

(Continued from page 28N)

on nuclear safety that all countries with operating nuclear power plants are required to submit.

For the 2012 special meeting, participant countries are being urged to address 9 topics in their reports: nuclear power plant design against external events, off-

site response to emergency situations (e.g., station blackout), emergency management and preparedness following worst case accident scenarios, safety consideration for operation of multiunits at the same nuclear power plant site, cooling of spent fuel storage in severe accident scenarios, training of nuclear

power plant operators for severe accident scenarios, radiological monitoring following nuclear power plant accident involving radiological release, public protection emergency actions, and communications in emergency situations.

*International Atomic Energy Agency*

---



---

## FROM THE LITERATURE

---



---

*Each month the editor of Newslines 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

---

#### Multimodality Monitoring of Breast Ca Therapy

In an article e-published on April 1 ahead of print in *Breast Cancer Research and Treatment*, Jacobs et al. from the Johns Hopkins University School of Medicine (Baltimore, MD) reported on a study determining the utility of advanced MR and PET/CT imaging in identifying radiologic biomarkers for treatment response in pa-

tients receiving preoperative systemic therapy (PST) for locally advanced breast cancer. The study included 6 women who were enrolled both in a study correlating PET/CT imaging and response to chemotherapy and in a study of advanced MR imaging parameters and response to chemotherapy. Each received 4 cycles of docetaxel at 14 d intervals, with or without 4 additional cycles of doxorubicin and cyclophosphamide. Patients underwent diagnostic breast MR,  $^{23}\text{Na}$  MR, and  $^{18}\text{F}$ -FDG PET/CT evaluation of breast lesions before and within 7 d after administration of the first cycle. Core biopsy samples were taken at baseline and after the first drug cycle for correlation of histopathologic and radiologic markers. Five patients experienced a pathologic partial response, and 1 experienced a pathologic non-response. Total tissue sodium concentration decreased by 21% in responders but increased in the nonresponder. Responders also saw a greater reduction (38%) in standardized uptake values on PET than did the nonresponder. MR imaging volumes decreased after the first drug cycle by 42% in responders and 35% in the nonresponder. The proliferation index declined in responders but increased in the nonresponder. The authors concluded that these results “demonstrate the feasibility of using multimodality proton,  $^{23}\text{Na}$  MRI, and PET/CT metrics as radiological biomarkers for monitoring response to PST in patients with operable breast cancer.”

*Breast Cancer Research and Treatment*

#### Multimodal Prostate SLN Guidance

van der Poel et al. from The Netherlands Cancer Institute–Antoni van Leeuwenhoek Hospital (Amsterdam) reported on March 30 ahead of print in *European Urology* on a pilot study designed to demonstrate combined preoperative, intraoperative, and postoperative sentinel lymph node (SLN) imaging in laparoscopic lymph node dissection using a multimodal tracer. The study included 11 men scheduled for robot-assisted laparoscopic prostatectomy with an increased risk of nodal metastasis. Before surgery, each participant underwent injection with a radioactive and fluorescent tracer, indocyanine green (ICG)- $^{99\text{m}}\text{Tc}$ -NanoColl, into the prostate. This was followed by lymphoscintigraphy and SPECT/CT imaging of pelvic nodes to preoperatively identify the location of sentinel lymph nodes. A fluorescence laparoscope, optimized for detection in the near infrared range, was used during surgery to visualize nodes identified on SPECT/CT. The authors found that SPECT/CT successfully identified SLNs and that fluorescence imaging enhanced intraoperative identification of these nodes, especially in areas with high radioactive background noise (such as the injection site). Histopathologic analysis showed a strong correlation between radioactive and fluorescent tracer content in excised lymph nodes. The authors cautioned that fluorescent tracers cannot take the place of radiotracers

(Continued on page 32N)

(Continued from page 30N)

in this application, because of severe tissue attenuation in the fluorescent signal. The authors concluded that “Initial data indicate that multimodal ICG-<sup>99m</sup>Tc-NanoColl, in combination with a fluorescence laparoscope, can be used to facilitate and optimize dissection of sentinel lymph nodes during robot-assisted laparoscopic prostatectomy procedures.”

