challenges that would be posed by radioisotope supplies in the United States: "It's in our national interest to have a domestic source of these basic, important materials. If we as a country can spend $8 billion on the Superconducting Super Collider, why can't we spend the relatively small sum it would take not only to develop new types of radionuclides but also to supply isotopes for clinical nuclear medicine?"

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.

FLT + FDG PET Tumor Imaging

Kadmas et al. from the University of Utah (Salt Lake City) reported in the February 7 issue of *Physics in Medicine and Biology* (2013;58:429–449) on an investigation of techniques for single-scan, dual-tracer ^{18}F-FDG and ^{18}F-fluorothymidine (^{18}F-FLT) PET tumor imaging. Although the 2 tracers provide complementary information, the combination is technically challenging because the tracers have similar half-lives and a short delay between injections. The authors described simulation studies performed to characterize dual-tracer signal-separation performance for imaging protocols with varying injection orders and with varied injection delays (10–60 min). They identified superior performance when ^{18}F-FLT was injected first and noted an optimal 30-min delay time between injections. They also investigated the robustness of these findings in PET/CT imaging of 5 patients with primary brain tumors. Data from separate scans of each tracer were combined to synthesize dual-tracer scans with known single-tracer components. The results showed similar dual-tracer signal recovery performance and confirmed the simulation study findings. The authors concluded that "rapid dual-tracer FLT + FDG tumor imaging is feasible and can provide quantitative tumor imaging measures comparable to those from conventional separate-scan imaging."

Physics in Medicine and Biology

ImmunoPET and Lymph Node Lymphangiogenesis

In an article in the January issue of *Methods in Molecular Biology* (2013;961:129–140), Mumprecht and Detmar from the Swiss Federal Institute of Technology (Zurich, Switzerland) reported on a PET-based noninvasive methodology for imaging lymphangiogenesis in vivo in mice, originally described by their group in *Cancer Research* (2010;70:8842–8851). In addition to reviewing current literature on the significant role of lymph node angiogenesis in tumor metastasis, inflammation resolution, and dendritic cell migration to the lymph nodes, the authors described their in vivo imaging approach using a radioactively labeled antibody against the lymphatic vessel endothelial hyaluronan receptor-1 (LYVE-1), which is almost exclusively expressed on lymphatic vessels. Initial investigations showing accumulation of the injected anti-LYVE-1 antibody in mouse lymphatic vessels were reviewed, and the authors discussed the potential translational and clinical implications of this technique.

Methods in Molecular Biology

Hypoxia-Targeted RT Dose Painting for HNSCC

Chang et al. from Austin Health (Victoria, Australia) reported on January 15 ahead of print in *Acta Oncologica* on a study investigating the use of ^{18}F-fluoromisonidazole (^{18}F-FMISO) PET-guided radiation therapy (RT) dose painting as a means for overcoming the radioresistant effects of hypoxia in head and neck squamous cell carcinoma (HNSCC). The study included 8 patients with HNSCC who were scheduled for definitive RT. Pre-RT PET imaging results were used to automatically generate hypoxic subvolumes, and 3 RT plans were generated for each patient: a standard (STD) plan to a dose of 70 Gy, a uniform dose escalation (UDE) plan to standard target volumes to a dose of 84 Gy, and a hypoxia dose–painted (HDP) plan with dose escalation only to the hypoxic subvolume to 84 Gy. Tumor control probabilities (TCP), normal tissue complication probabilities (NTCP), and uncomplicated tumor control probabilities (UTCP) were used to calculate and compare results with each of the plans for each of the patients. The mean TCPs increased to 73% with STD plans, 95% with the UDE plans, and 93% with the HDP plans. The mean parotid NTCP increased from 26% to 44% with the UDE plans, which also increased the mean mandible NTCP from 2% to 27%. The mean UTCP increased from 48% with the STD plans to 66% with the HDP plans and fell to 37% with the UDE plans. The authors concluded that these results suggest that "hypoxia-targeted radiotherapy dose painting for head and neck cancer using FMISO PET is technically feasible" and that "this approach is superior to uniform dose escalation."

