



Each month the editor of *Newsline* selects articles on diagnostic, therapeutic, research, and practice issues from a range of international publications. Many selections come from outside the standard canon of nuclear medicine and radiology journals. Note that although we have divided the articles into diagnostic and therapeutic categories, these lines are increasingly blurred as nuclear medicine capabilities rapidly expand. Many diagnostic capabilities are now enlisted in direct support of and, often, in real-time conjunction with therapies. 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.

## Diagnosis

### MR and SPECT in Facetogenic Back Pain

Kim and Wang from the University of Southern California Keck School of Medicine (Los Angeles) reported in the July issue of *Neurosurgery* (2005;59:147–156) on a study correlating findings on SPECT and MR scans in patients clinically identified as having facetogenic axial back pain. The study included 31 patients with severe axial back pain who underwent both lumbar MR and SPECT imaging. MR identified 230 facets and SPECT identified uptake in 29 joints. These findings were assessed and correlated. The authors described 4 morphologic patterns on the basis of synovial appearance on MR imaging: light, mottled, narrowed, and obliterated. The MR facets were graded from 1 to 4 using these architectures, a scale that most likely parallels the continuum of facet degeneration, with 4 representing the obliterated joint. Of the subtypes represented by the scale, grade 2, or

mottled, showed the highest specificity (90%) for SPECT and synovial fluid increase suggestive of inflammation. Synovial abnormalities correlated well with SPECT findings, and a grading scale was proposed to characterize the degeneration of a lumbar facet over time. The authors proposed a new subtype of SPECT-positive inflamed joint and called for additional studies to delineate the natural history of the lumbar facet.

*Neurosurgery*

### SPECT/CT and Neuroendocrine Tumors

In an article published in the July issue of *Clinical Oncology* (2006;61:579–587), Hillel et al. from the Sheffield Teaching Hospitals (UK) reported on the clinical effect of a combined <sup>111</sup>In-pentetreotide SPECT/CT system on somatostatin receptor imaging in patients with neuroendocrine tumors. The study included 29 patients, the majority of whom had carcinoid disease. All patients underwent SPECT/CT imaging. The SPECT images were first interpreted alone, and abnormal findings were reported in 15 of the 29 patients. These images were interpreted a second time with the addition of CT images for functional anatomic mapping. In 11 (73%) of the images reported as abnormal on SPECT, functional anatomic mapping either pointed to a previously unidentified lesion (7 patients) or changed the location of at least 1 previously identified lesion (4 patients). Overall, functional anatomic mapping changed patient management in 64% of the cases in which the additional anatomic information caused a change in the reported location of lesions. The authors concluded that these results suggest that functional anatomic mapping may improve the accuracy of SPECT somatostatin receptor imaging

and have a significant beneficial effect on patient management.

*Clinical Oncology*

### Sentinel Node Biopsy and Multicentric Breast Cancer

Knauer et al. from the General Hospital (Feldkirch, Austria) reported in the July 20 issue of the *Journal of Clinical Oncology* (2006;24:3374–3380) on a multi-institutional trial of the feasibility and accuracy of sentinel node (SN) biopsy in patients with multicentric invasive breast cancer. The study included 142 such patients enrolled in the Austrian Sentinel Node Study Group (ASNSG) trial and compared this group's data with those from 3,216 patients with unicentric cancer. A mean number of 1.67 sentinel nodes were excised in the multicentric group, and the incidence of SN metastases was 60.8%. These diagnoses were confirmed by axillary lymph node dissection in 125 patients. Of patients with positive SNs, 60.8% (48 of 79) showed involvement of nonsentinel nodes (NSNs), as did 3 patients with negative SNs. The sensitivity, negative predictive value, and overall accuracy of the SN technique in the multicentric group were 96.0%, 93.3%, and 97.3%, respectively. This group had significantly higher rates of SN metastases and nonsentinel node metastases than the patient group with unicentric cancer, but no differences were noted in detection or false-negative rates. The authors noted that these trials indicate that sentinel lymph node biopsy without routine axillary lymph node detection appears to be appropriate for multicentric breast cancer. They concluded that "Given adequate quality control and an interdisciplinary teamwork of surgical, nuclear medicine, and pathology units, SN biopsy is both feasible and accurate in this disease entity."

