

James Kereiakis, PhD, Eugene Saenger, MD, and Henry Wellman, MD, pioneered radioisotope dosimetry calculation studies in children (42). Wellman also was a pioneer in promoting the use of 123I radiopharmaceuticals.
From 1963 through 1972, new pediatric techniques were introduced by many other “pioneers,” including Leonard Rosenthal, MD, Michael J. Gelfand, MD, Joe Leonard, MD, Meg Parisi, MD, Helen Nadel, MD, and John Miller, MD. At the time, many researchers who believed they had developed new techniques had only to search the literature to discover that Rosenthal had done the same thing years before.

The University of Michigan group, under the leadership of William Beierwaltes, MD, contributed significantly to the welfare of children with their development and promotion of iodinated metaiodobenzylguanidine for the study of neuroendocrine tumors (43).

Kuhl, with engineer Roy Edwards, developed the first computed axial tomograph at the Hospital of the University of Pennsylvania in 1964 (44). The first emission computed tomography image of a human was acquired in 1966. SPECT and PET evolved from Kuhl’s concepts.

A number of individuals who primarily focused on adult nuclear medicine have also made significant contributions to pediatric practice. Among these were: John Freitas, MD, and his colleagues who pioneered radioisotope thyroid therapy in children for hyperthyroidism; Beierwaltes, who reported on the long-term consequences of radioisotope therapy in children; Phil Alderson, MD, who performed pediatric lung and cardiac studies in children; and Naomi Alazraki, MD, and Andrew “Tip” Taylor, MD, noted for work in developing $^{99m}$Tc-mercaptoacetyltriglycine ($^{99m}$Tc-MAG3), an ideal radiopharmaceutical for renal imaging in children (45–47). $^{99m}$Tc-MAG3 was one of the first radiopharmaceuticals approved by the U.S. Food and Drug Administration for use in children. This approval was subsequent to prospective phase III clinical trials sponsored by Mallinckrodt, Inc. Sue Weiss, CNMT, James Halama, PhD, James Everett, CNMT, and I furnished the phase III absorbed radiation dosage measurements for $^{99m}$Tc-MAG3 for the various age levels from infancy to teens (48).

Other significant contributors to the advancement of pediatric nuclear medicine include Gary Gates, MD, John Miller, MD, Richard Spencer, MD, Martin Charron, MD, Barry Shulkin, MD, Harriet Paltiel, MD, Rick Shore, MD, Monica Rossleigh, MD, Sidney Heyman, MD, and others.

Among the international contributors who come to mind are Gian Carlo Mussa, MD, of Torino, Italy, who primarily studied neonates; Rune Six, MD, in Sweden; Amnon (Amy) Piepsz, MD, in Brussels, Belgium; Isky Gordon, MD, and Andrew Hilson, MD, in England; Klaus Hahn, MD, in Munich, Germany, who has sponsored several pediatric nuclear medicine conferences and published an atlas of pediatric nuclear medicine; Joe Savage, MD, Robert Howman-Giles, MD, Shane Moroney, MD, and Proven Murray, MD, in Australia; Homai Da Costa, in Bombay, India; Daniel Schere, MD, in Buenos Aires, Argentina; Isabel Roca, MD, in Spain, who has conducted pediatric nuclear medicine meetings in recent years, and Enrique Olea, MD, in Santiago, Chile. Unfortunately, space does not permit appropriate recognition of many other practitioners and events.

The early innovations could not have been achieved without pioneer pediatric nuclear medicine technologists. Among the most notable were Weiss, in Chicago; Elizabeth Kilburn, RTNM, in Toronto; Royal Davis, CNMT, in Boston, MA; George Hoebring in Kansas City, MO; Barbro Ljung in Sweden; and Jill Freeman, Michele Maher, and Heather Bauer in Australia.

REFERENCES


(Continued on page 32N)
Q&A: Perspective on Pediatric Nuclear Medicine

Michael J. Gelfand, MD, is chief of the Section of Nuclear Medicine at Cincinnati Children’s Hospital Medical Center (OH) and a past president of SNM. He co-edited the 1994 text Pediatric Nuclear Imaging and has published more than 100 articles and 30 book chapters. Newsline spoke with Gelfand about the current status and future of pediatric nuclear medicine in the United States.

Newsline: What do you personally consider to be the biggest “stories” in contemporary pediatric nuclear medicine? What innovations are the most promising?

Gelfand: The number 1 innovation on my list is 18F-FDG PET. Almost every non–central nervous system solid tumor that we see in children and adolescents has high avidity for FDG. 18F-FDG PET imaging is ready to move into a major role in pediatric oncologic imaging. This is already occurring with both Hodgkins’ and non-Hodgkins’ lymphoma. The challenge will be to extend 18F-FDG PET imaging to less common pediatric solid tumors and to include 18F-FDG PET imaging as a mainline diagnostic imaging technique in as many as possible of the multicenter cancer treatment protocols for solid tumors.

A few other areas of innovation are notable. PET/CT is taking over from PET, just as in adult nuclear medicine. PET radiopharmaceuticals other than 18F-FDG are of considerable interest. 18F-fluoride has been used for bone scans in children at Boston Children’s Hospital. 11C-methionine has been used for brain tumor imaging in children in Turku, Finland. In body imaging, we have not yet found another general purpose radiopharmaceutical that is as good as 18F-FDG for tumor imaging, but we should keep looking. In the brain, we should be able to improve on 18F-FDG. We will find other radiopharmaceuticals that are potentially useful in children; the challenge will be to study these radiopharmaceuticals and establish clinical roles for them.

Then there is the whole question of molecular imaging—finding ways to use PET imaging in children that take advantage of the vast amount of knowledge that has been gained about the control of normal and abnormal processes in the body. Accomplishing this goal should allow us to use PET imaging to answer many more diagnostic, therapeutic, and research questions.

A final area of innovation is in cancer therapy. 131I-metiodobenzylguanidine is gaining a role in the treatment of advanced neuroblastoma, and it is possible that the anti-CD20 therapeutic agents will be used in the future in pediatric B-cell lymphomas.

Newsline: Our colleagues in radiology have been confronted in the past 5 years with well-publicized studies indicating that pediatric exposure in routine CT examinations has often been considerably higher than required for quality imaging. Yet we don’t hear that much about this topic in nuclear medicine. Now that hybrid imaging is securing a place in the nuclear imaging suite and also with the advent of new and more effective therapies, is this a topic that should be brought more to the forefront in nuclear medicine?

Gelfand: Diagnostic CT is a major source of medical radiation exposure in children and adolescents. My colleagues at Cincinnati Children’s Hospital have been leaders in dose reduction in pediatric CT, lowering beam current levels (mAs) to the lowest levels that are consistent with high-quality CT imaging. In general, dose reductions of about 50% have been achieved. Over the last 5 years, application of such lower dose levels has spread steadily from leading pediatric hospitals to other medical centers.

A tougher question is utilization. The number of CT examinations in children has grown rapidly. Some of this expansion is appropriate. At our hospital, a review of CT studies performed to rule out appendicitis indicated that our utilization was appropriate. But utilization should be monitored everywhere, formally or informally.

In nuclear medicine, the administered activity determines the radiation dose. Beginning 25 years ago, a number of physicians experienced in pediatric nuclear medicine have regularly published lists of suggested administered activities, usually based on weight, for pediatric nuclear medicine imaging. In the area where I live, it appears that word got out, because for the last 10 to 15 years, when we receive studies from other hospitals, the administered activities are usually reasonable.

The arrival of hybrid imaging, including PET/CT and SPECT/CT, is another challenge. At our hospital, the effective dose for a “low dose” diagnostic CT for a study of the chest, abdomen, and pelvis is about 50% higher than the effective dose for the 18F-FDG PET scan. The effective dose for a “localization” CT scan at minimum exposure settings is about 30% to 50% less than the PET scan, and
the effective dose for an attenuation-only scan is very low. As PET moves from oncologic imaging into imaging of benign conditions, how we perform the CT part of the PET/CT will be the most important determinant of total effective dose from the procedure. The same is true for SPECT/CT with $^{123}$I- or $^{99m}$Tc-labeled radiopharmaceuticals.