Acta Oncologica

Radiation Risk and Choroidal Melanoma Imaging

In an article in the January 1 issue of the *Journal of the American Medical Association. Ophthalmology* (2013;131:56–61), Wen et al. from the University of California, Los Angeles, reported on a study designed to determine the lifetime attributable risk of cancer associated with whole-body PET/CT and with CT of the chest, abdomen, and pelvis. The study looked at surveillance imaging for distant metastases performed at varying frequencies and intensities in patients with primary choroidal or ciliary body melanoma. The authors used the Biological Effects of Ionizing Radiation VII assumptions in calculating lifetime attributable cancer risks from the radiation data. Their calculations indicated that a 50-y-old who undergoes an annual CT of the chest, abdomen, and pelvis for 10 y will carry an elevated estimated lifetime attributable risk of cancer of 0.9% for men and 1.3% for women. Annual PET/CTs for the same period would carry attributable risks of cancer of 1.6% and 1.9% for male and female patients, respectively. The lifetime risk was estimated to be much higher in young females (as high as 7.9% for a 20-y-old woman undergoing PET/CT imaging every 6 mo for 10 y). The authors concluded that "aggressive surveillance protocols incorporating CT scanning or PET/CT scanning for detection of metastasis from primary choroidal or ciliary body melanoma appear to confer a significant substantial risk of a secondary malignant tumor in patients who do not succumb to metastatic melanoma within the first few posttreatment years."

Journal of the American Medical Association. Ophthalmology

^{11}C-AMT PET and Gliomas

Kamson et al. from Children's Hospital of Michigan (Detroit) reported on January 9 ahead of print in the *Journal of Neuro-oncology* on α-^{11}C-methyl-L-tryptophan (^{11}C-AMT) PET in pretreatment delineation of newly diagnosed gliomas and compared results with both MR imaging and histopathology results. The study included 28 patients with newly diagnosed World Health Organization grade II–IV gliomas. All patients underwent pretreatment ^{11}C-AMT PET, and both gadolinium-enhanced T1-weighted and T-2 weighted MR images were acquired. Imaging abnormalities with both modalities were assessed and compared. ^{11}C-AMT-accumulating grade I meningiomas were used to define a tracer uptake cutoff threshold that detected the tumor but excluded perimeningioma vasogenic edema. Histopathology was also studied to assess tumor infiltration in specimens from patients with glioblastoma. The mean ^{11}C-AMT PET-defined tumor volumes were greater than the T1 volumes but smaller than T2 abnormalities. The volume of tissue accumulating ^{11}C-AMT outside the MR-identified abnormalities increased with higher tumor proliferative index, with the largest volumes in glioblastomas. Histopathology confirmed tumor infiltration in regions that were ^{11}C-AMT-positive outside MR-demarcated glioblastoma masses, and no or minimal tumor cells were found in specimens that were ^{11}C-AMT negative. The authors concluded that these results suggest that "increased AMT accumulation on PET detects glioma-infiltrated brain tissue extending beyond the contrast-enhanced tumor mass" and that "although tryptophan uptake is low in peritumoral vasogenic edema, AMT PET can detect tumor-infiltrated brain outside T2-lesions." ^{11}C-AMT PET, then, may be useful in pretreatment delineation of tumor infiltration, particularly in high-grade gliomas.

Journal of Neuro-oncology

PET/CT in Clear Cell Renal Cell Cancer

In an article in the January issue of the *Journal of Clinical Oncology* (2013;31:187–194), Divgi et al. from Columbia University (New York, NY) reported on a study to characterize renal masses with PET/CT as part of the REDECT trial, which included an open-label multicenter analysis of ^{124}I-girentuximab PET/CT in patients with renal masses scheduled for surgery. The current analysis included images and datasets from 195 patients, each of whom underwent PET/CT and contrast-enhanced CT of the abdomen 2–6 d after intravenous administration of ^{124}I-girentuximab and before renal surgery. Images and histopathology were assessed for sensitivity and specificity for renal cell carcinoma. The average sensitivity was 86.2% for PET/CT and 75.5% for contrast-enhanced CT. The corresponding average specificities were 85.9% and 46.8%. Both inter- and intra-reader agreements were high, and the ^{124}I-girentuximab was well tolerated by patients. The authors noted that these results, to their knowledge, provided "the first clinical validation of a molecular imaging biomarker for malignancy." They concluded that ^{124}I-girentuximab PET/CT can "accurately and noninvasively identify clear cell renal cell carcinoma, with potential utility for designing best management approaches for patients with renal masses."

Journal of Clinical Oncology

PET and Hip Treatment Assessment

Frost et al. from King's College and King's Health Partners (London, UK) reported on January 15 ahead of print in the *Journal of Bone and Mineral Research* on the use of ^{18}F-fluoride PET as an early biomarker of bone treatment efficacy in the hips of women with osteopenia. The study included 27 treatment-naïve, postmenopausal women with osteopenia who were randomized to 1 of 2 study arms. One group of 13 women received calcium, vitamin D, and teriparatide (20 μg/d for 12 wk) (TPT group), and the other group, with 14 women, received calcium and vitamin D only (controls). All participants underwent ^{18}F-fluoride PET imaging of the proximal femur, pelvis, and lumbar spine at baseline and at 12 wk. Plasma

clearance (K_i) of the tracer to bone was measured at 4 regions of the hip, lumbar spine, and pelvis. In the TPT group, a significant increase in K_i was observed at all regions of interest, including the total hip, femoral neck, and hip trabecular and cortical regions of interest, as well as in the lumbar spine and pelvis. The control group showed no significant changes in K_i. The authors concluded that this study demonstrated that ^{18}F-fluoride PET "can be used as an imaging biomarker for determining treatment efficacy at the hip as early as 12 wk following initiation of therapy. "

