On behalf of the PET Center of Excellence and its first elected board of directors, I would like to welcome you to our center and our redesigned Web site. If you are a current member, you are already familiar with the excellent services and advantages of membership that are available to you and reserved for logged-in members only. Some of these features include this newsletter and an archival listing and weekly updates on all PET and PET/CT research that appears in the world literature. These features are extremely valuable to the practicing clinician and technologist.

As the new president of the PET Center of Excellence, I am very pleased and excited to be able to initiate another year of opportunity and growth. The center will continue to be dedicated to educational programs and practical issues directly related to PET and PET/CT, including clinical practice, procedure guidelines, and reimbursement. We will again conduct a CME track at the Annual Meeting this June in San Diego, similar to the one that proved highly successful in Toronto. The center also intends to conduct and sponsor a special workshop for the development of protocols for PET/CT dual modality imaging, with the goal of publishing these proceedings in a special supplemental issue of The Journal of Nuclear Medicine.

Please visit our Web site often and consider the advantages of membership in the PET COE. I welcome your suggestions and recommendations for activities that will assist us in continuing the mission of the center.

James W. Fletcher, MD  
President, PET Center of Excellence

National Oncologic PET Registry Almost Open for Business

When the Centers for Medicare & Medicaid Services (CMS) announced the formal approval of the National Oncologic PET Registry (NOPR) on February 9, it inaugurated a new method of assessing the efficacy of a given medical practice, with implications that go far beyond PET. But as this issue of the PCOE Newsletter goes to press, NOPR is not yet registering patients.

The registry is based on the concept of “coverage with evidence development.” This new model for coverage determination is an attempt to get around the classic catch-22 that has kept PET, and undoubtedly other expensive new technologies, from moving rapidly into mainstream medicine. The problem is that without insurance coverage, it is difficult to amass a sufficient number of case studies to prove (to the satisfaction of the people holding the purse strings) that a new and expensive technology is cost effective, but without that proof, insurers are not willing to provide coverage.

The PET Registry solves this problem. Because there is a body of research that offers highly suggestive, though not definitive, evidence that PET can provide oncologists with information that will improve cancer diagnosis and therapy planning, CMS will make Medicare coverage possible for almost all oncological indications, as long as timely information about each covered case is entered into the NOPR database. In effect, the registry creates a massive clinical trial of FDG PET as a diagnostic and therapy-monitoring tool.

“The launching of this registry is a milestone for cancer patients,” said SNM President Peter S. Conti, MD, PhD. Since CMS announced its intent to support a PET registry in January 2005, SNM representatives have assisted in developing the national, Internet-based, audited data repository. “SNM continues to work collaboratively with our colleagues from different associations to advance patient care,” noted Conti. SNM members collaborated with representatives of the Academy of Molecular Imaging, the project’s sponsor; the American College of Radiology and the American College of Radiology Imaging Network (ACRIN), the project’s managers; and the American Society of Clinical Oncology.

During a PET Champions Web conference sponsored by Cardinal Health in early February, two nuclear medicine physicians deeply involved in the design and implementation of NOPR—Edward Coleman, MD, vice-chair of the Department of Radiol-
biomarkers can be used to assess the impact of therapies and work with drug developers based on a common understanding of this type of evidence-based study will help both FDA and CMS if FDG-PET is a predictor of tumor response. Data resulting from patients being treated for non-Hodgkin’s lymphoma to determine researchers will use FDG-PET imaging technology in trials of and standardize the use of FDG-PET. Under the collaboration, biomarker development and evaluation.

According to Dr. Coleman, “A major concern in the design of the registry was the need to obtain the kind of comprehensive data that would lead to firm, evidence-based decisions on PET coverage while not over-burdening the referring physicians with paperwork.” The result was a five-question pre-PET form that the referring physician must fill out and give to the PET facility prior to the study and a one-page, three-to-six-question form that must be completed after the study. There are six versions of the post-PET form, depending on the original reason for the study.

