LEU ^{99}Mo Production at LANL

Los Alamos National Laboratory (LANL) announced on May 13 that irradiated uranium fuel had been recycled and reused for ^{99}Mo production, with "virtually no losses" in ^{99}Mo yields or uranium recovery. In a press release, LANL indicated that "this demonstrates the viability of the separation process, as well as the potential for environmentally and cost-friendly fuel recycling."

The National Nuclear Security Administration's Global Threat Reduction Initiative (GTRI) implements the U.S. policy to minimize and eliminate the use of highly enriched uranium (HEU) in civilian applications. In support of this objective, GTRI is working with U.S. commercial entities and the U.S. national laboratories to develop a diverse set of non-HEU-based technologies to produce ^{99}Mo in the United States. The U.S. national laboratories conduct research and development, engineering and design support, and proof of concept demonstrations. GTRI has been working with LANL to ensure its technical expertise is available to support GTRI's commercial partners, including Morgridge Institute for Research-SHINE Medical Technologies (MIR-SHINE), which proposes to use a particle accelerator to produce ^{99}Mo from a mildly acidic low-enriched uranium (LEU) solution.

Researchers at Los Alamos described their activities in successfully proving the technical viability of the initial stage of ^{99}Mo recovery from LEU solution through a direct scaled-down demonstration of the proposed industrial process. The researchers developed methodologies for preparing and analyzing uranium sulfate fuel, safely containing the fuel during irradiation at a the Los Alamos Neutron Accelerator Science facility, and performing chemical flow-sheet testing using a separation apparatus applicable to both low and high levels of radiation. Unlike traditional HEU-based processes, the challenge is to recover the ^{99}Mo from a large excess of LEU and leave the uranium in the same chemical form to allow for recycling. The team found that nearly all of the uranium could be recovered after ^{99}Mo separations were performed. The LEU fuel that passed through the column separation process was irradiated again, and once more the fission-generated ^{99}Mo was separated in high yield. When the same fuel was irradiated a third time, no observable loss was noted in the subsequent ^{99}Mo recovery. The results confirm the viability of both the ^{99}Mo separation process and uranium fuel recycling, which can lower operating costs and minimize waste generation.

Los Alamos National Laboratory

FROM THE LITERATURE

Each month the editor of Newsline selects articles on diagnostic, therapeutic, research, and practice issues from a range of international publications. Most selections come from outside the standard canon of nuclear medicine and radiology journals. 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. The lines between diagnosis and therapy are sometimes blurred, as radiolabels are increasingly used as adjuncts to therapy and/or as active agents in therapeutic regimens, and these shifting lines are reflected in the briefs presented here. We have also added a small section on noteworthy reviews of the literature.

Predicting Brain Amyloidosis in MCI

Tosun et al. from the University of California, San Francisco, and the VA Medical Center (San Francisco, CA) reported on May 18 ahead of print in *Annals of Neurology* on a study designed to identify an imaging signature predictive of brain amyloidosis with potential for routine use as a screening tool to identify those individuals with mild cognitive impairment (MCI) who are most likely to have high levels of brain amyloidosis. The study included 62 participants with MCI who underwent structural MR and ^{11}C-labeled Pittsburgh compound PET imaging. The researchers identified an anatomic shape variation–based neuroimaging predictor of brain amyloidosis and defined a structural MR–based brain amyloidosis score (sMRI-BAS). They validated the positive predictive abilities of the sMRI-BAS for β-amyloid in a separate group of 153 MCI patients with cerebrospinal fluid biomarker data positive for β-amyloid but without amyloid on PET imaging. The predictive powers of the sMRI-BAS were compared with those of the apolipoprotein E (ApoE) genotype and hippocampal volumes. The anatomic shape variations found to be predictive of brain amyloidosis included, as expected, the medial temporal lobe, temporal–parietal association cortices, posterior cingulate, precuneus, hippocampus, amygdala, caudate, and fornix/stria terminals. The ability of the sMRI-BAS combined with ApoE genotype status to predict β-amyloid positivity was significantly better than that of either predictor separately. Hippocampal volume was not found to be an independent predictor of brain amyloidosis in MCI. The authors pointed to these efforts as among "the first attempts to use an imaging technique that does not require amyloid-specific radioligands for identification of individuals with brain amyloidosis" and suggested that these findings "could lead to development of multidisciplinary/multimodality brain amyloidosis biomarkers that are reliable, minimally invasive, and widely available."

