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 recently 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 both 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.

DIAGNOSIS

^{123}I-β-CIT SPECT and Early Parkinson's Disease

Caretti et al. from the Vrije University Medical Center (Amsterdam, The Netherlands) reported on March 12 ahead of print in the *Journal of Neural Transmission* on a study investigating the relationship between thalamic ^{123}I-β-CIT binding on SPECT and early symptoms of Parkinson's disease (PD). The study included 32 drug naïve patients with PD (divided into groups with and without tremor) and 13 controls. All underwent SPECT imaging, and 26 of the patients underwent repeat imaging 17 months later. Depressive symptoms were evaluated in all participants. Results indicated that mean thalamic specific-to-nonspecific ^{123}I-β-CIT binding ratios were lower in patients than controls and that these ratios decreased in patients at follow-up. Average thalamic ratios were significantly lower in patients with tremor than in those without. The authors concluded that these findings, which indicate a decline in binding to thalamic serotonin transporters (5-HTT) in PD, "suggest a possible contribution to tremor onset."

Journal of Neural Transmission

SPECT and Memory Deficits in Early AD

In an article published in the March issue of *Dementia and Geriatric Cognitive Disorders* (2008;25:347–353), Hanyu et al. from the Tokyo Medical University (Japan) reported on a study using SPECT data to investigate the neuroanatomical substrates of unawareness of memory deficits in patients with early Alzheimer's disease (AD). The group had previously published research on this topic identifying impaired awareness of memory deficits in 65% of patients with mild AD and 34% of patients with mild cognitive impairment (*Nippon Ronen Igakkai Zasshi.* 2007;44:463–469). In the current study, regional perfusion deficits were compared in 19 AD patients with awareness of memory deficit and in 19 AD patients without such awareness. All patients underwent SPECT imaging. Statistical maps derived from imaging data showed more extensive and severe perfusion reduction in the unaware group in the right subcallosal, anterior cingulate and cingulate gyri and left orbital, subcallosal, and anterior cingulate gyri. The authors concluded that "functional damage to the inferior, medial and orbital frontal lobes as well as the anterior cingulate gyri may be associated with the lack of awareness in patients with early AD."

Dementia and Geriatric Cognitive Disorders

Imaging Neuropsychologic Sequelae to Toxins

Ozyurt et al. from Uludag University (Bursa, Turkey) reported in the March issue of *Clinical Toxicology* (2008;46:218–221) on a study using ^{99m}Tc-HMPAO SPECT to image regional cerebral blood flow in patients with either acute carbon monoxide exposure (n = 7) or acute organophosphate poisoning (n = 7). Similar perfusion changes were identified in the frontal, temporal, and parietal lobes in the first week after exposure in both groups. These imaging results were compared with long-term neuropsychological sequelae. Such sequelae developed in 5 patients after organophosphate poisoning and 6 patients after carbon monoxide exposure. Among the sequelae were disorientation (in those with hypoperfusion seen on SPECT heterogeneously or in the temporal or frontal lobes), mental confusion (in those with frontoparietal and frontal lobe changes), and parkinsonism (in those with parietooccipital, parietal, and frontal lobe lesions). The authors concluded that "the distribution of these lesions appears to predict the long-term sequelae of these poisonings" but cautioned that studies with larger numbers of patients will be needed to confirm the role of SPECT in imaging acute organophosphate and carbon monoxide exposure.

Clinical Toxicology

Risk Stratification for Cardiac Sarcoidosis

Mehta et al. from the Mount Sinai School of Medicine (New York, NY) reported on March 13 ahead of print in *Chest* on the diagnostic and prognostic value of cardiac MR and PET in the outpatient assessment of patients with sarcoidosis. The study included 62 such patients who were interviewed for cardiac symptoms and evaluated with electrocardiography, Holter monitoring, and echocardiography. Those with symptoms or abnormal results underwent cardiac MR or PET imaging, with diagnoses of cardiac sarcoidosis determined on the basis of imaging findings in 24 patients (39%). Seventeen of these patients were referred for electrophysiology for risk stratification. Patients with cardiac sarcoidosis

had more cardiac symptoms than those without and were more likely to have abnormal Holter and echocardiography results. Two patients received implantable cardioverter defibrillators. During a 2-y follow-up period, no deaths were reported and no other patients developed heart failure or arrhythmias that led to defibrillator therapy. The authors concluded that "a structured clinical assessment incorporating advanced cardiac imaging with PET or cardiac MR is more sensitive than established criteria for the identification of cardiac sarcoidosis." They added that sarcoidal lesions on cardiac MR or PET do not predict arrhythmias in ambulatory patients with preserved cardiac function and that these patients appear to be at low risk of near-term death.