PET facilities will bear most of the burden of collecting and recording the data. They are responsible for registering the patient no more than 14 days prior to the PET or PET/CT scan date as well as entering the pre- and post-scan data through the NOPR Web site. In order to bill for the scan, the pre-PET form must be entered by midnight the day of the study, and the post-PET form must be filed within 30 days. NOPR will send the appropriate post-PET report form to the referring physician one week after the scan is performed. The PET facility may bill CMS when all the required data are received at the NOPR Operations Office. The NOPR charges a $50 processing fee per patient. Facilities are expected to prepay the patient processing fees, which are held in an escrow account that should be periodically replenished by the PET facility.

Dr. Siegel pointed out that, contrary to rumors circulating last year, there are no accreditation requirements. “Any PET facility that can bill Medicare is eligible to participate in the program. All Medicare patients are eligible for coverage, including those participating in HMOs. Medicaid patients are not eligible, and private insurance companies are not participating,” he said. Facilities must register and pay a $50 fee per location before they can begin to register patients.

Cancer indications that are already covered by CMS will continue to be covered and are not eligible for the registry; indications where PET has been determined to be ineffective (breast cancer diagnosis and axillary nodal staging and melanoma regional nodal staging) are also not eligible for coverage under the registry. All other oncologic indications are eligible for coverage through the registry, but as the data accumulate and various indications are classified as covered or not covered, they will no longer be eligible for “coverage with evidence development.” The registry is expected to run for two years, possibly longer if needed to gather enough data to make determinations for rare cancers, according to Dr. Siegel.

Coverage determinations will be based on changes in intended management that result from the information provided by the PET and PET/CT scans. ACRIN will monitor the database, and if the frequency of change in intended management for a particular cancer indication is sufficient to suggest benefit, data and supporting literature will be provided to CMS with a request for coverage.

Dr. Siegel noted that in spite of the investigational nature of the NOPR, Institutional Review Board (IRB) approval is not required to participate, although each facility will need to request an exemption from its own IRB. The program is exempt under 45 CFR 46.101(b)(5) for all 45 CFR part 46 requirements because participation is required for Medicare reimbursement. Facilities not covered by an IRB have several options; guidance is provided on the NOPR Web site (www.cancerpetregistry.org). No special informed consent is required from patients.

The NOPR is accepting facility registrations, but not patient registrations, as this issue of the PCOE Newsletter goes to press. Patient registration is expected to open very soon. The Web site has copies of the reporting forms that can be downloaded along with information for PET facilities and referring physicians.

**Federal Biomarker Initiative Launches With Project to Test Value of FDG-PET in Predicting Tumor Response**

The Food and Drug Administration (FDA), the National Cancer Institute (NCI), and the Centers for Medicare & Medicaid Services (CMS) announced on February 14 the Oncology Biomarker Qualification Initiative (OBQI)—an agreement to collaborate on improving cancer therapies and outcomes through biomarker development and evaluation.

The first OBQI project to be implemented will serve to validate and standardize the use of FDG-PET. Under the collaboration, researchers will use FDG-PET imaging technology in trials of patients being treated for non-Hodgkin’s lymphoma to determine if FDG-PET is a predictor of tumor response. Data resulting from this type of evidence-based study will help both FDA and CMS work with drug developers based on a common understanding of the roles played by these types of assessments.

The collaboration will develop scientific understanding of how biomarkers can be used to assess the impact of therapies and better match therapies to patients. For instance, OBQI will address questions such as how particular biomarkers can be used to:

- Assess tumor response to therapy after one or two treatments;
- Determine more definitively if malignant cells are dying, even when a tumor is not shrinking;
- Identify which patients are at high risk for cancer recurrence after therapy;
- Determine if a specific cancer is likely to respond to a specific treatment; and
- Efficiently identify investigational therapies that are likely to be effective cancer treatments.

The goal of OBQI is to validate particular biomarkers so they can be used to evaluate new, promising technologies in a manner that will shorten clinical trials, reduce the time and resources spent during the drug development process, improve the linkage between drug approval and drug coverage, and increase the safety and appropriateness of drug choices for cancer patients.
PET in the Literature

The international literature on PET and PET/CT continues to grow at a pace that challenges both researchers and clinicians. In each issue, the PCOE Newsletter presents a tomographic slice of the breadth of PET literature that appears in publications around the world. Weekly lists of all published PET research are available to logged-in members in the PET Center of Excellence Web area at www.snm.org/pet in the PET References Archive under Resources. Articles selected for relevance to clinical oncologists are also featured weekly under PET News.