Journal of Bone and Mineral Research

Multimodal Breast Cancer Metastasis Imaging

In an article e-published on January 15 ahead of print in *Current Molecular Medicine*, Davison et al. from the Notre Dame Integrated Imaging Facility (IN) reported on techniques for multimodal optical, CT, and SPECT imaging in a mouse model of breast cancer. The study was designed to assess the complementarity and utility of multimodal imaging in a preclinical model of breast cancer metastasis in the lung. The authors described the labeling and injection of near-infrared fluorophore–labeled breast cancer cells into mice, with fluorescence imaging used to assess cell distribution in the body. Over the course of 6 wk, CT was used to evaluate longitudinal tumor cell accumulation in the lungs. Animals also underwent ^{99m}Tc-MAA SPECT during the same time period to assess lung perfusion. Results with both optical and CT imaging were positive, but SPECT assessment of lung perfusion did not correlate with segmented lung volumes on CT. The authors concluded that "the combination of animal models and noninvasive optical and CT imaging methods provides better research tools to study cancer cell differences at the molecular level."

Current Molecular Medicine

PET + CT in SBRT for NSCLC

Ebright et al. from Boston Medical Center/Boston University School of Medicine (MA) reported on January 12 ahead of print in the *Journal of Thoracic and Cardiovascular Surgery* on the efficacy of PET plus CT in detection of regional recurrence after stereotactic body radiation therapy (SBRT) for early non–small cell lung cancer (NSCLC). The study included the records of 35 patients treated with SBRT for biopsy-proven, early-stage NSCLC. PET and chest CT were performed ~3 mo after treatment. CT results were interpreted separately according to Radiation Therapy Oncology Group response criteria and then compared with PET and combined PET/CT results. Results were analyzed at a median follow-up of 12.8 mo, when 24 patients had stage IA, 7 stage IB, 3 stage IIA, and 1 stage IIB biopsy-proven NSCLC, with 2-y overall survival of 62%. Although CT imaging showed no regional recurrences, combined PET and CT indicated 10 regional recurrences. Four of these underwent salvage treatment with definitive chemoradiotherapy. The authors concluded that PET plus chest CT "enhances the detection of regional progression of NSCLC after SBRT over currently recommended practices" and noted that "in patients who are fit for salvage treatment, where early detection of recurrence can increase the likelihood of successful treatment, PET with diagnostic chest CT appears critical for follow-up."

Journal of Thoracic and Cardiovascular Surgery

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 January and February. In an article e-published on January 23 ahead of print in *Frontiers in Oncology*, Cuaron et al. from the Memorial Sloan–Kettering Cancer Center (New York, NY) described the "Role of FDG-PET scans in staging, response assessment, and follow-up care for non-small cell lung cancer." Glaudemans et al. from the University of Rome "Sapienza" (Italy) summarized current knowledge on "Leukocyte and bacteria imaging in prosthetic joint infection" in the January 16 issue of *European Cells and Materials* (2013;25:61–77). In an article in the January issue of *Cancer Control* (2013;20:60–71), Tomblyn et al. from the H. Lee Moffitt Cancer Center (Tampa, FL) reported on "The new golden era for radioimmunotherapy: not just for lymphomas anymore." Hillengass and Landgren, from the German Cancer Research Center (Heidelberg, Germany) described "Challenges and opportunities of novel imaging techniques in monoclonal plasma cell disorders: imaging 'early myeloma,'" which appeared online on January 4 ahead of print in *Leukemia and Lymphoma*. In an article e-published on January 10 ahead of print in the *International Journal of Cardiology*, Anagnostopoulos et al. from the Biomedical Research Foundation of the Academy of Athens (Greece) reviewed "Assessment of myocardial perfusion and viability by positron emission tomography." Miller, from Belfast City Hospital (Northern Ireland, UK), and an international team of colleagues also reported on January 10 ahead of print in the *International Journal of Cardiology* that "^{18}FDG-positron emission tomography has a role to play in the diagnosis and therapy of infective endocarditis and cardiac device infection." In an article to be published in the March issue of *Current Cardiology Reports* (2013;15:337), Rischpler et al. from the Technische Universität (Munich, Germany) summarized "PET and SPECT in heart failure." Pietrzyk and Herzog from the Forschungszentrum Jülich GmbH (Germany) reported on January 9 ahead of print in *MAGMA* on the question "Does PET/MR in human brain imaging provide optimal co-registration? A critical reflection."