*Journal of Clinical Oncology*

## Chernobyl Follow-Up Studies

The 20-year anniversary of the nuclear accident at Chernobyl has been the subject of numerous studies and reports in 2006. In the July 5 issue of the *Journal of the National Cancer Institute* (2006;98:897–903), Tronko et al. from the Institute of Endocrinology and Metabolism (Kiev, Ukraine) published the official results of the first cohort study of thyroid cancer among those exposed as children and adolescents. The study began with a solicitation to 32,385 individuals who had been younger than 18 years of age and resident in the most heavily contaminated areas in Ukraine at the time of the accident. These individuals were invited to be screened between 1998 and 2000 for any thyroid pathology by ultrasound and palpation. A total of 13,127 individuals (44% of the original cohort) were screened. Radiation measurements made shortly after the accident and interview data provided the bases for individual estimates of radiation dose to the thyroid. During this screening, 45 pathologically confirmed cases of thyroid cancer were identified. Thyroid cancer incidence showed a strong and approximately linear relationship with individual thyroid dose estimates, yielding an estimated excess relative risk of 5.25 per Gy. In the absence of the accidental exposure event, 11.2 thyroid cases would have been expected from this study group, rather than the 45 observed. Exposure to radioactive iodine, therefore, was strongly associated with increased risk of thyroid cancer among those exposed as children and adolescents. The authors cautioned, however, that these results should not be generalized to any future or hypothetical radiation accidents, “because of the potential differences in the nature of the radioactive iodines involved, the duration and temporal patterns of exposures, and the susceptibility of the exposed population.”

*Journal of the National Cancer Institute*

## SPECT/CT SLN Detection in Bladder Cancer

Sherif et al. from the Uppsala University Hospital (Sweden) reported in the July issue of *European Urology* (2006;50:83–91) on the use of SPECT/CT in preoperative sentinel lymph node (SLN) detection in patients with invasive bladder cancer. The study included 6 patients scheduled for radical cystectomy who underwent lymphoscintigraphy after transurethral injection of  $^{99m}\text{Tc}$ -albumin in the detrusor muscle peritumorally both with planar imaging and with SPECT/CT. Radical cystectomy began with extended lymphadenectomy and intraoperative detection of SLNs with a Geiger probe and dye marker. Conventional planar lymphoscintigraphy and fused SPECT/CT images were compared and correlated with the results of intraoperative SLN detection and subsequent histopathology. The researchers found that SPECT/CT provided anatomically detailed preoperative visualization of 21 SLNs in 5 of the 6 patients, but the planar images showed a total of only 2 SLNs in 2 of the 6 patients. SPECT/CT identified all metastatic SLNs, whereas conventional lymphoscintigraphy detected only 1 of 6. The authors concluded that, “The combination of lymphoscintigraphy with CT enhanced preoperative anatomic localization of sentinel nodes in bladder cancer and aided in the identification of sentinel nodes during surgery.”

*European Urology*

## $^{111}\text{In}$ -Octreotide Brain Scintigraphy

In an article e-published on July 19 ahead of print in the *Journal of Neurooncology*, Nathoo et al. from the Cleveland Clinic Foundation (OH) reported on the use of  $^{111}\text{In}$ -octreotide brain scintigraphy for noninvasive differentiation of meningiomas from other cranial dural-based pathology. The retrospective study included data from 50 patients (mean age, 62.4 years) over a median follow-up period of 2 years. Each patient underwent  $^{111}\text{In}$ -octreotide brain scintigraphy be-

fore proceeding to biopsy (4), resection (10), radiosurgery (21), external-beam radiation therapy (3), or continued observation (16). Two neuroradiologists reviewed the scintigraphy images without access to patient histories or status and assessed octreotide uptake at 6 and 24 hours after tracer injection. These results were correlated with those from  $^{18}\text{F}$ -FDG PET imaging (in 38 patients), MR imaging (50 patients), histology (14 patients), and angiography (1 patient). In those cases in which definitive diagnoses could be made, the sensitivity, specificity, and positive and negative predictive values for  $^{111}\text{In}$ -octreotide scintigraphy alone were 100%, 50%, 75%, and 100%, respectively. Scintigraphy in combination with MR imaging allowed precise differentiation of meningiomas from other lesions, whereas  $^{18}\text{F}$ -FDG PET alone correctly identified malignant pathology with 100% sensitivity and specificity. The authors concluded that  $^{111}\text{In}$ -octreotide brain scintigraphy “may increase the diagnostic specificity of conventional MRI when differentiating meningioma from other dural-based pathologies, while the addition of FDG PET differentiates benign from malignant lesions.”