Cardiology
Increased myocardial fatty acid metabolism in patients with type 1 diabetes mellitus.
Should PET replace SPECT for evaluating CAD? The end of the beginning. (16464710)
DiCarli MF, Hachamovitch R.

General Clinical Practice
Repetitive 18F-fluorodeoxyglucose positron emission tomography in giant cell arteritis: A prospective study of 35 patients. (16463425)
Acquiring new technology and surviving environmental pressures. (16443939)
McNally RD.

Instrumentation & Data
Validation of a Monte Carlo simulation of the Philips Allegro/GEMINI PET systems using GATE. (16467589)
Animal-specific positioning molds for registration of repeat imaging studies: comparative microPET imaging of F18-labeled fluorodeoxyglucose and fluoro-misonidazole in rodent tumors. (16459260)

Molecular Imaging
Potential of the FES-hERL PET reporter gene system—Basic evaluation for gene therapy monitoring. (16459270)
Applications of molecular imaging in cancer gene therapy. (16457650)

Neurology
Unique, common, and interacting cortical correlates of thirst and pain. (16461454)
Proc Natl Acad Sci U S A. 2006; Feb 3; [Epub ahead of print].
Evolution of brain activation with good and poor motor recovery after stroke. (16467276)

Oncology
Cancer therapy-associated CNS neuropathology: an update and review of the literature. (16463065)
Perry A, Schmidt RE.
Paraneoplastic cerebellar degeneration in a woman with ovarian cancer. (16462852)
Santillan A, Bristow RE.

Radiopharmacology
Antipsychotic drug action: targets for drug discovery with neurochemical imaging. (16466312)
Stone JM, Pilowsky LS.
PET Imaging of the AT(1) receptor with [11C]KR31173. (16459253)
Zober TG, Mathews WB, Seckin E, et al.
PET/CT Case: Lung Cancer

This 60-year old man presented to the emergency room with shortness of breath. A chest x-ray showed an ill-defined, left lung density. CT scanning showed this density to be a 2.4 cm lingular nodule, without evidence of adenopathy or other abnormalities. A follow-up PET/CT scan was ordered to help evaluate this nodule for malignancy.

The PET/CT showed markedly increased FDG uptake in the lingular nodule (Fig. 1). In addition, three other sites of uptake were seen in the regions of the right ribs, the upper lumbar spine, and the left pubic region (Figs. 2–4). After superimposition of the PET data with the CT images acquired as part of the exam, the latter three sites were seen to be lytic, expansile bone lesions. These finding were felt to be consistent with a left lung cancer with bone metastases. There was no evidence of hilar or mediastinal metastases.

How Did PET/CT Imaging Help?

PET/CT was able to show not only the malignant lung tumor but also that there were distant metastases, upstaging the patient to Stage IV. The CT portion of the study was able to document that the metastases were in bone and to exclude benign etiologies.

Recent studies have shown that PET and PET/CT in particular are the preferred methods for staging patients with non–small cell lung carcinoma (1,2).

Combination of PET, MR Imaging Shows White Matter Degeneration in Huntington’s Disease Patients

Released: February 14, 2006

Potential Exists to Possibly Prevent Disease Before Onset Symptoms Appear, Suggests Report in February’s Journal of Nuclear Medicine

RESTON, VA—Using both brain function (PET) and anatomical structure (MR) imaging studies, Italian researchers—within the context of an Italian-British collaboration—discovered that degenerative and dysfunctional events occur in individuals many years before the onset of Huntington’s disease—particularly in the brain’s white matter—an area not previously considered primarily involved with the disease. In fact, the brain’s white matter “progressively reduced” as individuals approached the first disease symptoms, according to a study published in February’s Journal of Nuclear Medicine.