The good news is that, as we move studies from $^{67}$Ga imaging to $^{18}$F-FDG PET, the effective radiation dose received by the patient from the radiopharmaceutical will fall significantly.

**Newsline:** It has been difficult to perform nuclear medicine research in pediatric patients because of limitations on radiation exposure. How can progress in adult nuclear medicine and basic research be translated to aid children with serious diseases? Should we urge the research community and regulatory bodies to endorse conscientious but extended nuclear medicine research in this population?

**Gelfand:** The performance of research studies in children and adolescents with new radiopharmaceuticals is a big problem. Everyone is aware of the incredible surge in knowledge in human molecular biology. This knowledge base is being constantly applied in pediatrics. The opportunities for research in molecular imaging are immense, but the barriers are high. In the United States, initial studies in adults can often be performed using the Radioactive Drug Research Committee (RDRC) mechanism. The current RDRC regulations have limited pediatric dose levels to 10% of those allowed in adults, which is too low to allow research studies with PET radiopharmaceuticals. We want to limit radiation dose in the pediatric population. However, useful research has been hampered by limits that may be appropriate for the general pediatric population but too restrictive for children with cancer and other serious diseases associated with shortened lifespans. The U.S. Food and Drug Administration (FDA) is currently working on a revision of the RDRC regulations. The pediatric nuclear medicine community in the United States has asked the FDA to liberalize the RDRC regulations to allow somewhat higher radiation doses for research in children with cancer and other diseases with reduced life expectancy, in order to facilitate research with PET radiopharmaceuticals in children with these diseases.

Research in the United States can also be performed under an Investigational New Drug (IND) exemption. The FDA has made real efforts to facilitate IND applications. Still, an IND application requires more effort for the investigator than an RDRC application, and, in some cases, the supporting data for an IND application cannot be acquired at reasonable cost.

**Newsline:** The numbers of individuals who have devoted their careers to pediatric nuclear medicine is relatively small (perhaps in part because of the long-held notion that children’s nuclear medicine should be merely a titrated version of adult diagnosis and therapy). Should we as a profession be encouraging more of our trainees to focus on this area of practice?

**Gelfand:** If nuclear medicine is going to move forward in the United States, with high-quality, proactive teaching, there must be well-trained individuals practicing nuclear medicine at academic medical centers and major hospitals. These are the people who can teach nuclear medicine, and some of them will be clinical researchers as well. They are in short supply. In pediatric nuclear medicine, the shortage is even more acute. Many of the leaders at the major children’s hospitals in the United States recognize that it is important to have an academic and research leader in nuclear medicine in their departments, but we need to train additional leaders. We need to encourage physicians who are going into nuclear medicine to train themselves for academic careers, and, particularly those who are going into pediatric radiology, to seriously consider additional training in nuclear medicine.

In reality, the physicians who currently practice nuclear medicine must provide the inspiration to the next generation of physicians to become the future leaders.
SNM 2006 Awards Include New Initiatives and Innovative Support for Research and Education

A series of research awards and competitive grant recipients were announced by the SNM at its Mid-Winter Educational Symposium in Tempe, AZ, on February 11. Several of these funding mechanisms are new in 2006 and represent a renewed effort by the SNM and the Education and Research Foundation (ERF) for the SNM to support a broad range of investigative and training activities at the forefront of molecular and nuclear medicine discovery.

SNM/GE Healthcare Grants

Three institutional recipients of the new $10,000 SNM/GE Healthcare Visiting Physician/Scientist Program grants were announced. These grants will allow nuclear/molecular imaging physicians and scientists from North America to lecture, consult, and train at 1 or more institutions or organizations in China and India. “International collaboration such as this benefits the entire molecular and nuclear imaging community as we work together to advance patient care around the globe,” said SNM President Peter S. Conti, MD, PhD, a professor of radiology, clinical pharmacy, and biomedical engineering at the University of Southern California, Los Angeles, and director of the PET Imaging Science Center at the Keck School of Medicine. “Together, we can broaden our knowledge, gain a better understanding of disease and collaborate on developing life-saving treatments.” Grant recipients are the Peking Union Medical College Hospital/Beijing Chapter of the Chinese Society of Nuclear Medicine, a premier health care facility with an 8-year program in clinical medicine; the Second Hospital of Zhejiang University, a center of health care, medical education, and scientific research in the Zhejiang Province in China; and the Society of Nuclear Medicine, India, a membership association that encourages research in and provides a forum for the exchange of ideas and experience among scientists.

The SNM/GE Healthcare Visiting Physician/Scientist Program Grant for China and India will cover travel and per diem costs. During a 1- or 2-week period, a visiting physician/scientist will spend time lecturing, training, and consulting on molecular and nuclear imaging. Eligible applicants included clinical centers, hospitals, academic institutions, and consortia of institutions with active molecular and nuclear imaging programs in China and India. International societies of nuclear medicine based in these countries could also apply. Program visits will take place during the 2006 calendar year.

Student Fellows; Bradley–Alavi Fellows

The recipients of 5 fellowships for students involved in full-time clinical and basic research activities in molecular and nuclear imaging were also announced at the Mid-Winter meeting. These fellowships are funded by the ERF for SNM and provide $3,000 for each recipient. Eligible students are enrolled in medical, pharmacy, or graduate schools or are undergraduates who demonstrate outstanding competence in molecular and nuclear imaging research.

The top 3 recipients of these awards are also designated as Bradley–Alavi Fellows, in honor of the late Stanley E. Bradley, a professor of medicine at Columbia University College of Physicians and Surgeons and a prominent researcher in the fields of renal physiology and liver disease, and Abass Alavi, MD, professor of radiology and chief of the division of nuclear medicine at the University of Pennsylvania Medical Center. This year’s Bradley–Alavi Fellows include: Mai Lin, BA, MS, University of Texas Southwestern Medical Center at Dallas; Guillem Pratx, School of Medicine, Stanford University (CA); and Shu-An Lin, School of Medicine, Stanford University (CA).

Student fellowships were awarded to: David Yerushalmi, BS, MS, Stanford University (CA); and Gang Ren, MD, University of Texas Southwestern Medical Center at Dallas.

SNM/Mallinckrodt Seed Grant

Meixang Yu, PhD, associate professor and chief PET radiochemist at the University of Tennessee Health Science Center in Memphis, was named the first recipient of the SNM/Mallinckrodt Seed Grant in Molecular Imaging/Nuclear Medicine Research. This competitive grant is designed to assist researchers in conducting new and innovative pilot projects that have potential for future support from foundations, corporations, or government agencies. The grant for Yu’s research project, “Molecular Imaging and Biological Evaluation of 124I Avastin Anti-VEGF Antibody: Implications for Cancer Diagnosis and Treatment Response,” was made possible by a $25,000 donation from Tyco Healthcare/Mallinckrodt. “This research project will extend our knowledge of how an existing radiotracer may be eventually used to fight colorectal and lung cancer in humans,” added ERF Vice President Robert F. Carretta, MD.

Yu earned a doctorate in radiological chemistry in 1996 from Peking University and completed postdoctoral work at Kuopio University in Finland. She received her bachelor’s degree in chemistry in 1990 from Peking University in
China and a master’s degree in analytical chemistry in 1993 from the China Institute of Atomic Energy. Yu has been involved with PET tracer development for more than 10 years and has experience in PET data processing, including modeling calculation.

**Ashburn Pilot Research Grant**

The ERF also funded the William L. Ashburn, MD, Pilot Research Grant, which is supported by Digirad Corporation in memory of the cofounder of the company, a physician researcher whose career in molecular and nuclear imaging spanned almost 40 years. Steven Burrell, MD, assistant professor at the Queen Elizabeth II Health Sciences Center (Halifax, Nova Scotia), received $10,000. His research project is “Cardiac 123I-Metaiodobenzylguanidine Imaging as a Means of Predicting Automatic Implantable Cardioverter Defibrillator Events.”

