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. We have added a special section on molecular imaging, including both radionuclide-based and other molecular imaging efforts, in recognition of the extraordinary activity and promise of diagnostic and therapeutic progress in this area. 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.

MOLECULAR IMAGING/THERAPY

Nanoparticle PET/CT in Aneurysms

Nahrendorf et al. from the Massachusetts General Hospital/Harvard Medical School (Boston, MA) reported on January 20 ahead of print in *Arteriosclerosis, Thrombosis, and Vascular Biology* on a study using ^{18}F-labeled nanoparticle PET/CT to gauge the extent of local inflammation in aortic aneurysms by directly detecting macrophages. The study was conducted in apolipoprotein E(-/-) mice in which aneurysms were induced by systemic administration of angiotensin II, followed by PET/CT with a monocyte/macrophage-targeted iron oxide nanoparticle. PET/CT detected the aortic aneurysms (mean diameter = 1.85 ± 0.08 mm, compared with 1.07 ± 0.03 for normal aorta). PET signal was significantly higher in these aneurysms (standard uptake value = 2.46 ± 0.48, compared with 0.82 ± 0.05 for aortas in normal mice). A range of histologic and imaging validation studies confirmed that nanoparticles localized predominantly to monocytes and macrophages within the aneurysm wall. The authors concluded that PET/CT with "^{18}F-cross-linked iron oxide nanoparticles allows quantitation of macrophage content in a mouse model of aortic aneurysms."

Arteriosclerosis, Thrombosis, and Vascular Biology

EGFR Expression in Prostate Cancer

In an article e-published on January 20 ahead of print in the *International Journal of Oncology,* Malmberg et al. from Uppsala University (Sweden) reported on investigations of ^{111}In-labeled imaging agents targeting epidermal growth factor receptors (EGFRs) for in vivo molecular profiling of disseminated prostate cancer. The technique leverages the upregulation of the tyrosine-kinase EGFR in progressively higher grade, androgen-insensitive, and metastatic tumors. The in vitro study evaluated binding and cellular processing of radiolabeled EGFR-targeting conjugates by 3 prostate cancer cell lines: DU145 (brain metastasis of prostate cancer, hormone insensitive), PC3 (bone metastasis of prostate cancer), and LNCaP (lymph node metastasis of prostate cancer, androgen- and estrogen-receptor–positive). Receptor expression of EGFR and uptake/internalization of anti-EGFR monoclonal antibodies (cetuximab) and Affibody molecule (Z2377) (both labeled with ^{111}In) were assessed. Both conjugates were found to bind to prostate cancer cells. Although EGFR expression levels were relatively low, they correlated with the degree of hormone independence. Internalization of Affibody molecules was slower in all cell lines than was internalization of monoclonal antibodies. The authors concluded that "the level of EGFR expression in these cell lines is sufficient for in vivo molecular imaging" and that "slow internalization indicates possibility of the use of nonresidualizing labels for Affibody molecules."

International Journal of Oncology

MRI of Anorexigenic Effects

Hankir et al. from the Imperial College London (UK) reported ahead of print on January 19 in the *Journal of Neuroendocrinology* on the use of manganese-enhanced MR imaging to assess the effects of peptide YY (PYY[3-36]) and pancreatic polypeptide (PP), 2 appetite-suppressing hormones released postprandially from the ileum and pancreas, respectively, on neuronal activity affecting food intake. The study was based on previous investigations suggesting that both peptides have anorexigenic effects through signaling in the brainstem and the arcuate nucleus (ARC) of the hypothalamus. In fasted mice injected subcutaneously with PP, a significant reduction in signal intensity was noted in the ARC, ventromedial hypothalamus, and paraventricular nucleus. The same administration of PYY(3-36) resulted in a trend toward decreased signal intensity in the hypothalamus, although this was nonsignificant. Neither peptide induced signal intensity changes in the area postrema of the brainstem. The authors noted that these marked differences in signal intensity profile in the hypothalamus were found despite the fact that both peptides produce similar reductions in food intake, suggesting that separate hypothalamic pathways control the anorexigenic responses induced by peptides. The authors also performed serial manganese-enhanced imaging of mice at 3 time periods within 6 h of injection of PYY(3-36) and a potent analog, PYY(3-36)(LT).

The reduction in ARC signal intensity at 2–4 h after PYY(3-36) (LT) injection was significantly greater than that for saline controls or for PYY (3-36) in fasted mice. The physiologic differences between PYY(3-36) and the analog were also seen in the long-term effects on food intake, with the analog producing a more sustained anorexigenic effect. The authors concluded that these and other data suggest that manganese-enhanced MR imaging "can be used to study the long-term effects of gut peptide delivery on activity within the hypothalamus and brainstem."