Annals of Neurology

PET/CT, CLL, and Richter's Transformation

In an article e-published on May 9 ahead of print in *Leukemia and Lymphoma*, Papajik et al. from Palacky University (Olomouc, Czech Republic) reported on a prospective study designed to evaluate the benefit of ^{18}F-FDG PET/CT in newly diagnosed or relapsed chronic lymphocytic leukemia and Richter's transformation. The study included 23 patients with newly diagnosed disease, 13 of whom had relapsed disease and 8 with suspected or confirmed Richter's transformation. All patients underwent ^{18}F-FDG PET/CT, and maximum standardized uptake values (SUV_{max}) were calculated. The median SUV_{max} was 3.4 (range, 1.5–6.3) and 3.1 (range, 1.2–5.9) in newly diagnosed and relapsed patients, respectively. In patients with suspected or histopathologically confirmed Richter's transformation, the median SUV_{max} was significantly different at 16.5 (range, 7.2–25.3). ^{18}F-FDG PET/CT showed inflammatory lesions in 7 patients (16%) and synchronous tumors in 2 newly diagnosed patients. The authors concluded that "^{18}F-FDG PET/CT may be a beneficial imaging method when used in individuals with chronic lymphocytic leukemia and suspected Richter's transformation."

Leukemia and Lymphoma

PET/CT Staging of DLBCL

Khan et al. from Guy's and St Thomas' Foundation Trust (London, UK) reported on May 9 ahead of print in *Blood* on a study investigating whether PET/CT can identify clinically important bone marrow involvement in diffuse large B-cell lymphoma (DLBCL) with sufficient accuracy to replace routine staging bone marrow biopsy. The study included the records of 130 patients with DLBCL who had been staged with PET/CT. Of these, 35 (27%) were found to have marrow involvement. PET/CT identified involvement in 33 of these patients, whereas marrow histology identified only 14. PET/CT identified all clinically important marrow lymphoma, whereas marrow biopsy did not upstage any patients. The sensitivity and specificity of PET for bone marrow involvement were 94% and 100%, respectively. The respective figures for iliac crest biopsy were 40% and 100%. In those patients with marrow deposits identified by PET/CT but not biopsy, progression-free and overall survival were similar to that in stage 4 disease without involved marrow. Those patients with positive marrow biopsy histology saw significantly inferior progression-free survival. The authors concluded that these data suggest that "in experienced hands PET/CT has a high level of accuracy for identifying marrow disease in DLBCL and provides new insight into the nature and clinical significance of marrow involvement."

Blood

No-Denial and Imaging Utilization

In an article e-published online on April 27 ahead of print in the *Journal of the American College of Radiology*, Robinson et al. from the University of Washington (Seattle) looked at whether initiation of a no-denial policy resulted in increased utilization of imaging services. The study looked at the records of a large U.S. health plan both before and after initiation of a no-denial preauthorization system for all CT, MR, PET, and nuclear cardiac imaging studies. The records included 247,117 advanced imaging requests made 21 mo before and 16 mos after elimination of the denial provision, as well as a matched control population that underwent no such change. After elimination of the denial provision, utilization decreased slightly more in the no-denial group than in the control group. Rates of request approval, examination modification, withdrawal, and no consensus after peer-to-peer consultation did not significantly change after initiation of the no-denial preauthorization or between the 2 groups. The authors concluded that, contrary to most predictions, "eliminating denial provisions in utilization management for advanced diagnostic imaging does not result in increased utilization of such imaging."