*Journal of Neurooncology*

## PEM in Primary Breast Cancer

Berg et al. from American Radiology Services and Johns Hopkins Green Spring (Lutherville, MD) reported in the July/August issue of *Breast Journal* (2006;12:309–323) on a multicenter study of the diagnostic performance of a high-resolution PET scanner using mild breast compression (positron emission mammography [PEM]). The study included 94 women with known or suspected breast cancer who underwent  $^{18}\text{F}$ -FDG PEM imaging. PEM readings were correlated with histopathology for 92 lesions in 77 women: 77 index lesions (42 malignant), 3 ipsilateral lesions (3 malignant), and 12 contralateral lesions (3 malignant). Of 48

cancers, 16 (33%) were clinically evident; 11 (23%) were ductal carcinoma in situ (DCIS), and 37 (77%) were invasive (30 ductal, 4 lobular, and 3 mixed). PEM showed 10 of 11 (91%) DCIS and 33 of 37 (89%) invasive cancers and was positive in 1 of 2 T1a tumors, 4 of 6 T1b tumors, 7 of 7 T1c tumors, and 4 of 4 instances in which tumor size was unavailable. PEM sensitivity for detecting cancer was 90%, specificity was 86%, positive predictive value was 88%, negative predictive value was 88%, and accuracy was 88%. PEM was the sole approach that accurately visualized malignant lesions in 3 patients. The authors concluded that  $^{18}\text{F}$ -FDG PEM has high diagnostic accuracy for breast lesions.

*Breast Journal*

### Microglial Activity Maps in Stroke

In an article published in the July issue of *Stroke* (2006;37:1749–1753), Price et al. from the University of Cambridge and Addenbrookes Hospital (Cambridge, UK) reported on nuclear medicine techniques to establish temporal and spatial patterns of microglial activity in the periinfarct zone as part of the neuroinflammatory response in the subacute phase of ischemic stroke. The study included 4 patients who had experienced carotid territory ischemic stroke and 4 age-matched controls, all of whom underwent  $^{11}\text{C}$ -R-PK11195 PET imaging. Controls were imaged once, and patients were imaged at 3 time windows up to 30 days after ictus. The resulting data were coregistered with T1-based MR images to identify significant binding in core infarction, contralateral hemisphere, and within a defined periinfarct zone. Significant binding potential elevations were identified beyond 72 hours and extended to 30 days in core infarction, contralateral hemisphere, and the periinfarct zone. Minimal microglial activation was seen in the initial period up to 72 hours. The authors suggested that this may “represent a therapeutic op-

portunity that extends beyond time windows traditionally reserved for neuroprotection.”

*Stroke*

### PET Predictive Powers in Glioma Treatment

In an article e-published on July 11 ahead of print in the *International Journal of Radiation Oncology, Biology, Physics*, Charnley et al. from the University of Manchester (UK) reported on a study assessing the ability of  $^{18}\text{F}$ -FDG PET to predict response among patients with glioma to temozolomide therapy alone or to temozolomide combined with radiotherapy. The study included 19 patients with high-grade glioma, including 8 patients with recurrent glioma, who received only temozolomide for a period of 7 weeks, and 11 newly diagnosed patients, who received temozolomide plus radiotherapy over 6 weeks, followed by 6 cycles of adjuvant temozolomide beginning 1 month after the last radiotherapy. Both PET and MR images were acquired at baseline and 7 and 19 weeks after first temozolomide administration. The authors found that patients in the temozolomide-only group who survived more than 26 weeks showed a greater reduction in glucose metabolic rate at 7 weeks than those who would not survive to 26 weeks. Also in the temozolomide-only group, PET responders (defined as glucose metabolic rate  $\geq 25\%$ ) survived longer than nonresponders. MR imaging was not predictive of these responses, nor was PET predictive in the group receiving both temozolomide and radiotherapy.