*European Urology*

## Imaging Activated Platelets in Carotid Arteries

In an article e-published on March 30 in the online journal *PLoS One*, Heidt et al. from the University of Freiburg (Germany) described construction of a radiolabeled single-chain antibody targeting the ligand-induced binding site (LIBS)-epitope of activated platelets to selectively depict platelet activation and wall-adherent nonocclusive thrombosis in a mouse model using in vitro and ex vivo autoradiography as well as small animal SPECT/CT. LIBS and a control antibody were labeled with <sup>111</sup>In (<sup>111</sup>In-LIBS and <sup>111</sup>In-control, respectively). In vitro autoradiographic studies showed that activated platelets incubated with <sup>111</sup>In-LIBS had significantly higher ligand uptake than <sup>111</sup>In-controls. In a mouse model of carotid artery thrombosis, ligand uptake of <sup>111</sup>In-LIBS was significantly higher in the presence of small thrombi than in noninjured tissue, as confirmed by ex vivo studies. In vivo studies also confirmed these findings, with <sup>111</sup>In-LIBS SPECT/CT of the injured carotid artery showing a significant increase in the target-to-background ratio compared to that with <sup>111</sup>In-control SPECT/CT. With SPECT/CT, wall-adherent activated platelets in carotid arteries were easily depicted in vivo. The authors concluded that these “results encourage further studies elucidating the role of activated platelets in plaque pathology and atherosclerosis and might be of interest for

further developments towards clinical application.”

*PLoS One*

## Imaging Sialylated Tumor Cell Glycans

Neves et al. from the Cambridge Research Institute (UK) reported on April 14 ahead of print in the *FASEB Journal* on a bioorthogonal metabolic labeling strategy to detect tumor cell surface glycans (involved in cell-cell interactions and migration) using in vivo fluorescence and radionuclide imaging of sialylated glycans in a mouse model. The authors described the injection of a metabolic precursor for biosynthesis of 5-azidoneuraminic acid. Azidosialic acid-labeled cell surface glycans were then reacted with a biotinylated phosphine injected intraperitoneally. NeutrAvidin, labeled with either a far-red fluorophore or <sup>111</sup>In, was injected, and 24 h later mice underwent optical and SPECT imaging. Results showed a significant increase in tumor-to-tissue contrast correlated with the labeling. The authors concluded that “the technique has the potential to translate to the clinic, where, given the prognostic relevance of altered sialic acid expression in cancer, it could be used to monitor disease progression.”

*FASEB Journal*

## THERAPY

### Radioimmunotherapy + Chemoimmunotherapy

In an article e-published on April 5 ahead of print in *Molecular Cancer Therapeutics*, Sharkey et al. from the Garden State Cancer Center (Belleville, NJ) reported on a study designed to determine whether chemoimmunotherapy with antibody-drug conjugates can be combined with radioimmunotherapy (RIT) to enhance efficacy in a mouse model of solid tumors without increases in toxicity. The study was conducted in mice bearing human pancreatic cancer xenografts. The mice were treated with a single dose of <sup>90</sup>Y-labeled antimucin antibody alone or

in combination with an anti-Trop-2-SN-38 conjugate, administered twice weekly over 4 wk. The regimen was found to control tumor progression and cure established xenografts significantly better than the RIT or chemotherapeutic approaches separately and to accomplish this without enhanced toxicity. The authors conducted additional studies to determine optimal timing of chemotherapy and RIT and optimal antigen targeting with specific agents. They concluded that “these studies show the feasibility of combining chemoimmunotherapy with antibody-drug conjugates and RIT for improved efficacy without increased toxicity.”

*Molecular Cancer Therapeutics*

## DIAGNOSIS

### Small Animal PET/MR

In the April 21 issue of *Physics in Medicine and Biology* (2011;56:2459–2480), Maramraju et al. from Stony Brook University (NY) described the development of instrumentation for and initial experiences with a 9.4-T MR unit capable of simultaneous PET/MR small animal imaging. The PET detector in the unit included 12 detector blocks, each a 4 × 8 array of lutetium oxyorthosilicate crystals coupled to matching nonmagnetic avalanche photodiode arrays. These detector blocks formed a 38-mm inner diameter ring with an 18-mm axial extent. MR coils fit inside the PET device, operating in transceiver mode. The PET insert was integrated with a Bruker 9.4-T 210-mm diameter MR scanner. The article described the acquisition of simultaneous PET/MR images of phantoms, in vivo rat brain, and cardiac-gated mouse studies using <sup>11</sup>C-raclopride and <sup>18</sup>F-FDG. Resulting images indicated that gradient echo and high-duty-cycle spin echo radio frequency pulses resulted in a 7% and a 28% loss, respectively, in PET counts. Calibration of the activity concentration of PET data during MR pulsing was reproducible within <6%.