**Blahd Pilot Research Grant**

In addition, the ERF funded the Mitzi and William Blahd, MD, Pilot Research Grant, which honors the couple’s dedication to philanthropic support for education and research in nuclear medicine. Jun Zhao, PhD, a research scientist at the Research Foundation of Mental Hygiene Inc., New York State Psychiatric Institute, at Columbia University (New York City), received $8,000 for his project, “Development of NMDA/Glycine Site PET Radioligands.”

**Pilot Research Grants**

Recipients of 2006 pilot research grants have also been named. These grants, each totaling $8,000, support clinical and basic research by young investigators who are interested in testing innovative ideas while other major grant support is being sought. Recipients include: Datta E. Ponde, PhD, research assistant professor, University of Pennsylvania (Philadelphia), for “Comparison of Radiolabeled Choline and Ethanolamine as a Probe for Cancer Detection and for Measuring Cell Proliferation”; Jinsong Ouyang, PhD, physicist at Brigham & Women’s Hospital and instructor at Harvard Medical School (Boston, MA), for “Fast and Accurate Iterative Reconstruction for Simultaneous Dual-Isotope SPECT Using Parallel Computing”; Feng Quing, MD, PhD, PET fellow, University of Iowa Hospitals and Clinics, PET Center (Iowa City), for “Perfusion and Oxygenation in Mouse Tumors Using 133Xe Gamma Imaging and Oxygen Electrodes”; and Mike F. Georgiou, PhD, research assistant professor, University of Miami Hospital and Clinics/Sylvester Cancer Comprehensive Center (FL), for “A PET Gating System for Respiratory Motion Compensation of Lung Lesions.”

The ERF has supported the molecular imaging/nuclear medicine community for more than 35 years. The foundation’s mission is to advance excellence in health care through education and research in molecular imaging/nuclear medicine by provision of grants and awards. For more information about these awards or the ERF, contact Kathy Bates, SNM director of development, at 703-708-9000, ext. 1028, or kbates@snm.org. Information is also posted on the SNM Web site at www.snm.org/grants.

**SNM Newsline**

**SNMTS Announces 2006 Scholarship and Grant Recipients**

At the SNM Mid-Winter Educational Symposium in Tempe, AZ, on February 11, the SNMTS released the names of 37 molecular and nuclear medicine technologist students and researchers who will be awarded a total of $58,000 in scholarships and grants in 2006. “Through its scholarship and grants program, SNMTS invests in the future of the nuclear medicine technology profession by supporting both the development of future practitioners and research,” said SNMTS President Valerie R. Cronin, CNMT, in announcing these awards. “SNMTS remains committed to encouraging individuals to pursue careers in molecular and nuclear imaging.”

**Professional Development Education Fund Research Grant**

The awards include the Professional Development Education Fund (PDEF) Research Grant, which provides $10,000 to encourage technologists to initiate innovative research projects that advance knowledge of the profession in either clinical practice, education, or professional development. Gregory G. Passmore, PhD, CNMT, associate professor of biomedical and radiological technologies with the School of Allied Health Sciences and the School of Graduate Studies at the Medical College of Georgia, Augusta, is the recipient of this award. Passmore’s research project, “Testing of DU Collimator for Removal of Tl/Tc Dual-Isotope Cross-Talk,” applies basic physics principals to a clinical nuclear medicine technology problem.

**Mickey Williams Minority Student Scholarships**

Two Mickey Williams Minority Student scholarships, which each provide $5,000 to a minority student entering or enrolled in a 2- or 4-year molecular imaging/nuclear medicine technologist program, were awarded. One recipient is
Christina Araujo of Omaha, NE, an undergraduate student in the nuclear medicine program at the University of Nebraska Medical Center in Omaha. The other is Starr White of Easton, PA, an undergraduate student with the nuclear medicine technology program at Cedar Crest College (Allentown, PA).

PDEF Professional Development Scholarship

In addition, a $5,000 PDEF Professional Development Scholarship, which supports a nuclear medicine technologist who is pursuing a master’s or doctoral degree, was awarded to Said Diabes Figueroa, MS, CNMT, RT(N), of Columbia, MO, a doctoral student in the Nuclear Science and Engineering Institute at the University of Missouri–Columbia. He received an extension on a 2-year PDEF Professional Development Scholarship to pursue doctoral research on imaging and dosimetry related to new radiation-based therapeutic agents.

Paul Cole Scholarships

A total of 33 Paul Cole scholarships were announced at the Mid-Winter meeting. These $1,000 awards provide support for students enrolled in or accepted for enrollment in associate, baccalaureate, or certificate programs in nuclear medicine technology. Awards are based on financial need, statements of goals, academic performance, and program director recommendations. The recipients and their academic affiliations include: Travis Fogelman, Delaware Technical and Community College (Wilmington); Katherine Weigel, College of Health Sciences, Florida Hospital (Orlando); Michelle Kraus, Medical Sciences Education Department, St. Vincent’s Medical Center (Jacksonville, FL); Susie Zumbahlen, St. Louis University (MO) (funded by SNM’s Central Chapter); Georgianna Stefanatos, Elmhurst College/Northwestern Memorial Hospital (Chicago, IL) (funded by SNM’s Central Chapter); Marjan Muvceski, School of Medicine, Indiana University (Indianapolis); Brittni Jackson, School of Health Sciences, Mayo Clinic (Rochester, MD); Karly Sopic, University of Iowa Hospitals and Clinics (Iowa City); Brandi Huber, University of Iowa Hospitals and Clinics (Iowa City); Jami Hogan, Ferris State University (Big Rapids, MI); Michelle Benaske, Ferris State University (Big Rapids, MI); Louis Mbiib, College of Medicine, Mayo Clinic (Rochester, MD); Flint Ansden, School of Nuclear Medicine, Central Maine Medical Center (Lewiston); Garrett Holzum, University of Missouri (Columbia); Jaykumar Patel, School of Health Related Professions, University of Medicine and Dentistry of New Jersey (Columbia); Deanna Saldana, Nuclear Medicine Institute, University of Findlay (OH); Charity Harris, Kent State University/Salem (OH); Jenny Duval, University of Arkansas for Medical Sciences (Little Rock); Audrey Willett, Health Science Center, Department of Radiologic Technology, University of Oklahoma (Oklahoma City); Lindsay Wilson, University of Oklahoma Health Science Center (Oklahoma City); Stacey Trone, Lancaster General College of Nursing and Health Sciences (PA); Shelly States, Nuclear Medicine Institute, University of Findlay (OH); Jonathan Crites, Kent State University/Salem (OH); Megan Berkstresser, Indiana University of Pennsylvania (Indiana, PA; joint program with the University of Findlay); Laura Dee Trinnen, Medical College of Georgia (Augusta); Nealy Cook, Midlands Technical College (Columbia, SC); Melissa Dutton, Midlands Technical College (Columbia, SC); Ryan Raml, Southeast Technical Institute (Sioux Falls, SD); Jaime Reid, Nuclear Medicine Institute, University of Findlay (OH); Amanda Wanta, Aurora St. Luke’s Medical Center, University of Wisconsin (La Crosse); Ashley Mroczenski, College of Medicine, Mayo Clinic (Rochester, MN); Robert McPherson, University of Toronto (Ontario; joint program with Michener Institute, Toronto, Ontario); Lindsey Doble, University of Toronto (Ontario; joint program with Michener Institute, Toronto, Ontario); and Joshua Clayton, Atlantic Health Sciences Corporation, New Brunswick Community College/University of New Brunswick (Saint John).

The PDEF Research Grant, the PDEF Mickey Williams Minority Student scholarships, and the PDEF Professional Development Scholarship are funded by the Corporate Friends of PDEF: Biogen Idec, Bristol-Myers Squibb, Capintec Inc., GE Healthcare, Mallinckrodt Inc., and MDS Nordion. The Education and Research Foundation (ERF) for the SNM works to advance excellence in health care through education and research in molecular imaging/nuclear medicine by provision of grants and awards. For more information about these awards or to learn more about the PDEF or the ERF, contact Kathy Bates, SNM director of development, at 703-708-9000, ext. 1028, or at kbates@snm.org. Information is also posted on the SNM Web site at www.snm.org/grants.
Our Preferred Future

As physicians, technologists, and scientists, we strive to be wise and enlightened guides to the young women and men who are our profession’s future. We discuss—and often passionately express—our feelings about the necessary level of education needed for entry into the molecular and nuclear imaging profession. Future professionals—our residents, fellows, and recent graduates—debate this educational issue as well—most recently in online discussions on the Young Professionals Committee (YPC) listserv.