*International Journal of Radiation Oncology, Biology, Physics*

### Receptor Imaging in Bipolar Disorder

Cannon et al. from the National Institute of Mental Health reported in the July issue of the *Archives of General Psychiatry* (2006;63:741–747) on a study using  $^{18}\text{F}$ -FP-TZTP, a selective muscarinic 2 (M2) receptor

radioligand, for PET imaging in the assessment of M2 receptor binding in individuals with major depressive disorder and bipolar disorder. The study included 17 patients with major depressive disorder, 16 with bipolar disorder, and 23 healthy controls. All participants underwent  $^{18}\text{F}$ -FP-TZTP PET imaging and were unmedicated at the time of imaging. The authors assessed tracer distribution volumes and compared illness severity as measured by clinical rating metrics with these volumes. Mean anterior cingulate cortex distribution volumes differed significantly in the group with bipolar disorder, with significantly lower binding potential, and these reductions correlated with severity of depressive symptoms in this group but not in controls or individuals with major depressive disorder. The authors suggested that these data provide the “first direct evidence that altered M2 receptor function contributes to mood dysregulation in bipolar disorder.”

*Archives of General Psychiatry*

### PET/MR Imaging in Autism

Haznedar et al. from the Mount Sinai School of Medicine (New York, NY) reported in the July issue of the *American Journal of Psychiatry* (2006;163:1252–1263) on the use of coregistered PET and MR imaging to map volumetric and metabolic abnormalities in structure and function within the dorsal striatum and thalamus in 17 patients with autism or Asperger’s disorder and 17 age-matched controls. All participants underwent MR and  $^{18}\text{F}$ -FDG PET imaging. In addition, participants were asked to perform a serial verbal learning test during the PET tracer uptake period. PET and MR images were coregistered, with MR region-of-interest coordinates applied to the PET scan for each participant. The authors found that individuals with autism spectrum disorders had greater volumes in the right caudate nucleus than did control subjects, as well as a reversal of the expected left-greater-than-right hemispheric asymmetry. Patients also had lower relative glucose metabolic

rates bilaterally in the ventral caudate, putamen, and thalamus. Patients with autism had lower metabolic activity in the ventral thalamus than those with Asperger's disorder but did not differ from comparison subjects in metabolic activity in the caudate nucleus. They concluded that these results are consistent with the existence of a deficit in the anterior cingulate-ventral striatum-anterior thalamic pathway in patients with autism spectrum disorders.

*American Journal of Psychiatry*

## PET and GRPR Imaging in Breast Cancer

In an article e-published on July 13 ahead of print in *Breast Cancer Research and Treatment*, Parry et al. from the Washington University School of Medicine (St. Louis) reported on research designed to assess the feasibility of using positron-labeled bombesin analogs for PET detection of gastrin-releasing peptide receptor-(GRPR) expressing breast cancers. The study employed dedicated, small animal imaging PET technology and mice bearing T-47D human breast cancer cells. The authors first investigated a series of bombesin analogs that could be labeled with  $^{64}\text{Cu}$ , and the most promising were evaluated in the mouse model. Biodistribution studies indicated that a bombesin analog with an 8-carbon linker had the highest tumor uptake but also had high normal tissue uptake in the liver. The analogs containing the 6- or 8-carbon linkers also showed good tumor uptake. The authors concluded that these results indicate "the feasibility of using positron-labeled bombesin analogs for PET detection of GRPR-expressing breast cancer."

*Breast Cancer Research and Treatment*

## Genetic Influences in Fitness

Hannukainen et al. from the University of Turku (Finland) reported on July 6 ahead of print in the *Journal of Applied Physiology* on a study investigating the heredity-dependent or -independent effects of increased

physical activity and aerobic fitness on skeletal muscle free fatty acid (FFA) uptake and perfusion at rest and during exercise. The study included 9 pairs of young adult male monozygotic twins. Members of each pair had significant differences in routine physical activity and aerobic fitness. All were imaged with PET before and after various exercises. Submaximal knee-extension exercise increased perfusion, FFA uptake, and oxygen uptake in quadriceps femoris muscles 6–10 times over resting values. The more active twins tended to utilize more oxygen, but no differences were found in muscle perfusion or FFA uptake between twins. Exercise decreased both perfusion and FFA uptake heterogeneity within the muscles similarly in both groups. The authors found that although a long-term history of moderately increased physical activity tended to enhance muscle oxidative metabolism, it had no significant influence on FFA uptake or perfusion rates or their heterogeneity in skeletal muscle. They concluded that "the genetic influence is more important to determine the heterogeneity of perfusion and FFA uptake in skeletal muscle than exercise training."