Journal of Neuroendocrinology

NIRF Optical Imaging of Tumor Vasculature

Chen et al. from the University of Southern California (Los Angeles) reported on January 7 ahead of print in *Amino Acids* on a study of a Cy5.5-labeled phage-displayed peptide probe for near-infrared fluorescence (NIRF) optical imaging of tumor vasculature in living mice. Previous investigations reported by these researchers showed that the GX1 peptide, identified by phage-display technology, is a tumor vasculature endothelium–specific ligand. For the current study, the tumor-targeting efficacy of the Cy5.5-conjugated GX1 peptide was evaluated in a subcutaneous U87MG glioblastoma xenograft model. In vitro flow cytometry showed dose-dependent binding of the peptide to the glioma cells, and in vivo optical imaging showed rapid tumor targeting at 30 min after injection of the Cy5.5-GX1 probe and high tumor-to-background contrast at 4 h. Tumor specificity of the probe was confirmed, and additional studies showed a high tumor-to-muscle ratio for the probe at 24 h. The authors concluded that "Cy5.5-GX1 is a promising molecular probe for optical imaging of tumor vasculature," with clinical potential for early detection of tumor angiogenesis and monitoring of response to antitumor vasculature therapy.

Amino Acids

THERAPY

RIT After Colorectal Liver Mets Resection

In an article e-published on January 6 ahead of print in the *Annals of Surgery*, de Jong et al. from Radboud University Nijmegen Medical Center (The Netherlands) reported on a study designed to determine whether adjuvant radioimmunotherapy (RIT) prevents recurrent liver metastases and/or results in improved survival after tumorectomy in an experimental model. The study was conducted in rats in which liver metastasis was induced by intrahepatic injection of CC531 tumor cells, followed at 2 wk by tumor resection. The study included 3 groups of rats, including groups injected with ^{177}Lu-labeled monoclonal antibody MG1 (directed against a cell surface antigen on CC531 tumors), a ^{177}Lu-labeled sham antibody, or saline only. ^{177}Lu-MG1 was found to preferentially accumulate in tumors in the liver, with a peak accumulation at 3 d after injection. No adverse signs were noted, except for a transient decrease in weight in both groups receiving radiolabeled injections. Those rats receiving the ^{177}Lu-MG1 survived longer than the other 2 groups. Survival after early administration was not significantly different from that after delayed administration. The authors concluded that this study provided "proof of principle that RIT can be an effective adjuvant treatment modality after surgical treatment of colorectal liver metastases."

Annals of Surgery

DIAGNOSIS

Occult Metastases in Oral Carcinoma

Christensen et al. from the University of Copenhagen (Denmark) reported on January 13 ahead of print in *The Laryngoscope* on a study designed to examine the prevalence of isolated tumor cells and micrometastases in nonsentinel lymph nodes using additional step-serial sectioning and immunohistochemistry as for sentinel lymph nodes. The study included 51 patients with oral cavity squamous cell carcinoma who underwent surgical treatment, including sentinel node biopsy–assisted selective neck dissection. Each patient also underwent dynamic and planar lymphoscintigraphy and SPECT/CT to identify and localize sentinel lymph nodes. Both harvested nonsentinel nodes and the sentinel nodes underwent the same histopathologic step-serial sectioning, staining, antibody testing, and visual examination. Results were compared with previous routine examination of the nonsentinel nodes. An average of 8 nonsentinel nodes were studied per patient, and only 1 patient had positive findings in a nonsentinel node not found on routine examination. This patient also had metastases in sentinel nodes as well as in other nonsentinel nodes detected on using the routine examination protocol. The authors concluded that these results indicate that "the risk of nonsentinel lymph node involvement would seem to be extremely low in patients with early oral cavity squamous cell carcinoma and negative sentinel nodes" and noted that this study provides additional validation of sentinel node biopsy as an accurate staging tool in this disease setting.