These discussions indicate that there is concern about the future job market of nuclear medicine physicians. Will newly graduated nuclear medicine physicians be able to find positions? The overall positive impression is that most recent American Board of Nuclear Medicine (ABNM)–certified nuclear medicine physicians (72%) do find full-time positions within a year of graduation (79%), according to an informal, 28-question, online survey distributed by the YPC. Heather Jacene, MD, YPC chair, and Darlene F. Metter, MD, Academic Council president, acknowledge this concern. The council intends to investigate this issue on a national scale, document the facts, develop a national network, and build academic bridges with our radiology colleagues.

Does the current training address all the needs of young professionals? It’s not surprising that survey respondents ranked knowledge of general nuclear medicine and PET/CT training as skills most necessary to receive a job offer. Many of our residents do not have a radiology background, and, in fact, many PET/CT practitioners may not be radiologists or current in CT. We know that molecular imaging will lead to a much greater ability to characterize diseases, diagnose them at a very early stage, treat them effectively, and monitor the effectiveness of such treatment. PET, PET/CT, SPECT, SPECT/CT, and other new techniques now in development have advanced our knowledge beyond any expectations, captivated the imagination of the current generation of professionals, and ignited the evolution of our profession.

The Accreditation Council for Graduate Medical Education (ACGME)—a private, nonprofit council that evaluates and accredits medical residency programs in the United States—recognizes that new, major technologies are being used and need to be included in educational training. As part of new ACGME requirements beginning in July 2007, the length of training for nuclear medicine residents who have had only an internship will be increased from 2 to 3 years. In addition, the requirement for training in CT is “substantially strengthened.”

In response, ABNM, the primary certifying organization for nuclear medicine in the United States, is changing its formal requirements for entry to its certifying exam to match the ACGME Residency Review Committee program requirements, according to Christopher J. Palestro, MD, ABNM chair. On future examinations, candidates for both certification and recertification can expect an increasing emphasis on morphologic—especially cross-sectional—imaging studies and therapeutic medicine, he said.

Our young professionals—and our members—continue to look to SNM for answers, for training, and for a professional connection. We need to adapt to changes in technology, practice, and patients’ needs. Is SNM at the forefront of this adaptation? Most definitely, yes. What is the preferred future we seek? It is one where molecular and nuclear imaging professionals must be versed in both functional and anatomic imaging—and SNM has taken up the educational challenge.

For young professionals, the society is a powerful resource, offering essential training opportunities, a network of personal contacts, a job bank, and inclusion on our many committees. For young professionals and members, SNM offers an essential collection of CT courses. In addition, as our Lifelong Learning and Self-Assessment Program (LLSAP) continues to grow over the year, Web-based modules will be available covering recent developments in molecular, nuclear, and correlative imaging in numerous specialty fields and basic sciences. The topics addressed will include the technical aspects, evaluation, and treatment of patients using CT, PET, PET/CT, SPECT, SPECT/CT, and other new techniques. In recent good news, ABNM and the American Board of Radiology both approved several LLSAP modules for self-assessment continuing medical education credit.

As you can see, SNM is leading the way for the next generation of trained physicians who will have a bright future with extended educational opportunities.
SNM Works with USP, Congress, NRC on Diverse Issues

USP: MEDMARX Data
On January 18 the United States Pharmacopeia (USP) released a MEDMARX database report on medication errors occurring in radiology services, cardiology cath labs, ICUs, and nuclear medicine departments during the period of 2000–2004. The data implied that very low numbers of dispensing errors occurred in U.S. nuclear medicine departments last year—approximately 40 errors in 20 million procedures. Many of the errors associated with nuclear medicine cited by the USP analysis are attributable to moving of patients between various departments in the hospital rather than the actual procedures performed within the nuclear medicine department.

SNM is committed to working with the USP staff on all issues pertaining to nuclear medicine patient care. For more information, please read the SNM press release about the USP MEDMARX data report online at: http://interactive.snm.org/index.cfm?PageID=4786.

CARE Legislation: Technologist Licensure
Senator Michael B. Enzi (R-WY) and Senator Edward M. Kennedy (D-MA) introduced the RadCARE bill (S 2322) on February 17. The RadCARE bill is the Senate companion to the House of Representatives’ Consumer Assurance of Radiologic Excellence (CARE) bill (HR 1426).

The fact that the RadCARE bill was introduced by the chairman and ranking minority member of the committee of jurisdiction—the Health, Education, Labor and Pensions (HELP) Committee—is extremely encouraging and a monumental accomplishment for the advocacy network led by the American Society of Radiologic Technologists (ASRT) and the SNM Technologist Section. There is little doubt that RadCARE is now in the most favorable position it has ever been in to move through committee.

The House version of the CARE legislation currently has 113 cosponsors approximately one year after its reintroduction in the 109th Congress.

For more information about the CARE and RadCARE legislation and to track the status of these bills, please visit the SNM online legislative action center at http://capwiz.com/snm/home/.

NRC Comments: NARM and Crane Petition
The SNM Nuclear Regulatory Commission (NRC) Task Force sent a letter to the 5 commissioners outlining our ideas and concerns regarding the regulations currently being written to enforce Section 651(e) of the Energy Policy Act of 2005, which granted the NRC regulatory authority over naturally occurring and accelerator-produced radioactive material (NARM). The letter to the commissioners is part of an ongoing effort to keep the medical/scientific community involved in the rulemaking process for NARM, and contains concepts previously shared with the NRC and other stakeholders at the public meeting on November 9, 2005.

The SNM NRC Task Force also developed and submitted comments in response to the September 2, 2005, petition submitted by Peter G. Crane, entitled “Re: Petition for Partial Revocation of the Patient Release Criteria Rule.” In the petition, Crane requested that 10 CFR part 35, “Medical Use of Byproduct Material,” be changed to partially revoke the 1997 amendment to 10 CFR 35.75, “Release of Individuals Containing Radiopharmaceuticals or Permanent Implants” (62 FR 4120; January 29, 1997, Patient Release Criteria Rule). The partial revocation would prohibit the release of patients from radioactive isolation with more than the equivalent of 30 mCi of 131I in their systems. The SNM’s response stated that the Crane petition, and its term dose equivalent of 30 mCi of 131I, is misinformed and, if taken seriously, would be a significant step backward for radiation safety and patient care.
DOE/NIH Study to Evaluate Nuclear Medicine Effectiveness

Details of a $700,000 Department of Energy (DOE)/National Institutes of Health (NIH) study to determine the importance of nuclear medicine research came to light during a press briefing on “The Future of Medical Imaging: Transforming Health Care,” held in Washington, DC, on January 31. In the question-and-answer period, SNM President Peter S. Conti, MD, PhD, queried Elias Zerhouni, MD, NIH director, about the $23 million cut in funding in the DOE fiscal year 2006 budget, a cut that effectively eliminated all money for basic nuclear medicine and molecular imaging research. Zerhouni responded by revealing plans for a planned National Academies study that will perform a “state-of-the-science” review of nuclear medicine.

“I was able to publicly raise the issue of nuclear medicine research funding directly with the NIH director, and the proposed study will provide the opportunity to validate the importance of basic nuclear medicine research,” said Conti, a professor of radiology, clinical pharmacy and biomedical engineering at the University of Southern California, Los Angeles.

According to a summary published online, 15 experts will be appointed to carry out the review over a 1-year period. Project officer for the initiative is Belinda Seto, deputy director of the National Institute of Biomedical Imaging and Bioengineering at NIH. DOE and NIH plan to contract with the National Academies’ Nuclear and Radiation Studies Board (NSRB) and the Board of Health Science Policy to conduct the investigation. The NRSB has agreed in principle to participate, board director Kevin Crowley told Diagnostic Imaging. Implementation will proceed after the DOE and NIH resolve final details concerning funding. DOE is set to spend $496,000 on the study, and NIH will contribute $248,000. The final report should be ready for publication about 14 months after organizing efforts begin.