*Journal of Applied Physiology*

## Mouse Model for Radiation Bone Loss

In a study widely covered in the popular media, Hamilton et al. from Clemson University (SC) and Loma Linda University (CA) reported on June 8 ahead of print in the *Journal of Applied Physiology* on a study designed to evaluate bone loss in a murine model of radiation-induced osteoporosis. The research involved exposing mice to gamma, proton, carbon, or iron radiation at 2-Gray doses, representing both a clinical treatment fraction and projected exposures on exploratory space flights. Mice were killed 110 days after irradiation, and proximal tibiae and femur diaphyses were analyzed using microCT. Results showed profound changes in trabecular architecture for

all types of radiation. Bone loss was 29% for gamma, 35% for proton, 35% for carbon, and 34% for iron irradiation. Connectivity density, thickness, spacing, and number were also affected. Although much of the popular attention on this research focused on the effects of radiation on astronauts during space travel, these results with relatively low levels of radiation also reinforce recent studies suggesting significant increases in fractures among individuals who have undergone radiation therapy. In addition to providing a novel animal model for future investigations, these results point to the need for continued investigations into imaging methods that can accurately assess and characterize bone loss.

*Journal of Applied Physiology*

## Therapy

### Caregiver Exposure After $^{131}\text{I}$ Therapy

In an article e-published ahead of print on July 6 in *Radiation Protection and Dosimetry*, Marriott et al. from Hamilton Health Sciences (Ontario) reported on a study designed to assess radiation exposure to caregivers of patients who had received high-dose radioiodine therapy for differentiated thyroid cancer. The study consisted of radiation dose measurements on family members designated as the primary caregiver in 25 instances of high-dose therapy with 3.7 GBq of  $^{131}\text{I}$  and 2 additional instances in which the dose varied slightly. Radiation doses for the caregivers were monitored each hour for 1 week with electronic personal dosimeters. The average penetrating dose was  $98 \pm 64 \mu\text{Sv}$ , and the maximum penetrating dose was 283  $\mu\text{Sv}$ . Dose rate profiles indicated that approximately one-third of the total caregiver dose was received during the trip home from the hospital. The resulting dose rate profiles showed rapid clearance of  $^{131}\text{I}$ , but suggested that this clearance occurs in 3 distinct phases associated with specific events:

<1 hour, corresponding to the ride home; 21 hours, corresponding to clearance of the radioisotope from the patient; and 8 days, corresponding to the persistence of small quantities of radioiodine in the home.

*Radiation Protection and Dosimetry*

## RIT Approach Reviewed

In an article e-published on July 6 ahead of print in *Cancer*, Weigert et al.

from the University of Munich (Germany) reviewed literature and guidelines on radioimmunotherapy (RIT) with  $^{90}\text{Y}$ -ibritumomab tiuxetan in patients with follicular lymphoma or B-cell non-Hodgkin's lymphoma. They surveyed the results of trials leading to the approval of the treatment regimen in the United States, as well as other current trials assessing efficacy in other subtypes of lym-

phoma, such as diffuse large-cell and mantle-cell lymphoma. Current challenges were reviewed, including how best to integrate this RIT approach into existing established treatment planning approaches. The authors also evaluated current recommendations and future prospectives and provided practical recommendations for patient management.

*Cancer*

(Continued from page 24N)

own Web site. In a recent development—and in response to changing technology that makes the Internet an economical and efficient conduit for delivery of information—the society's board of directors elected to make *JNM* an open-access journal, allowing full-text, online articles to be available for free 12 months after publication. This move expands the journal's audience to include medical researchers, physicians and other health care providers, patients and their advocates, students, and the global public. Such unrestricted access to scientific knowledge is bound to have a major impact on medical practice and on promoting the benefits of molecular imaging and therapy.

The first issue of a Chinese edition of the journal was published last month through a unique arrangement with Blackwell Publishing, and a Japanese version of *JNM* has been printed for about 2 years. The publication of these 2 language editions, overseen by editors selected from

*JNM*'s review board, accelerates the journal's professional impact.

SNM has almost completed an archiving project, having scanned nearly 50 years of *JNM* issues, which will be available online before the end of this year. This will improve access to articles that are often still used and cited. Public relations efforts introduce published research to a wider audience every month. The journal is a valuable SNM member benefit, with new supplements being planned. One coming this year will focus on clinical PET/CT and patient care.

Where is the journal going in the future? *JNM* continues to parallel the society's direction: As the profession expands and merges with molecular biology, molecular medicine, and medical imaging, so too will *JNM* continue to follow and report those developments.

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