Chest

Long-Term Prognosis for Medullary Thyroid Cancer

In an article e-published on March 10 ahead of print in *Clinical Endocrinology (Oxford)*, Rendl et al. from the Paracelsus Private Medical University (Salzburg, Austria) reported on a study of factors in long-term survival after diagnosis of medullary thyroid carcinoma (MTC). The study focused on the survival of 32 patients with an average age at diagnosis of 42 y and median follow-up of 9.5 y (range, 0.5–39 y). The mortality associated with progressive MTC was 15.6%, with 5-, 10-, and 15-y survival rates of 96%, 91%, and 85%, respectively. Mean survival time after initial diagnosis was 31 y. As expected, patients achieving complete remission had significantly longer survival times than those with biochemical persistent disease or metastasis. The authors noted that in 5 patients PET/CT identified additional tumor burden (lymph node metastases in 4 patients and a local tumor recurrence in another). They concluded that despite the fact that the biochemical cure rate is lower in MTC than in differentiated types of thyroid cancer, the overall prognosis of MTC is favorable. They added that additional studies are needed to determine whether the "identification of further tumor sites by advanced imaging procedures such as PET/CT translates into better prognosis in patients with persistently elevated calcitonin levels."

Clinical Endocrinology (Oxford)

Improving Parathyroid Reoperation

Hessman et al. from University Hospital (Uppsala, Sweden) reported on March 12 ahead of print in the *World Journal of Surgery* on the investigation of techniques for localization diagnosis to improve success rates in parathyroid reoperations. The study included 144 patients with nonmalignant hyperparathyroidism who underwent reoperation after previous parathyroid surgery. Forty-six of these patients and 14 patients who underwent thyroid surgery before primary parathyroid operation were studied with ^{99m}Tc-sestamibi scintigraphy, ^{11}C-methionine PET/CT, and ultrasound. In patients in whom imaging was considered inadequate, additional studies, including ultrasound-guided fine-needle aspiration biopsy and selective venous sampling with rapid parathyroid hormone analysis, were performed. Overall, reversal of hypercalcemia was achieved by reoperation in 134 of 144 (93%) patients. In the group that underwent imaging, ^{99m}Tc-sestamibi scintigraphy, ^{11}C-methionine PET/CT, and ultrasound had respective sensitivities and predictive values of 90% and 88%, 79% and 87%, and 72% and 93%. Both ultrasound-guided fine-needle aspiration biopsy and selective venous sampling with rapid parathyroid hormone analysis provided advantages in accurate localization and in guiding surgical decision making. In 45 of the 46 patients with previous parathyroid surgery and 14 of the 14 patients with previous thyroid surgery, reversal of hypercalcemia and apparent cure were obtained after reoperation, indicating a success rate of 98% for the imaging protocols. The authors concluded that in the challenging setting of reoperative parathyroid surgery, "results can be improved by consistently applied sensitive methods of preoperative imaging, and reoperative procedures may then achieve nearly the same success rates as primary operations."

World Journal of Surgery

PET and PET/CT in Monitoring Uterine Sarcoma

In an article e-published on February 27 ahead of print in *Gynecologic Oncology*, Park et al. from the University of Ulsan College of Medicine (Seoul, Republic of Korea) reported on the clinical accuracy of PET or PET/CT in detecting tumor recurrence in patients treated for uterine sarcoma. The retrospective study included the records and imaging studies of 35 patients who underwent either PET or PET/CT after treatment for uterine sarcoma. Of the total of 48 such scans the group underwent, 30 (8 PET and 22 PET/CT) were performed to assess for disease recurrence and 18 (4 PET and 14 PET/CT) were performed as part of routine posttherapy monitoring. Imaging findings were compared with histopathology or clinical outcome at least 6 mo after imaging. In patients with suspected recurrence, the sensitivity, specificity, accuracy, and positive and negative predictive values for imaging were 92.9%, 100%, 94.4%, 100%, and 80%, respectively. These values were 87.5%, 95.5%, 93.3%, 87.5%, and 95.5%, respectively, in asymptomatic patients. Imaging changed management in 12 patients (33.3%), accelerating treatment in 8 and avoiding previously planned treatment in 4. The authors concluded that "PET or PET/CT was highly effective in discriminating true recurrence in patients with suspected recurrence and was highly sensitive in detecting recurrence in asymptomatic patients."