Journal of the American College of Radiology

Serial Changes in FDG Spinal Cord Uptake

Chong et al. from Chosun University (Gwangiu, Korea) reported in the April issue of the *Chonnam Medical Journal* (2013;49:38–42) on a study designed to determine average changes in ^{18}F-FDG uptake in the spinal cord between 2 serial PET/CT scans in healthy individuals. The retrospective study included the cancer screening records of 30 individuals who underwent 2 PET/CT scans at a median interval of 2.80 ± 0.94 y. The standardized uptake value (SUV_{max}) in the spinal cord of each midvertebral body was obtained by drawing a region of interest on an axial image of PET/CT. The cord-to-background ratio (CTB) was assessed, and differences in pattern, sex, age, and intervals between serial PET/CT scans were included as variables. On average, significant change on the second scan was seen only at the level of the C6 and T10 vertebrae. Mean CTB showed a decreasing pattern from cervical to lumbar vertebrae, with 2 peaks at the lower cervical level (C4–6) and at the lower thoracic level (T12). The authors suggested that these findings are "valuable as a baseline reference in the follow-up of metabolic changes in the spinal cord."

Chonnam Medical Journal

PET and Whole-Body CT in Stage III Melanoma

In an article e-published on April 24 ahead of print in *Annals of Surgical Oncology*, Niebling et al. from the University of Groningen (The Netherlands) looked at the outcomes of PET and whole-body CT staging in patients with stage III melanoma to assess which factors are independently prognostic for survival. The study included 252 patients with palpable and histologically or cytologically proven lymph node metastases from melanoma

who also underwent ^{18}F-FDG PET and whole-body CT. Melanoma-specific survival and disease-free survival were analyzed for patients who were PET and CT positive or negative. Average overall 5-y melanoma-specific survival was 38.2%. This percentage was 47% for PET- and CT–negative patients and 16.9% for PET- and CT–positive patients. Forty-six percent of PET- and CT–negative patients were disease free at 5 y. Among the independent predictors for melanoma-specific survival in all patients were sex, lymph node metastases in axillae (compared to in the head or neck), and presence of extranodal growth, but PET- and CT-positive status was the most significant prognostic factor. The authors concluded that because "staging melanoma patients with palpable lymph node metastases is more accurate when whole-body FDG-PET and CT is added to the diagnostic workup," then "FDG PET and CT, preferably combined, are indicated in the staging of clinical stage III melanoma patients."

Annals of Surgical Oncology

Percutaneous Laser Ablation in PTC

Mauri et al. from the Azienda Ospedaliera Ospedale di Circolo di Busto Arsizio (Italy), the Regina Apostolorum Hospital (Albano, Italy), and Hadassah Hebrew University Medical Center (Jerusalem, Israel) reported on May 10 ahead of print in the *Journal of Clinical Endocrinology and Metabolism* on a study assessing the use of percutaneous laser ablation (PLA) in difficult-to-treat metachronous cervical lymph node metastases from papillary thyroid carcinoma. The retrospective analysis included data on 15 patients with previous resection of papillary thyroid carcinoma with elevated serum levels of thyroglobulin (Tg) or anti-Tg antibodies (TgAbs). The group had 24 metachronous nodal metastases treated with PLA over a 20-mo period and were followed with ^{18}F-FDG PET/CT and contrast-enhanced ultrasound at 6 and 12 mo posttreatment. Technical success without major complications was achieved in all patients. Local control was achieved in 11 of 15 patients (73%) at 6 mo, 6 of whom had serum Tg/TgAb normalized. At 6 mo, 20 of 24 (83%) nodes were negative on PET/CT and ultrasound. Four were PET/CT positive, and 3 of these were ultrasound positive. Local control was achieved in 10 of 14 (71.4%) patients at 12 mo. Four of these patients had serum Tg/TgAb normalized. At 12 mo, 16 of 20 nodes (80%) were negative on PET/CT and ultrasound. Four were PET/CT positive, and 2 of these were ultrasound positive. The authors concluded that "PLA is potentially feasible, safe, and effective for the treatment of metachronous cervical nodal metastases from papillary thyroid carcinoma" and "may reduce or delay a large number of highly invasive repeat neck dissections."