The report will provide findings and recommendations on: future needs for radiopharmaceutical development for the diagnosis and treatment of disease; future needs for computational and instrument development for more precise localization of radiotracers in normal and aberrant cell physiologies; national impediments to the efficient entry of promising new radiopharmaceutical compounds into clinical feasibility studies and strategies to overcome these problems; and effects of shortages of isotopes and highly trained radiochemists on nuclear medicine research and short- and long-term strategies to alleviate such shortages.

Although Conti was encouraged by this news, he noted that SNM will continue to fight to restore funding for basic research in the DOE FY 2007 budget and will explore ways to continue existing programs through supplemental funding, reprogramming, or other mechanisms to cover the gap created by these cuts.

2007 DOE Budget Requests Presented

On February 2, U.S. Secretary of Energy Samuel W. Bodman announced President Bush’s fiscal year (FY) 2007 budget for the Department of Energy (DOE), requesting $23.6 billion, a $124 million increase over the FY 2006 request. “This budget signifies an investment in our future,” Bodman said. “Continued support for scientific discovery and the development of alternative energy sources is vital to America’s energy and economic security. From new global threats of the 21st century, to recognizing the importance of providing our next generation of scientists, teachers, and engineers with a strong educational foundation, DOE’s FY 2007 budget represents a comprehensive approach to addressing both the near- and long-term challenges America faces.”

Despite these positive words, the proposed budget does not include renewed funding for Office of Science nuclear medicine–related programs that suffered severe cuts and, in some cases, were terminated under the 2006 budget. As a part of the American Competitiveness Initiative, the Office of Science FY 2007 budget requests $4.1 billion, a $505 million (14%) increase over FY 2006, to support funding for basic scientific research. Funding will pursue new technologies in cutting-edge scientific fields such as nanotechnology, material science, biotechnology, and high-speed computing. “The American Competitiveness Initiative will continue America’s preeminence in science, and will ignite innovation to keep America competitive,” said Dr. Raymond Orbach, Director of the Office of Science. “This funding will be coupled with efforts to make much more effective use of our national laboratories for research and development leadership in the physical sciences.”

Among the Office of Science programs with increased funding are the Basic Energy Sciences Program ($286.4 million increase); Biological and Environmental Research ($54.6 million increase); High Energy Physics Program ($58.4 million increase); Nuclear Physics Program ($87 million increase); Fusion Energy Sciences Program ($31.3 million increase); Advanced Scientific Computing Research Program ($84.0 million increase), and the Workforce Development for Teachers and Scientists Program ($3.8 million increase).
Individual budget requests for each of the DOE funding areas are available at: www doe gov/media/FY 2007 Budget/FY _2007_1pg_fact_sheets.PDF.

U.S. Department of Energy

NIH Launches Large-Scale Alzheimer's Neuroimaging Study

The National Institute on Aging (NIA) of the National Institutes of Health (NIH) announced on February 10 an initiative to recruit 800 older adults to participate in a study aimed to identify biological markers of memory decline and Alzheimer’s disease (AD), as part of the Alzheimer’s Disease Neuroimaging Initiative (ADNI). The $60 million, 5-year ADNI study is the most comprehensive effort to date to identify brain and other biological changes associated with memory decline. The project was begun by NIA and is supported by more than a dozen other federal agencies and private-sector companies and organizations. Investigators at 58 local study sites across the United States and Canada will be asking individuals ages 55–90 to become a part of this research.

“We encourage people to participate in this important study because it will help us to identify needed biological markers of memory decline and Alzheimer’s disease. These biomarkers could become comparable to the cholesterol measures now used as biomarkers for heart disease,” said Susan Molchan, MD, program director for the ADNI project at the NIA. “In addition, using what we learn from the brain scans and other tests, we hope to lessen the time and cost of testing drugs and to bring treatments to patients much sooner.”

The ADNI researchers will employ serial MR imaging, PET, hematologic tests, and clinical and neuropsychological assessments to track mild cognitive impairment (MCI) and early AD progression. The study’s principal investigator is Michael W. Weiner, MD, of the San Francisco Veterans Affairs Medical Center and the University of California, San Francisco. The Northern California Institute for Research and Education, a foundation affiliated with the U.S. Department of Veterans Affairs, has been awarded the multicenter ADNI grant. Three groups of individuals are being recruited for the study: approximately 200 cognitively normal older people, who will be followed for 3 years; 400 people with MCI, who will be followed for 3 years; and 200 people with early AD, who will be followed for 2 years. At the end of the study, the researchers will compare neuroimaging, biological, and clinical information from the participants, looking for correlations among the data to develop standards for tracking the progression of memory decline. A unique feature of the project is the development of an imaging and biomarker database that can be tapped by researchers in both the public and private sectors as they develop and test drugs for memory decline. “Our goal is to ‘see’ critical brain changes and to identify biochemical indicators that may be useful in evaluating treatments aimed at slowing memory decline and AD,“ explains Weiner.

ADNI is the largest public–private partnership on brain research underway at the NIH. In addition to the NIA, the federal ADNI partners include the National Institute of Biomedical Imaging and Bioengineering, also part of NIH, and the U.S. Food and Drug Administration. Partnership with private-sector funders is managed through the not-for-profit Foundation for the National Institutes of Health, established by the U.S. Congress to facilitate support of and involvement with NIH programs. Corporate and nonprofit participants are: Pfizer Inc; Wyeth Research; Bristol-Myers Squibb; Eli Lilly and Company; GlaxoSmithKline; Merck & Co., Inc.; AstraZeneca AB; Novartis Pharmaceuticals Corporation; Eisai Global Clinical Development; the Alzheimer’s Association; Elan Corporation, plc; and the Institute for the Study of Aging. Siemens, Philips, and General Electric are providing software support for the imaging aspects of the project.

Other investigators for the project are: Leon Thal, MD, University of California at San Diego, (Coordinating Center); Ronald Petersen, MD, PhD, of the Mayo Clinic, Rochester, MN (Clinical Aspects); Clifford Jack, MD, Mayo Clinic (Neuroimaging/MRI Core); William Jagust, MD, University of California, Berkeley (Neuroimaging/PET Core); John Q. Trojanowski, MD, PhD, University of Pennsylvania (Biomarker Core); Arthur W. Toga, PhD, University of California, Los Angeles (Bioinformatics Core); and Laurel Beckett, PhD, University of California, Davis (Biostatistics Core). Other investigators are at more than 60 participating sites in the United States and Canada.

Information about participating in the research is available through NIA’s Alzheimer’s Disease Education and Referral (ADEAR) Center at 800-438-4380 or by visiting the ADNI section of the ADEAR Web site at www.alzheimers.org/imagine.

The Cost of Developing Imaging Agents

AD Nunn, from Bracco Research USA (Princeton, NJ) reported in the March issue of Investigative Radiology (2006;41:206–212) on the financial cost of developing imaging agents for routine clinical use and on the potential effects of these costs on the future clinical imaging agent environment. Cost estimates were based on publicly available financial data from annual reports of major companies developing and selling imaging agents. These estimates were compared with more in-depth data and analyses available for the development costs of therapeutic drugs. The author estimated that the cost of developing a drug for diagnostic imaging is in the $100–$200 million range, and that “blockbuster” imaging drugs (those with wide utility and high numbers of procedures) have current sales of $200–$400 million. These blockbuster imaging drugs tend to be mainstays of routine imaging that have been on the market for some time and represent a segment of the market that changes slowly. Future agents, Rudd
DOE Awards
Supercomputing Time

On February 1, Secretary of Energy Samuel W. Bodman announced that the DOE Office of Science had awarded a total of 18.2 million hours of computing time on some of the world’s most powerful supercomputers to help researchers in government labs, universities, and industry who are working on projects that range from designing more efficient engines to developing a better understanding of Parkinson’s disease. The allocations of computing time are made under the DOE Innovative and Novel Computational Impact on Theory and Experiment (INCITE) program, now in its third year of providing resources to computationally intensive research projects in the national interest.