Gynecologic Oncology

Preoperative PET/CT Colonography

Nagata et al. from the Showa University Northern Yokohama Hospital (Japan) reported on March 11 ahead of print in *Diseases of the Colon and Rectum* on a study evaluating the utility of ^{18}F-FDG PET/CT colonography in the preoperative diagnosis of tumors proximal to obstructive colorectal cancers. The study included 13 patients

with colorectal cancers that could not be traversed colonoscopically. The authors' protocol include integrated whole-body PET/CT for tumor staging and CT colonography in a single examination with no bowel preparation. Imaging results were compared with intraoperative results, histopathology, and follow-up colonoscopy. PET/CT colonography correctly identified 13 primary obstructive colorectal cancers (100%) and 2 synchronous colon cancers (100%) proximal to the obstruction, with no false-negatives or false-positives. PET/CT of the 2 synchronous colon cancers (which were missed in other preoperative studies) facilitated removal in single-stage surgical procedures. The authors concluded that in the setting of obstructive colorectal cancers "preoperative PET/CT colonography provided valuable anatomic and functional information" on the entire colon to properly address surgery of colorectal cancer.

Diseases of the Colon and Rectum

Receptor Scintigraphy in Pediatric Brain Tumors

Khanna et al. from the University of Iowa (Iowa City) reported in the March issue of *Pediatric Blood Cancer* (2008; 50:561–566) on a study evaluating the role of somatostatin receptor scintigraphy (SRS) in posttreatment surveillance of pediatric brain tumors. The study included 20 children and young adults (ages, 7 mo–24 y; mean, 9 y) who underwent serial SRS and MR imaging after therapy. Imaging results were compared with clinical outcomes and with somatostatin receptor expression as determined by immunohistochemistry in available tumor specimens. SRS was true-positive in 15 of 16 patients with proven disease identified after resection ($n = 5$) or during follow-up ($n = 11$). In these same patients, MR imaging was positive in 12, false-negative in 2, and equivocal in 2 (could not distinguish between radiation necrosis and tumor recurrence). SRS was negative in the 4 patients with no evidence of disease on follow-up. Although SRS was false-negative in 1 patient with a true-positive MR study, no immunohistochemistry evidence of somatostatin receptor expression was found in this individual. The authors concluded that SRS is a useful adjunct to MR imaging for posttreatment surveillance of somatostatin receptor expression–positive pediatric brain tumors, with special utility when MR imaging is equivocal.

Pediatric Blood Cancer

SLN Biopsy Experience in Pediatric Patients

Kayton et al. from the Memorial Sloan–Kettering Cancer Center (New York, NY) reported on March 13 ahead of print in *Cancer* on a 10-y review of the pathology, lymphoscintigraphy, and clinical records of pediatric and young adult patients who underwent ^{99m}Tc-sulfur colloid–guided sentinel lymph node (SLN) biopsy. The study included 30 patients (ages, 2–21 y) who underwent a total of 31 SLN biopsies. ^{99m}Tc-sulfur colloid alone was used for 13 of the 31 SLNs and combined with isosulfan blue dye in 18. Thirty of 31 SLNs were identified preoperatively, and the remaining node was identified during surgery. Positive SLNs were identified in 1 of 9 patients with rhabdomyosarcoma and 2 of 5 patients with breast cancer, and in each of these patients SLN results were used to guide management decisions. No other patients had positive SLNS, and, despite a lack of lymph node basin irradiation or formal node dissection, no recurrences were seen in a median follow-up of 48 mo in patients with nonrhabdomyosarcoma soft-tissue sarcomas. The authors concluded that not only is SLN biopsy for pediatric soft-tissue tumors safe, it can provide valuable information that can alter management decisions both for children with rhabdomyosarcoma and adolescents with breast cancer. The authors noted that data obtained in this investigation "should prompt the prospective study of SLN biopsy as a modality that might help guide the administration or withholding of regional therapy among pediatric patients with nonrhabdomyosarcoma soft-tissue sarcoma."

Cancer

^{99m}Tc-HMPAO SPECT and Autism

Degirmenci et al. from the Dokuz Eylul University Medical School (Izmir, Turkey) reported in the April 15 issue of *Psychiatry Research* (2008; 162:236–243) on a study using ^{99m}Tc-HMPAO SPECT to investigate and characterize perfusion patterns in autistic children and their families. The study included 10 children with autism (9 boys, 1 girl), 5 age-matched children (3 boys, 2 girls) as controls, immediate family members of 8 children with autism (8 mothers, 8 fathers, 7 siblings), and age- and sex-matched control groups for parents and siblings. All participants underwent brain perfusion imaging with ^{99m}Tc-HMPAO SPECT. In children with autism, hypoperfusion was seen on imaging in the right posterior parietal cortex ($n = 3$), the bilateral parietal cortex in ($n = 1$), bilateral frontal cortex ($n = 2$), left parietal and temporal cortex ($n = 1$), and right parietal and temporal cortex ($n = 1$). Asymmetric perfusion was seen in the caudate nucleus in 4 children with autism. Semiquantitative analysis confirmed significant hypoperfusion in the right inferior and superior frontal, left superior frontal, right parietal, right mesial temporal, and right caudate nucleus in these children. Significant hypoperfusion was noted in the right parietal and bilateral inferior frontal cortex in parents of children with autism but not in matched controls. Significant decreases in perfusion in the right frontal cortex, right nucleus caudate, and left parietal cortex were noted in siblings of children with autism but not in matched controls. The authors concluded that these findings indicate the existence of regional brain perfusion alterations in children with autism and in their first-degree family members.