Journal of Clinical Endocrinology and Metabolism

^{99m}Tc-IDA SPECT and Liver Function in RT

In an article e-published on May 17 ahead of print in the *International Journal of Radiation Oncology, Biology, Physics,* Wang et al. from the University of Michigan (Ann Arbor) investigated whether regional hepatic function assessed before and during radiation therapy (RT) using ^{99m}Tc-iminodiacetic acid (^{99m}Tc-IDA) SPECT could predict regional liver function reserve after RT. The study included 14 patients with intrahepatic cancers who underwent dynamic ^{99m}Tc-IDA SPECT before, during, and 1 mo after completion of RT. In addition, indocyanine green (ICG) tests of overall liver function were performed within 1 d of each scan, and hepatic extraction fraction (HEF) dose–response functions during and after RT were generated. The researchers developed 3 models (termed dose, priori, and adaptive) to assess whether regional HEFs measured before and during RT helped predict later regional hepatic function. The mean of the volumetric liver HEFs was found to be significantly correlated with ICG clearance half-life time at all imaging time points. In 12 patients, correlations between local doses and regional HEFs 1 mo after RT were significant. Two models proved predictive: in the priori model, regional HEF after RT was predicted by the planned dose and regional HEF assessed before RT, and, in the adaptive model, regional HEF after RT was predicted by regional HEF reassessed during RT and the remaining planned local dose. The authors concluded that the fact that ^{99m}Tc-IDA SPECT obtained during RT could be used to assess regional hepatic function and helped predict post-RT regional liver function reserve suggests that this technique "could support individualized adaptive radiation treatment strategies to maximize tumor control and minimize the risk of liver damage."

International Journal of Radiation Oncology, Biology, Physics

PET and Midbrain Function in PD

Brown et al. from the Washington University School of Medicine (St. Louis, MO) reported on May 20 ahead of print in *Annals of Neurology* on a study comparing presynaptic PET tracer uptake in the substantia nigra with cell loss and motor impairment in a 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP)–treated macaque model of Parkinson disease. PET images with 6-^{18}F-fluorodopa, ^{11}C-2β-methoxy-3β-4-fluorophenyltropane (^{11}C-CFT), and ^{11}C-dihydrotetrabenazine (^{11}C-DTBZ) were acquired in the animals to measure specific substantia nigra and striatum uptake before and after a variable dose of MPTP. The resulting PET data were compared with motor impairment assessments, post mortem tyrosine hydroxylase–positive cell counts, and striatal dopamine concentration. ^{11}C-CFT and ^{11}C-DTBZ uptake in the substantia nigra each had strong and significant correlation with dopaminergic cell counts, a correlation that was lacking with ^{18}F-fluorodopa. Specific uptake of ^{11}C-CFT and ^{11}C-DTBZ in the substantia nigra also had a linear relationship with motor impairment. The

authors noted that these finding "demonstrate that PET measured binding potentials for CFT and DTBZ for a midbrain volume of interest targeted at the substantia nigra provide faithful correlates of nigral neuronal counts across a full range of lesion severity," and, because these measures correlate with both nigral cell counts and parkinsonian ratings, they suggested that "these substantia nigra PET measures are relevant biomarkers of nigrostriatal function."