“The INCITE program, the department’s scientific computing resources will continue to allow researchers to make discoveries that might otherwise not be possible,” Bodman said in announcing the latest INCITE grants. “We live in an exciting time as researchers make advances that potentially can help us all.” Funded projects range from aviation science to molecular physics to computer animation, with several projects requiring millions of supercomputing hours for completion.

One project of interest to the nuclear medicine community is “Simulation and modeling of synuclein-based ‘protofibril structures’ as a means of understanding the molecular basis of Parkinson’s Disease.” The University of California, San Diego, was awarded 16,000 processing hours at Argonne National Laboratory on the IBM Blue Gene supercomputer. This study will combine high-end computation with biochemical and NMR experiments to model the molecular basis for alpha synuclein aggregation. By combining the theoretical findings with experimental validation, the researchers hope to identify key amino acid interactions that favor amyloid pore formation and to use this information in new drug identification and development.

For the first time in the 3-year history of INCITE, proposals from private sector researchers were specifically encouraged. In return, much of the resulting knowledge will be made publicly available.

U.S. Department of Energy

BioShield Contract for Radiation Countermeasures

The Department of Health and Human Services (HHS) announced on February 13 the award of a $21.9 million BioShield program contract to Akorn, Inc. of Buffalo Grove, IL, for the manufacture and delivery of 2 medical countermeasures for radiological or nuclear incidents. Akorn, Inc. will deliver 390,000 doses of Ca-DTPA (pentetate calcium trisodium injection sterile solution) and 60,000 doses of Zn-DTPA (pentetate zinc trisodium injection sterile solution). The initial number of doses being purchased under the new contract is based on the Department of Homeland Security’s threat assessment and the interagency Weapons of Mass Destruction Medical Countermeasures Subcommittee’s evaluation of medical consequences of a radiological or nuclear incident. Under the terms of the 5-year contract HHS has the option to purchase up to 500,000 additional doses of Ca-DTPA and 500,000 additional doses of Zn-DTPA.

Akorn, Inc. has an exclusive marketing and distribution license agreement for the United States with Hameln Pharmaceuticals, Gmbh, of Hameln, Germany. Hameln Pharmaceuticals is the only manufacturer with Food and Drug Administration (FDA) approval for Ca-DTPA and Zn-DTPA to treat internal contamination from radioactive elements. FDA granted Hameln Pharmaceuticals orphan drug exclusivity until 2011. The Ca-DTPA and Zn-DTPA chelators are radiolabeled with plutonium, americium, or curium to treat internal radiation contamination. The HHS Office of Public Health Emergency Preparedness, which oversees the research and procurement efforts under the Project BioShield program through its Office of Research and Development Coordination, will manage the DTPA contract.

U.S. Department of Health and Human Services

Nuclear Medicine in Germany

In an article in the January issue of Nuklearmedizin (2006;45:1–9), Stamm-Meyer et al. reported on the frequency and collective effective doses of diagnostic nuclear medicine procedures in Germany between 1996 and 2002. The authors estimated the application frequencies for 10 groups of common nuclear medicine procedures by accessing official reimbursement data provided by German health insurance companies. Mean effective doses for these examinations were estimated from data on types of radiopharmaceuticals and administered activities at 14 clinics and 10 practices. These data led to the estimation that during the study period, a total of approximately 3.5 million nuclear medicine procedures were performed in an average year, corresponding to a mean annual application frequency of approximately 47 examinations per 1,000 inhabitants. More than 90% of the examinations were scintigraphies...
of the thyroid (37%), skeleton (25%), myocardium (13%), lungs (8%), and kidneys (8%). The mean annual effective per capita effective dose was approximately 0.12 ± 0.02 mSv. Three types of procedures were responsible for about 80% of the total collective effective dose: scintigraphies of the myocardium (36%), skeleton (33%), and thyroid (10%). Averaged over all procedures, the mean effective dose per examination was 2.7 ± 0.8 mSv. The authors concluded that the average effective dose per inhabitant and year caused by nuclear medicine examinations is markedly lower than that resulting from medical X-ray procedures.

Nuclear medicine

Reluctant Radiologists?
According to the results of a survey released in January, 29% of radiologists practicing in the United States in 2005 would not choose medicine if given the opportunity to go back in time and choose another career, an increase of 24% since the question was last asked in 1997. The survey results were reported by the physician-recruiting firm, LocumTenens.com, which asked similar questions of other medical specialists.

Compensation is not the key issue in dissatisfaction. “Compensation for radiologists has skyrocketed over the past decade because there aren’t enough of them to meet demand,” said LocumTenens.com Vice President Katie Thill. Respondents to LocumTenens.com reported average annual compensation for a radiologist in the United States at $354,260. “However, most physicians choose medicine for reasons beyond a paycheck and many of them today are seeking better work/life balance,” said Thill.

Although almost half (49%) of radiologists responding to the survey indicated they had no plans to make a job change, half said they planned to change jobs in the next 3 years (23% within 6 months). Fifty-three percent of those indicating an upcoming change cited lifestyle issues (“better community for self/family” or “better work environment”) as their top reason for making the change.

In part, this reflects a competitive market for imaging services that allows flexibility. In the last decade U.S. health care facilities, particularly those in rural areas, have experienced a shortage of radiologists. The demand for radiology services is likely to outpace physician supply into the foreseeable future.

“Improving medical technology and aging baby boomers are increasing the number of imaging procedures, while the pool of radiologists remains fairly stable,” Thill said. She referred to American Medical Association data indicating the number of residents entering radiology practice between 1990 and 2002 declined by 1%. Meanwhile, locum tenens industry sources indicate demand increased by 16% in a much shorter time frame (1997–2001).

A recent study of demand by National Imaging Associates indicated patient use of imaging technology triples after age 65. According to the August 1 issue of RT Image, the number of imaging procedures will likely grow to nearly half a billion outpatient and 100-million inpatient scans annually by 2008.

Although the survey included some radiologists who include nuclear medicine techniques in their practices, results for nuclear medicine practitioners were not included separately in the study. LocumTenens.com

(Continued from page 20N)

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 diagnostic and therapeutic 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.

Therapy

111In-Labeled Carbon Nanotubes in Drug Delivery

Researchers from England and France reported on February 21 ahead of print in the Proceedings of the National Academy of Sciences USA on the pharmacokinetics and apparent safety of intravenously administered radio-labeled carbon nanotubes, a step that brings this innovative drug and therapeutic gene delivery approach closer to clinical application. Singh and colleagues from the University of London (UK), and the Centre National de la Recherche Scientifique, Immunologie, et Chimie Therapeutiques (Strasbourg, France) functionalized water-soluble, single-walled carbon nanotubes with the chelating molecule diethylenetriaminepentaacetic (DTPA) labeled with 111In. The nanotubes were administered intravenously in a mouse model, and subsequent gamma scintigraphy indicated that the tubes were not retained in the liver or spleen and were cleared rapidly from the blood through renal excretion. In addition, studies using both single-walled and multiwalled nanotubes indicated that both types of tubes were excreted intact. The authors concluded that the rapid blood clearance of the nanotubes and short half-life (3 hours) of the tracer “have major implications for all potential clinical uses.”

“This certainly removes the shroud that has made many people nervous about using nanotubes, especially for medical applications,” Pulickel M. Ajayan, a Rensselaer Polytechnic Institute (Troy, NY) nanotube researcher told Chemical and Engineering News, one of many scientific media sources to cover the article. “This is the first time carbon nanotubes have been administered intravenously and fundamental pharmacokinetic parameters have been obtained,” said senior study author Kostas Kostarelos. “It is also the first report showing blood clearance and urine excretion of the nanotubes.”