Psychiatry Research

THERAPY

Scintigraphy and Salivary Function After RT

Tenhunen et al. from the Helsinki University Central Hospital (Finland)

reported on March 6 ahead of print in *Radiotherapy and Oncology* on a study evaluating the use of ^{99m}Tc-pertechnetate scintigraphy in predicting salivary flow after radiation therapy. The study included 20 patients who were diagnosed with head and neck cancer and treated with intensity-modulated radiation therapy to save salivary gland function. Each patient underwent salivary gland scintigraphy before therapy. The researchers measured total quantitative saliva secretion before and at 6 and 12 mo after therapy. Two models were developed, 1 based on overall averages of saliva produced in healthy individuals and 1 based on saliva produced by each gland in patients as measured by scintigraphy before therapy. The scintigraphy-based model was found to accurately predict posttreatment saliva flow rates. Relative changes in salivary flow rates were found to be dependent on the cumulative radiation dose received in treatment. The authors concluded that "salivary gland function assessed by scintigraphy prior to radiotherapy is useful in prediction of the residual salivary flow after radiotherapy."

Radiotherapy and Oncology

RIT and NHL

In an article e-published on March 12 ahead of print in *Lancet Oncology*, Zinzani et al. from the University of Bologna (Italy) expanded on previously published results (*Cancer.* 2008;112: 856–862) of a prospective, open-label, nonrandomized phase 2 trial of combined fludarabine and mitoxantrone chemotherapy plus ^{90}Y-ibritumomab tiuxetan radioimmunotherapy (RIT) in patients with untreated nonfollicular non-Hodgkin's lymphoma (NHL). The current multicenter results included 61 patients with stage III or IV untreated indolent follicular NHL who were treated with 6 cycles of fludarabine and chemotherapy. Patients with a partial response, normal platelet and granulocyte counts, and bone marrow infiltration $<25\%$ at 4–6 wk after completion of chemotherapy proceeded to consolidation treatment at 6–10 wk with a course of ^{90}Y-ibritumomab tiuxetan therapy. An overall initial chemotherapeutic response was seen in 60 of 61 patients (98%; 43 with complete and 17 with partial responses). Fifty-seven patients (43 with complete and 14 with partial responses) proceeded to ^{90}Y-ibritumomab tiuxetan therapy. Fifty-five of these 57 patients then achieved complete responses, including 12 of the 14 patients who had previously achieved only partial responses. Over a median follow-up of 30 mo, the 3-y progression-free and 3-y overall survival rates were 76% and 100%, respectively, for those undergoing RIT. Hematologic toxic effects were observed in more than half of those undergoing RIT, and blood transfusions were required in 21 patients. As in their previous study, the authors concluded that these results provide evidence "for the feasibility, tolerability, and efficacy of fludarabine and mitoxantrone plus ^{90}Y-ibritumomab tiuxetan in untreated patients with follicular NHL."

Lancet Oncology

Amifostine in High-Dose ^{131}I Treatments

Kim et al. from the Pusan National University Hospital (Busan, Republic of Korea) reported in the March issue of *Thyroid* (2008;18:325–381) on a study using serial quantitative analysis of salivary gland scans to investigate the effectiveness of amifostine as a cytoprotective adjuvant in ^{131}I treatment of differentiated thyroid cancer. The study included 80 newly diagnosed patients (9 men, 71 women), who were divided into 2 treatment groups: 42 patients received amifostine intravenously before ^{131}I therapy and 38 patients received ^{131}I therapy alone. In both groups, quantitative salivary scintigraphy after therapy showed statistically significant declines in function. Amifostine did not prevent parenchymal damage to major salivary gland function and showed no benefits in preventing xerostomia in the setting of ^{131}I treatment for differentiated thyroid cancer.