“Our observations—made by analyzing the results of the largest group of subjects studied to date—may suggest new methodologies and drug trials for therapy,” said Ferdinando Squitieri, MD, PhD, who works in the Neurogenetics Unit and Centre for Rare Diseases of IRCCS Neuromed in Pozzilli, Isernia, Italy. “It is possible to approach the disease at the presymptomatic stage by monitoring the brain tissue volumes and the basal ganglia and cortex dysfunction. If so, we may be able to prevent Huntington’s disease before onset symptoms by using proper drugs,” added the co-author of “Brain White-Matter Volume Loss and Glucose Hypometabolism Precede the Clinical Symptoms of Huntington’s Disease.”

The Huntington’s gene has been determined; however, it’s unclear how the gene leads to damage of nerve cells in the brain, including the basal ganglia and cerebral cortex.

“Our findings are opening a new field in molecular medicine—the predictive medicine to prevent pathologies,” explained Squitieri. “Our study suggests that there’s a potential presymptomatic biomarker—a volumetric change of white matter—that can possibly be used for monitoring neuroprotective treatments,” he said. “For the first time, we are providing in vivo evidence that glial cells—the supportive cells in the central nervous system—are involved in early disease,” he noted.

CMS Provides Final Approval to Launch the National Oncologic PET Registry for Cancer Patients

Released: February 14, 2006

SNM Plays Important Role in Project’s Development

RESTON, VA—The Center for Medicare & Medicaid Services (CMS) has formally approved the National Oncologic PET Registry (NOPR) project that will significantly expand Medicare’s coverage for PET imaging. Since CMS announced its intent to support a PET registry in January 2005, SNM representatives have assisted in developing NOPR, a national, Internet-based, audited data repository designed to gather PET data from beneficiaries and providers and to report on that data.

“The launching of this registry is a milestone for cancer patients,” said SNM President Peter S. Conti, MD, PhD, professor of radiology, clinical pharmacy, and biomedical engineering at the University of Southern California (USC), Los Angeles. “SNM continues to work collaboratively with our colleagues from different associations to advance patient care,” noted Conti, who as SNM president represents more than 16,000 physician, technologist and scientist members.

SNM members collaborated with representatives of the Academy of Molecular Imaging, the project’s sponsor; the American College of Radiology and the American College of Radiology Imaging Network, the project’s managers; and the American Society of Clinical Oncology. “NOPR affords oncologists and nuclear medicine physicians a unique opportunity to make PET available to Medicare beneficiaries and to improve our understanding of the role of PET in oncology practice,” said SNM member Barry Siegel, MD, who is also an ACRIN researcher and co-chair of the NOPR Working Group.

For more information about NOPR, please visit www.cancerpetregistry.org.

SNM Opposes New Payment Caps on Imaging Services Detailed in Federal Deficit Reduction Act

Released: February 7, 2006

Budget-Cutting Bill Impacts Payments to Physicians’ Offices Beginning in 2007

RESTON, VA—SNM opposes a provision of the federal Deficit Reduction Act that impacts its members: payment caps to physicians’ offices with imaging equipment that are set to begin in 2007.

The five-year, $39 billion budget-cutting bill, which is scheduled to be signed into law Feb. 8 by President George W. Bush, calls for payment caps on imaging and computer-assisted imaging services. “The bill limits reimbursement for the technical (as opposed to the professional or interpretation) component to what would be paid under the hospital outpatient prospective payment system (HOPPS) or Medicare fee schedule payment (MFSP), whichever

(Continued on page 6)
is less,” explained Gary L. Dillehay, MD, chair of SNM’s Coding and Reimbursement Committee. The caps apply to molecular and nuclear imaging (including positron emission tomography), X-rays, ultrasounds, magnetic resonance imaging, computed tomography and fluoroscopy, said the associate professor of radiology at Loyola University Medical Center in Maywood, Ill.

In addition, the act eliminates the 4.4 percent reduction in claims payments for physicians’ services, freezing the payment at 2005 rates. Officials at the Centers for Medicare and Medicaid Services indicate that the freeze will be applied retroactively to services paid between Jan. 1 and the date of the bill’s enactment. 