Chemical and Engineering News

Embryonic Stem Cell Therapy Visualization

In the February 21 issue of Circulation (2006;113:1005–114), a team of researchers from the Stanford University School of Medicine (CA) reported on work with embryonic stem cells that stably express fluorescence, bioluminescence, and PET reporter genes with a resulting imaging platform that can monitor the kinetics of stem cell survival, proliferation, and migration. Cao et al. noted that monitoring of stem cell therapy in vivo is currently limited by the use of conventional histologic tests and imaging modalities. Murine embryonic stem cells were stably transduced with a lentiviral vector carrying a novel triple-fusion reporter gene. Embryonic stem cells carrying the reporter gene were injected into the myocardium of adult nude rats, and control animals received nontransduced embryonic stem cells. Bioluminescence and PET imaging were conducted first on day 4 and at regular intervals thereafter. Signals increased progressively from the first through the fourth week, indicating stem cell survival and proliferation. Histologic analyses showed the formation of intracardiac and extracardiac teratomas; animals treated with intraperitoneal injections of ganciclovir did not develop teratomas. The authors concluded that this “versatile imaging platform should have broad applications for basic research and clinical studies on stem cell therapy.”

Circulation

HAMA Titers and Survival in RIT

Azinovic et al. from the Hospital San Jaime (Torrevieja, Spain) and the University of California, Davis (Sacramento), reported on February 22 ahead of print in Cancer Immunology, Immunotherapy on the relationship between human antimume antibody (HAMA) and survival in patients with B-cell malignancies administered a mouse antilymphoma monoclonal antibody (mAb), Lym-1, directed against a unique epitope of HLA-DR antigen that is up-regulated on malignant B-cells. The study included 51 patients with B-cell malignancies who had been treated with 131I-Lym-1 radioimmunotherapy (RIT) and who were followed both before and after therapy until HAMA negative. In addition to determining the relationship of HAMA to survival, the researchers also assessed the relationships of HAMA to prior chemotherapies and absolute lymphocyte counts before initiation of RIT. Eighteen patients (35%) developed HAMA after RIT, and maximum HAMA titers were found to be significantly associated with survival. Among 39 patients who survived at least 16 weeks, median survival of those with HAMA <5 µg/mL was 61 weeks, compared
with 103 weeks for patients with HAMA > 5 µg/mL. For the 5 patients with the highest maximum HAMA, median survival was 244 weeks. An inverse relationship was noted between maximum HAMA titer at 16 weeks and number of previous chemotherapies. The authors concluded that the longer survival of patients with B-cell malignancies who developed high HAMA titers “was not explained by risk factors or histologic grade, suggesting the importance of the immune system.”

Cancer Immunology, Immunotherapy

**131I-Metuximab in Hepatocellular Carcinoma**

In a study e-published on March 20 ahead of print in Cancer Biology and Therapy, Zhang et al. from the Fourth Military Medical University (Xi’an, China) reported on research on the biodistribution, localization, and imaging characteristics of 131I-labeled metuximab radioimmunotherapy (RIT) in patients with hepatocellular carcinoma. The study included 24 patients with hepatocellular carcinoma who were divided into 3 groups to receive 18.5, 27.75, and 37 MBq/kg body weight of 131I-labeled metuximab. 99mTc-sodium phytate SPECT imaging was performed 2 days before and 7 days after RIT. The percentage of injected dose and time-dependent 131I tumor-to-nontumor (T/NT) ratios were calculated at 12, 48, 96, and 192 hours after injection. Positive post-RIT imaging results in 24 patients indicated that the RIT agent accumulated more in tumor. Biodistribution studies indicated that the optimal imaging time for the highest T/NT ratio in liver was at 192 hours. The authors concluded that 131I-labeled metuximab could deliver “relatively selective radiation” to tumor tissues and may have potential efficacy in treating hepatocellular carcinoma.

Cancer Biology and Therapy

**Diagnosis**

**18F-Labeled Insulin for PET**

Guenther et al. from McMaster University (Hamilton, ON) and Hamilton Health Sciences (ON) reported in the February 23 issue of the Journal of Medical Chemistry (2006;49:1466–1474) on a novel method for the preparation of 18F-labeled insulin for use as a PET tracer and outlined the results of initial in vitro evaluation. The preparation of the tracer was described in detail, as well as verification studies. An insulin receptor phosphorylation assay using cells overexpressing recombinant human insulin receptors showed no statistical difference in the extent of autophosphorylation stimulated by the 18F-labeled insulin and by human insulin, nor were uptake differences noted in 3T3-L1 mouse adipocytes treated with the labeled insulin and human insulin. The authors concluded that “results support the use of the 18F-insulin analogue as a PET tracer for imaging the distribution of insulin in vivo.”

Journal of Medical Chemistry

**18F-FLT and 18F-FDG PET in Thoracic Tumors**

In a study published in the February issue of Chest (2006;129:393–401), Yap et al. from the University of California at Los Angeles School of Medicine compared the use of 18F-FDG and 18F-FLT in PET tumor staging and other characteristics in individuals with solitary pulmonary nodules (11 patients) and with non–small cell lung cancer (NSCLC; 11 patients). PET imaging with each of the tracers was performed in each patient, and uptake was assessed by standardized uptake values (SUVs). Histologic evaluation after biopsy or surgery (99 samples in total) served as the gold standard and included assessment of tumor proliferation. One-third (33.3%) of these samples were positive for tumor tissue (22 pulmonary, 9 lymph node, and 2 extrapulmonary). 18F-FDG PET was false-positive in 3 and false-negative in 2 pulmonary lesions, whereas 18F-FLT PET was false-positive in 1 and false-negative in 6 pulmonary lesions. 18F-FDG uptake in lesions subsequently identified as positive was significantly higher than that of 18F-FLT. These results led the authors to conclude that, compared with 18F-FDG PET, “detection of primary and metastatic NSCLC by 18F-FLT PET is limited by the relatively low 18F-FLT uptake of the tumor tissue.” However, a significant correlation was observed between 18F-FLT uptake of pulmonary lesions and histologic assessment of tumor proliferation, an association not noted with 18F-FDG. The authors added that “the correlation between 18F-FLT uptake and cellular proliferation suggests that future studies should evaluate the use of 18F-FLT PET for monitoring treatment with cytostatic anticancer drugs.”

Chest

**18F-FDG PET in RT Planning**

Dietl et al. from the University of Regensburg (Germany) reported on February 21 ahead of print in Auris, Nasus, Larynx on the results of a prospective clinical analysis of the diagnostic and therapeutic effect of 18F-FDG PET on planning radiotherapy in patients with advanced head and neck cancer (stages III/IV). The study included 49 patients who were imaged with PET before radiotherapy to exclude systemic disease, synchronous second tumors, and unknown primary tumors. PET findings were compared with data from conventional imaging and clinical follow-up. In 21 patients (42.8%), PET provided new diagnostic information with therapeutic implications. Therapeutic management was changed in 14 patients, and minor modifications in portal design were made for 6 patients. PET supported a curative strategy in 9 patients and a palliative approach in 11 patients. The authors concluded that 18F-FDG PET is a “useful and important diagnostic tool mainly for exclusion of systemic disease in advanced head and neck cancer.”