Annals of Neurology

SPECT/CT and Meningioma Grading

In an article e-published on May 9 ahead of print in the *Journal of Neuro-oncology*, Wang et al. from the Fourth Military Medical University (Shaanxi, China) reported on a study designed to elucidate the relationship between ^{99m}Tc-HYNIC-octreotide SPECT/CT somatostatin receptor scintigraphy (SRS) with pathology grading and expression of somatostatin receptor 2 (SSTR2) in meningioma. The study included 30 patients with meningiomas who had undergone both MR and ^{99m}Tc-HYNIC-octreotide SPECT/CT SRS. Tissues were graded in pathology and stained for SSTR2 expression. SPECT/CT tumor-to-nontumor (T/TN) ratios were calculated and compared with results from pathology. SRS was 100% sensitive in detecting the meningiomas, whereas CT sensitivity was 83%. The 20 grade I meningiomas had an average T/NT ratio of 3.80 ± 1.67, significantly lower than the 10 grade II cases (9.57 ± 3.78). Immunohistochemical staining detected SSTR2 expression in all meningiomas. The T/NT ratio was positively associated with pathology grading and expression of SSTR2. The authors concluded that "^{99m}Tc-HYNIC-octreotide SPECT/CT SRS is a sensitive technique for detecting meningioma, and the T/NT ratio of the SRS data closely correlates with the pathological grade of meningioma and the expression of SSTR2."

Journal of Neuro-oncology

PET/CT in T1 Breast Cancer

Koolen et al. from the Antoni van Leeuwenhoek Hospital (Amsterdam, The Netherlands) reported on May 14 ahead of print in *Acta Oncologica* on a study evaluating the accuracy of ^{18}F-FDG PET/CT in visualizing primary tumors and detecting locoregional and distant metastases in T1 breast cancer. The study included 62 women with invasive T1 breast cancer who underwent PET/CT imaging of the thorax and whole body. Imaging results were compared with clinical and histopathology data. PET/CT visualized the primary tumor in 54 (87%) patients, identifying 59% of tumors ≤10 mm in diameter and 98% of tumors >10 mm. All triple-negative and HER2-positive tumors and 40 of 48 (83%) estrogen-receptor–positive/HER2-negative tumors were visualized with PET/CT. PET/CT sensitivity and specificity in detection of axillary metastases were 73% and 100%, respectively. PET/CT showed periclavicular nodes in 2 patients. Of 12 distant lesions identified, 1 proved to be a lung metastasis, 3 were false-positive, and 8 were new primary proliferative lesions. The authors concluded that with optimal imaging acquisition, "the majority of T1 breast carcinomas can be visualized with PET/CT, and specificity in the detection of axillary metastases is excellent." However, sensitivity was limited and additional whole-body imaging "has a low yield in this specific patient group."

Acta Oncologica

REVIEWS

Review articles provide an important way to stay up to date on the latest topics and approaches by providing valuable summaries of pertinent literature. The Newsline editor recommends several reviews accessioned into the PubMed database in April and May. In an article in the April 25 issue of *Frontiers in Oncology* (2013;3:104), Götz and Grosu from University Freiburg (Germany) published "^{18}F-FET PET imaging for treatment and response monitoring of radiation therapy in malignant glioma patients: a review." Hruska and O'Connor from the Mayo Clinic (Rochester, MN) reviewed "Nuclear imaging of the breast: translating achievements in instrumentation into clinical use" in the May issue of *Medical Physics* (2013; 40:050901). In an article e-published on May 10 ahead of print in the *Journal of Pharmacokinetics and Pharmacodynamics*, Varnäs et al. from the Karolinska Institutet (Stockholm, Sweden) highlighted "Molding of PET data in CNS drug discovery and development." Caprioli et al. from the University of Cambridge (UK) described "Translating positron emission tomography studies in animals to stimulant addiction: promises and pitfalls" online on May 8 ahead of print in *Current Opinion in Neurobiology.* In an article e-published on May 3 ahead of print in *Trends in Pharmacological Sciences*, Whittle et al. from the University of Cambridge (UK) reported on "Pharmacological strategies for targeting BAT thermogenesis." Rowe and Villemagne, from the University of Melbourne (Australia) summarized recent findings in "Amyloid imaging with PET in early Alzheimer disease diagnosis" in the May issue of *Medical Clinics of North America* (2013; 97:377–398).