SNM Provides $75,000 in 2005 Grants, Awards for Molecular Imaging/Nuclear Medicine Researchers

Released: February 1, 2006

First SNM/Mallinckrodt Seed Grant Provides $25,000 for Molecular Imaging/Nuclear Medicine Cancer Research

RESTON, VA—SNM recently awarded $75,000 in grants and awards, funded by its Education and Research Foundation, for molecular imaging/nuclear medicine researchers. 

Meixang Yu, PhD, associate professor and chief PET radiobiologist 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.

Additionally, 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 in New York City, received $8,000 for his project, “Development of NMDA/Glycine Site PET Radioligands.”

SNM Submits Comments to FDA on PET Drugs CGMP Draft Rule and Guidance

Released: December 20, 2005

The Society of Nuclear Medicine commented on the draft rule and guidance for current good manufacturing practice for positron emission tomography drugs (21 CFR Part 212). 

Society of Nuclear Medicine Debuts New Online Lifelong Learning and Self-Assessment Program

Released: November 28, 2005

Nuclear/Molecular Imaging Physicians, Technologists and Radiologists Can Register for Oncology PET and PET/CT Modules, Developed in Response to Maintenance of Certification Requirement

RESTON, VA—The Society of Nuclear Medicine has debuted its new, convenient online Lifelong Learning and Self-Assessment Program, easing the way for nuclear/molecular imaging professionals to demonstrate competence—and accountability—to patients, colleagues, managed care companies and government regulators.

“Over the next 14 months, the SNM LLSAP program will offer numerous Web-based self-assessment modules covering the recent developments in nuclear medicine and correlative imaging in the specialty fields of oncology, cardiology, neurology, endocrinology, pulmonology, gastroenterology, musculoskeletal and genitourinary disorders, and basic sciences. The topics addressed will include the technical aspects and evaluation and treatment of patients using computed tomography (CT), positron emission tomography (PET) and PET/CT, single photon emission tomography (SPECT) and SPECT/CT and therapy with unsealed radioactive sources,” said Dominique Delbeke, MD, PhD, chair of SNM’s Committee on Maintenance of Certification (MOC). 

SNM’s first self-assessment module—Oncology PET and PET/CT—is now available and offers the first two of nine self-assessment sections: Hematologic Malignancies and Gastrointestinal Malignancies.

Other PET and PET/CT oncologic sections to come include Artifacts and Pitfalls of PET Imaging, Solitary Pulmonary Nodules and Lung Cancer, Melanoma-Sarcoma-Neuroendocrine Malignancies, Central Nervous System Malignancies, Head and Neck Tumors, Male Genitourinary Malignancies, and Breast and Gynecologic Cancers.

In addition, the SNM LLSAP program will soon offer self-assessment modules in Cardiovascular SPECT and PET, with sections on New Developments in SPECT Myocardial Perfusion Imaging, PET Myocardial Imaging, Cardiovascular CT and Hybrid PET/CT; Neurology SPECT and PET, with sections on Overview and Dementia, Head Trauma and Movement Disorders, Cerebrovascular Disease, Epilepsy and Brain Tumors; and Endocrinology, with sections on Benign Thyroid Disease, Parathyroid Disorders, Adrenal Disorders and Neuroendocrine Disorders. Additional self-assessment modules are under development addressing non-PET diagnostic oncology and oncology therapy, pulmonology, gastroenterology, musculoskeletal and genitourinary disorders and basic sciences.

To register or learn more about SNM LLSAP program, please go online to http://www.snm.org/llsap.
**PET on the Net**

Below we present a small sample of some interesting articles that were recently turned up by the PCOE Newsletter’s search engine as it mined the Internet for mentions of positron emission tomography. Click the headline to read the full story.

**Non-invasive Tests May Miss Breast Cancer, AHRQ Study Finds**
Agency for Healthcare Research and Quality, February 15, Washington, DC, USA
The report finds that each of the four tests—magnetic resonance imaging, ultrasonography, positron emission tomography scanning, and scintimammography—would miss a significant number of cases of cancer, compared with immediate biopsy for women at high-enough risk to warrant evaluation for breast cancer....