Auris, Nasus, Larynx

**PET SUVs Predict Survival After Esophageal Surgery**

In a study published in the March issue of the Annals of Thoracic
Surgery (2006;81:1076–1081), Rizk et al. from the Memorial Sloan–Kettering Cancer Center (New York, NY) reported on a retrospective review of patients undergoing 18F-FDG PET imaging before surgical resection for esophageal adenocarcinoma to determine whether PET results could predict overall survival independently of clinical and/or pathologic stage. The study included the records of 50 patients who underwent CT and PET imaging before surgery and most of whom also underwent endoscopic ultrasound evaluation. Surviving patients were followed for a median of 27 months, and maximum standard uptake value (SUVmax) on PET was found to correlate with survival. The 3-year survival was 57% for patients with an SUVmax > 4.5 and 95% for patients with an SUVmax ≤ 4.5. The survival advantage of the SUVmax second group was also seen in clinically early-stage patients, as well as in patients with pathologically early-stage disease. The authors concluded that not only does 18F-FDG PET stage disease. The authors concluded patients with pathologically early-stage disease. The study included 26 such patients who underwent stereotactic radiotherapy in patients with intracranial meningiomas. The study included the records of 50 patients who underwent CT and PET imaging before surgery and most of whom also underwent endoscopic ultrasound evaluation. Surviving patients were followed for a median of 27 months, and maximum standard uptake value (SUVmax) on PET was found to correlate with survival. The 3-year survival was 57% for patients with an SUVmax > 4.5 and 95% for patients with an SUVmax ≤ 4.5. The survival advantage of the SUVmax second group was also seen in clinically early-stage patients, as well as in patients with pathologically early-stage disease. The authors concluded that not only does 18F-FDG PET stage disease. The authors concluded patients with pathologically early-stage disease. The study included 26 such patients who underwent stereotactic radiotherapy in patients with intracranial meningiomas. The study included the records of 50 patients who underwent CT and PET imaging before surgery and most of whom also underwent endoscopic ultrasound evaluation. Surviving patients were followed for a median of 27 months, and maximum standard uptake value (SUVmax) on PET was found to correlate with survival. The 3-year survival was 57% for patients with an SUVmax > 4.5 and 95% for patients with an SUVmax ≤ 4.5. The survival advantage of the SUVmax second group was also seen in clinically early-stage patients, as well as in patients with pathologically early-stage disease. The authors found the benefits of including DOTATOC as a tracer because of its ability to target the high expression of somatostatin receptor subtype 2 in meningiomas and concluded that 68GA-DOTATOC PET improves target definition for patients undergoing radiotherapy for intracranial meningiomas.

PET/CT in Low Rectal Cancer

Gearhart et al. from the Johns Hopkins Medical Institution (Baltimore, MD) reported in the March issue of the Annals of Surgical Oncology (2006;13:397–404) on a study of the staging utility of pretreatment PET/CT in patients with low rectal cancer. The study included 37 previously untreated patients with rectal cancer who underwent transrectal ultrasonography or MR imaging, CT, and 18F-FDG PET/CT. Tumor location (low, mid, or high) and carcinoembryonic antigen levels were noted. Discordant findings between spiral CT and PET/CT were resolved by histologic analysis or additional imaging follow-up. PET/CT identified discordant findings in 14 patients (38%), resulting in upstaging of 7 and downstaging of 3. Discordant PET/CT findings were significantly more common in patients with low rectal cancer than in those with mid or high rectal cancers. Discordant PET/CT findings resulted in a deviation in the proposed treatment plan in 27% of patients. The authors concluded that PET/CT “frequently yields additional staging information in patients with low rectal cancer” and that improvements in the technique will allow for more appropriate stage-specific therapy.

Annals of Surgical Oncology

Preoperative PET in High-Risk Melanoma

In an article e-published ahead of print on February 15 in the Annals of Surgical Oncology, Brady et al. from the Memorial Sloan–Kettering Cancer Center (New York, NY) reported on the use of preoperative whole-body 18F-FDG PET in addition to routine CT (chest, abdomen, and pelvis) in high-risk patients with melanoma. The study included 103 patients who underwent imaging before surgery, with histopathology or clinical follow-up within 4–6 months used to determine the accuracy of imaging. Preoperative imaging led to changes in management in 36 (35%) patients. This information proved accurate in 32 (89%) of these patients. PET alone was responsible for changes in management in 14 patients and in combination with CT was responsible for changes in 20 patients. The most common change was the decision to cancel surgery (19 of 36 patients in whom management changed on the basis of imaging). PET was more sensitive than CT in detecting occult disease (68% and 48%, respectively), but both modalities were highly specific (92% and 95%, respectively). The authors concluded that “PET imaging in addition to CT scanning should be strongly considered before operation in patients at high risk for occult metastatic disease.”

Annals of Surgical Oncology

PET/CT in Carcinoma of the Larynx

Gordin et al. from the Rambam Medical Center and the Carmel Medical Center (Haifa, Israel) reported in the February issue of Laryngoscope (2006;116:273–278) on a study designed to compare the efficacies of 18F-FDG PET/CT with PET or CT alone in patients with carcinoma of the larynx. The study included 42 patients,
whose imaging results were interpreted prospectively with knowledge of clinical histories and previous imaging tests. The performances of imaging modalities were compared by study type and lesion type for sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy. For PET/CT, sensitivity = 92%, specificity = 96%, PPV = 96%, NPV = 92%, and accuracy = 94%. For PET alone, these respective percentages were 92%, 73%, 76%, 91%, and 82%, and for CT alone, these percentages were 88%, 8%, 48%, 40%, and 51%. PET/CT led to changes in management in 25 patients (59%); by canceling additional diagnostic procedures in 13 patients, changing planned therapy in 9 patients, and by redirecting biopsy area in 3 patients. The authors concluded that “the performance of PET/CT is better than standalone PET or CT in patients with cancer of the larynx.”

**PET vs Scintigraphy in Staging of Nasopharyngeal Cancer**

Liu et al. from the Chang Gung Memorial Hospital (Taipei, Taiwan) reported in the February issue of the *Journal of Clinical Oncology* (2006;24:599–604) on a study comparing 18F-FDG PET and skeletal scintigraphy in the detection of bone metastasis in endemic nasopharyngeal carcinoma (NPC) at initial staging. The study included 212 patients with untreated NPC who underwent both PET and skeletal scintigraphy. Thirty (15%) of these patients were found to have bone metastases. PET was more sensitive than scintigraphy in both the patient-based analysis and a region-based analysis at the spine. The results also indicated that advanced stage at initial diagnosis and the coexistence of hepatic metastases were significant predictors of poor survival. The authors concluded that 18F-FDG is more sensitive than skeletal scintigraphy for detecting bone metastases in NPC at initial staging and that skeletal scintigraphy should be considered “supplementary” in this setting.

*Journal of Clinical Oncology*

**SPECT/CT and Functional Mapping of Brain Tumors**

In a study published in the February issue of *Cancer Biotherapy and Radiopharmaceuticals* (2006;21:41–48), Filippi et al. from the University Tor Vergata (Rome, Italy) reported on research to assess the clinical usefulness and incremental value of fused 99mTc-tetrofosmin SPECT/CT for the functional anatomical mapping of brain tumors. The study included 30 patients, 20 of whom were imaged with both modalities in a single session before surgery and 10 of whom were imaged after surgery and before radiotherapy planning. SPECT images alone were assessed first and then reinterpreted after fusion with CT images. SPECT/CT was found to have a significant clinical effect in 13 (43.3%) patients. Of specific note was the fact that SPECT/CT accurately characterized 8 lesions near sites of physiologic uptake and localized viable tumor tissue in 5 patients imaged after surgery. The authors concluded that SPECT/CT with 99mTc-tetrofosmin using their hybrid device “represents a useful clinical tool in brain tumor imaging, both correctly categorizing focal areas near sites of physiological uptake and localizing viable tumor tissue after surgery.”

*Cancer Biotherapy and Radiopharmaceuticals*

**Hurthle Cell Thyroid Cancer Therapy**

Besic et al. from the Institute of Oncology (Ljubljana, Slovenia) reported in the January issue of *Thyroid* (2006;16:67–72) on a study designed to determine the factors associated with survival in patients with Hurthle cell papillary thyroid carcinoma (HCPTC) in Slovenia, an iodine-deficient region. Out of a total of 1,552 patients with thyroid carcinoma seen at the authors’ institution over an almost 30-year period, 42 patients (33 females, 9 males; age range, 10–85; tumor diameters, 1–9 cm) had histopathologically verified HCPTC. Nineteen patients were found to have extrathyroid tumor growth, 13 patients had lymph node metastases, and 2 patients had distant metastases. Thirty-nine patients underwent total or near-total thyroidectomy, 2 underwent lobectomy, 37 underwent radioiodine ablation of thyroid remnant, 14 received external irradiation, and 3 underwent chemotherapy. The 5- and 10-year survivals were 94% and 87%, respectively, with respective disease-free intervals of 93% and 81%. Factors significantly correlated with survival included age, extrathyroid tumor growth, primary tumor stage, and regional and distant metastases. The authors concluded that long-term survival and locoregional control of disease are likely after radical tumor resection, radioiodine ablation of the thyroid remnant, and external irradiation.

*Thyroid*