The Laryngoscope

MR vs PET/CT in Compression Fx

In an article e-published on January 7 ahead of print in the *Journal of Neurosurgery. Spine*, Cho and Chang from the Korea Institute of Radiological and Medical Science (Seoul) reported on a study comparing MR and ^{18}F-FDG PET/CT imaging in the differential diagnosis of benign and malignant vertebral compression fractures (VCFs). The retrospective study included records from 96 patients with a total of 102 VCFs (67 fractures in 65 patients were benign, 35 fractures in 31 patients were malignant). All patients underwent MR imaging, and 37 underwent ^{18}F-FDG PET/CT (17 in the benign group and 20 in the ma-

lignant group). Among the variables assessed were prevalence of posterior cortical bulging, epidural mass formation, and pedicle enhancement on MR imaging and radiotracer uptake and standardized uptake values (SUVs) on PET/CT. Uptake on PET/CT was seen in all 20 (100%) of the malignant lesions and 12 (71%) of the benign lesions evaluated (sensitivity of 100%, specificity of 29%), with a significant difference in mean maximum SUVs between malignant and benign lesions. The most reliable threshold for SUV_{max} was 4.25, providing a sensitivity of 85% and specificity of 71%. Sensitivity and specificity for MR variable prediction of malignancy were, respectively, 74% and 55% for posterior cortical bulging, 77% and 74% for epidural mass formation, and 90% and 61% for pedicle enhancement. All 3 significant features were found in 21 (64%) of the malignant and 8 (17%) of the benign lesions (sensitivity of 64%, specificity of 83%). The authors concluded that "when MR imaging findings are equivocal, FDG-PET/CT can be considered as an adjunctive diagnostic method for differentiating malignant from benign VCFs."

Journal of Neurosurgery. Spine

PET/CT in Congenital Hyperinsulinism

Zani et al. from the Institute of Child Health and Great Ormond Street Hospital for Children (London, UK) reported in the January issue of the *Journal of Pediatric Surgery* (2011; 46:204–208) on a study evaluating the accuracy of preoperative ^{18}F-l-3,4-dihydroxyphenylalanine (^{18}F-DOPA) PET/CT imaging to differentiate between diffuse and focal congenital hyperinsulinism of infancy and assist in anatomical localization of focal lesions. The study included 19 children with congenital hyperinsulinism scheduled for laparoscopic or open surgery. Each patient underwent ^{18}F-DOPA PET/CT imaging, the results of which were correlated with subsequent histology. PET imaging showed diffuse pancreatic uptake in 5 children, in whom histology confirmed these findings. PET imaging indicated focal pancreatic uptake in 14 children, which also corresponded to histologic results; however, in 5 of the study's patients (36%), PET failed to define the location and/or size of the lesion, leading to 1 inaccurate pancreatic resection.

The authors concluded that although ^{18}F-DOPA PET/CT "discriminates between diffuse and focal forms of congenital hyperinsulinism of infancy" and in focal disease is useful in 2/3 of patients in defining the site and dimension of the focal lesion, "intraoperative histologic confirmation of complete focal lesion resection is needed."

Journal of Pediatric Surgery

PET and Prediction of Multiple Myeloma Relapse

In an article e-published on January 2 ahead of print in the *European Journal of Haematology,* Elliott et al. from the Mount Sinai Medical Center (New York, NY) compared the predictive values for ^{18}F-FDG PET with concurrent laboratory testing results (and the combination of imaging and labs) in prediction of 12-mo relapse/progression in multiple myeloma. Median time to progression was 29.8 mo (range, 1.6–130+ mo), and overall survival and survival without progression at last follow-up were 84% and 49%, respectively. The sensitivity of PET for predicting relapse/progression was 67% and that for lab data was 89%, but PET was more specific than lab data (89% and 79%, respectively). When both sets of data were combined, a positive result for either imaging or labs was 89% sensitive and a positive result for both was 100% specific for predicting 12-mo disease progression. The authors concluded that "PET with laboratory data improves the accuracy of prediction of relapse/progression within 12 mo compared with each test alone" and that "integration of PET into myeloma follow-up is recommended, and the impact of this approach on management should be explored."

European Journal of Haematology

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 late December and January. In an article e-published on January 15 ahead of print in *Current Cardiology Reports,* Giedd and Bergmann from the Beth Israel Medical Center (New York, NY) provided an overview of "Fatty acid imaging of the heart." On January 5, also ahead of print in *Current Cardiology Reports*, Nekolla and Saraste from the Technischen Universität München (Germany) described "Novel F-18-Labeled PET myocardial perfusion tracers: bench to bedside." Owen et al. from the Hammersmith Hospital (London, UK) on January 6 ahead of print in *Multiple Sclerosis* authored "Towards molecular imaging of multiple sclerosis." In the January issue of *Seminars in Hematology* (2011;48:22–31), Mena et al. from the National Institutes of Health (Bethesda, MD) reviewed "Molecular imaging in myeloma precursor disease."