**Alzheimer’s Disease Neuroimaging Study Launched Nationwide by the National Institutes of Health**
National Institute on Aging, February 9, Washington, DC, USA
The Alzheimer’s Disease Neuroimaging Initiative (ADNI)—a project developed by the National Institutes of Health (NIH)—is seeking 800 older adults to participate in a study aimed at identifying biological markers of memory decline and Alzheimer’s disease (AD). Ultimately, scientists hope that brain and biological changes can be detected before memory decline and other symptoms appear, allowing the effectiveness of drugs to be evaluated at the earliest possible time....

**National Institute of Radiological Sciences Confirms That PET Is Useful in Antipsychotic Dosage Selection**
Japan Corporate News, February 1, Tokyo, Japan
The National Institute of Radiological Science announced on January 30 that it has confirmed the utility of positron-emission tomography imaging in determining the optimal dosage of antipsychotics....

**Alaska Man Plans 20-Ton Domestic Cyclotron**
The Register, December 2, London, England, UK
A 55-year-old Alaska man has met determined local resistance to his plan to assemble a 20-ton nuclear particle accelerator in his Anchorage home... The Scandiatronix MC16 is used to brew up radioactive material, which is injected into people prior to cancer-seeking positron emission tomography (PET) scans....

**Brain Scan, Cerebrospinal Fluid Analysis May Help Predict Alzheimer’s**
Record, November 18, Washington University, St. Louis, MO, USA
A combination of brain scanning with a new imaging agent and cerebrospinal fluid (CSF) analysis has left neuroscientists encouraged that they may finally be moving toward techniques for diagnosing Alzheimer’s disease before its clinical symptoms become apparent....

**PET Imaging Applied to Immune System**
Xagena.it, 2005, Italy
In a series of experiments with genetically engineered mice, a team of researchers from the Howard Hughes Medical Institute (HHMI) at the University of California Los Angeles (UCLA) has demonstrated the ability to peer inside the body non-invasively and see the immune system at work....

**JHM Alliance Provides First Two Grants for Tech Development**
Johns Hopkins Gazette, January 17, Baltimore, MD, USA
First, Pomper and colleagues inject a radioactive agent, thymidine kinase (Tk) substrate 2’-deoxy-1-ß-D-arabinofuranosyl-5-[124I]iodouracil (FIAU), which is trapped by bacteria inside the body. Then they use the noninvasive imaging technique positron emission tomography, combined with computed tomography for anatomic detail, to identify the site of the infection....

**New Microchip Technology for PET Biomarkers Developed**
Medgadget.com, December 19, San Francisco, CA, USA
Researchers demonstrated a new technology, a programmable chip that can dramatically accelerate the development of many new molecular imaging molecules for PET. As a proof of principle, this group of academic and commercial scientists demonstrated that FDG could be synthesized on a “stamp-size” chip....
PET Shows Promise, Innovation in Detecting, Monitoring Cancers Specific to Women

Released: November 8, 2005

Imaging With FDG “Underutilized” in Studying Cervical, Ovarian, Endometrial, Vulvar, and Vaginal Cancers, According to Article in Society of Nuclear Medicine Publication

RESTON, VA—The use of positron emission tomography (PET) with the radiotracer fluorodeoxyglucose (FDG) is “underutilized” in diagnosing and treating cancer of the reproductive organs—the cervix, uterus, ovaries, fallopian tubes, vagina and vulva—according to an article in the November issue of The Journal of Nuclear Medicine. Doctors are beginning to see the potential of using PET to look inside a woman’s body to find gynecologic disease and its progression—and to follow how a treatment works.

PET imaging with FDG is having a “great impact” in determining the extent of spread of cancers of the reproductive system, especially when doctors get ambiguous results from other conventional imaging tests such as ultrasound, magnetic resonance imaging, (MRI) or computed tomography (CT), said Neeta Pandit-Taskar, MD, a nuclear medicine physician at Memorial Sloan-Kettering Cancer Center in New York City. While a woman’s reproductive organs are the potential source of life, they can be the starting point of deadly disease in which abnormal body cells grow and spread. Reports indicate that 80,000 women in the United States—or 10 women an hour—are diagnosed with a cancer of the reproductive organs....

(Continued from page 6)