Thyroid

MOLECULAR IMAGING

Nanobody-Based SPECT EGFR Imaging

In an article e-published on February 23 ahead of print in *Molecular Imaging and Biology*, Huang et al. from the Vrije Universiteit Brussel (Brussels, Belgium) reported on a technique for in vivo SPECT nanobody-based radioimmunodetection of epidermal growth factor receptor (EGFR)–overexpressing tumors. The authors described the development of ex vivo and in vivo studies with a llama single-domain antibody fragment nanobody labeled with ^{99m}Tc. Pinhole SPECT verified selective tumor targeting in mice bearing xenografts of tumor cells with either high or moderate EGFR overexpression and provided discrimination between these tumors. In vivo blood clearance of the radiolabeled nanobody was fast, indicating a relatively short half-life of 1.5 h. The authors concluded that the high specificity and selectivity for EGFR-overexpressing cells, the feasibility of discriminating SPECT analysis, and the favorable biodistribution results corroborate the suitability of these nanobodies for in vivo tumor imaging.

Molecular Imaging and Biology

Direct Stem Cell Injection in Refractory Ischemia

Pompilio et al. from the Centro Cardiologico Monzino (Milan, Italy) reported in the March issue of *Thoracic and Cardiovascular Surgeon* (2008;56: 71–76) on research on direct intramyocardial injection of bone marrow–derived stem cells in patients with refractory ischemia. The study included 5 patients with untreatable angina pectoris who received injections of 4–12 million bone marrow–derived stem cells directly into myocardial segments with stress-induced ischemia as assessed by gated SPECT. Patients were followed up with gated SPECT, an exercise test, echocardiography, and coronary angiography at baseline, 6 mo, and 1 y to assess exercise capacity, myocardial perfusion, left ventricular

function, and coronary anatomy. No early or long-term complications from stem cell therapy were observed, and all patients experienced significant improvement in symptoms at an average of 3.8 wk after injection. Serial SPECT showed improved rest and stress perfusion at 6 mo. In 4 of the 5 patients, clinical improvement remained unchanged at a mean follow-up of 36.5 mo. The authors concluded that these long-term clinical and perfusion improvements in the absence of adverse events point to the potential benefits of stand-alone bone marrow–derived stem cell therapy as an alternative to conventional approaches to refractory ischemia.

Thoracic and Cardiovascular Surgeon

Microbubbles and Therapeutic Angiogenesis

In an article published in the March issue of the *Journal of Ultrasound in Medicine* (2008;27:453–460), Li et al. from the Second Affiliated Hospital of Chongqing University of Medical Sciences (China) reported on a study exploring the feasibility of therapeutic angiogenesis induced by hepatocyte growth factor (HGF) mediated by ultrasound-targeted microbubble destruction as a potential treatment for myocardial infarction. The study was conducted in a rat model of myocardial infarction in which 40 rats were divided into equal groups and treated with: (1) HGF, ultrasound, and microbubbles (ultrasound-targeted microbubbles were loaded with the HGF gene and triggered electrocardiographically); (2) HGF and ultrasound; (3) HGF and microbubbles; and (4) surgery alone. All rats were killed 14 d after transfection, and laboratory, immunohistochemical, and histopathologic studies were performed. Enhanced green fluorescent protein expression was detected in the myocardium of group 1 and a few areas of HGF expression were detected only in small vessels and the capillary endothelium, but no expression was found in the other groups. Microvessel density was found to be highest in the myocardium of rats in group 1, and the amount of HGF in the myocardium was highest in this group as well. The authors concluded that these results suggest that "ultrasound-targeted microbubble destruction could deliver HGF into the infarcted myocardium and produce an angiogenesis effect, which could provide a novel strategy for gene therapy of myocardial infarction."

Journal of Ultrasound in Medicine

MR Imaging and Diabetogenic Cell Response

Medarova and colleagues from the Massachusetts General Hospital and the Masschusetts Institute of Technology (Boston) reported in the April issue of *Magnetic Resonance in Medicine* (2008; 59:712–720) on a study using MR imaging with a novel superparamagnetic iron oxide nanoparticle–based contrast probe to track the accumulation of diabetogenic CD8+ T-cells during type 1 diabetes progression. Nonobese diabetic mice of different ages (5, 8, 15, and 24 wk) were imaged before and after injection with the probe or with unmodified iron oxide nanoparticles. Semiquantitative MR imaging analysis indicated that accumulation of the probe was antigen specific, age dependent, and well correlated with the numbers of labeled CD8+ T-cells recovered from the pancreas in treated mice. The authors concluded that this approach represents a "promising new avenue for noninvasive imaging of lymphocyte inflammation in organ-specific autoimmunity and transplantation."

Magnetic Resonance in Medicine