(Continued on page 34N)

(Continued from page 32N)

The authors concluded that these “initial results demonstrate the feasibility of performing simultaneous PET and MRI studies in adult rats and mice using the same PET insert in a small-bore 9.4-T MRI.”

*Physics in Medicine and Biology*

### Intraoperative Handheld PET Probe

González et al. from the Memorial Sloan-Kettering Cancer Center (New York, NY) reported on April 22 ahead of print in *Surgical Endoscopy* on the development of a handheld PET probe to evaluate suspicious nodes intraoperatively and correlate these findings with those seen on preoperative PET. The study was conducted in rats inoculated with a lymphogenic mesothelioma tumor line. Rats were imaged weekly with PET until suspicious lymph nodes were identified. The PET probe was then used to guide dissections and select high-risk nodes on the basis of tracer uptake. From a total of 10 rats, 52 nodes were harvested, 8 of which were suspicious on preoperative PET. Using a tracer-to-background ratio of 2.5, the probe localized all suspicious nodes previously seen on PET scans. Both  $\gamma$  and  $\beta$  probes showed excellent areas under the curve in receiver operating characteristic analysis. Both probes had an area under the curve of 0.95 for localizing suspicious nodes on PET. The area under the curve for detecting malignancy for the  $\gamma$  probe was 0.90 and for the  $\beta$  probe was 0.97. The authors concluded that this “novel tool may be used synergistically with the PET scan examination to maximize intraoperative nodal selection and sampling.”

*Surgical Endoscopy*

### Predictive Postablation $^{131}\text{I}$ Imaging

Ciappuccini, from the Centre François Baclesse (Caen, France) reported on April 6 ahead of print in the *European Journal of Endocrinology* on a study designed to assess the ability of postablation  $^{131}\text{I}$  scintigraphy (a whole-body scan [WBS] and neck and

thorax SPECT/CT) and previously known relevant factors to predict persistent or recurrent differentiated thyroid cancer. The study included 170 patients, all of whom underwent postablation  $^{131}\text{I}$  WBS and neck and thorax SPECT/CT. Other factors assessed were stimulated serum thyroglobulin (Tg) and Tg antibody levels, TNM status, age, sex, macroscopic lymph node involvement, and disease-free survival over an average 29-mo follow-up. Persistent or recurrent disease was seen in 32 (19%) patients over this period. Only positive WBS with SPECT/CT was related to an increased risk of persistent or recurrent disease. In patients without Tg antibodies, however, both positive WBS with SPECT/CT and serum Tg levels 58 ng/mL were correlated with an increased risk. The authors concluded that in “patients with differentiated thyroid cancer, the cross analysis of postablation  $^{131}\text{I}$  scintigraphy with neck and thorax SPECT/CT and of stimulated serum Tg level enables early assessment of the risk of persistent or recurrent disease.”

*European Journal of Endocrinology*

### Manganese Exposure in Welders

The connection between manganese exposure and the development of parkinsonism has been explored in several studies that have focused on environmental and/or occupational risk, particularly among miners and welders. Criswell et al. from the Washington University School of Medicine (St. Louis, MO) reported in the April 12 issue of *Neurology* (2011; 76:1296–1301) on a study using  $^{18}\text{F}$ -fluoro-1-DOPA ( $^{18}\text{F}$ -FDOPA) PET to determine whether occupational exposure to manganese fumes is associated with damage to nigrostriatal neurons in asymptomatic welders. The study included 60 individuals: 20 active asymptomatic welders exposed to manganese fumes, 20 subjects with idiopathic Parkinson disease, and 20 normal controls. All participants underwent  $^{18}\text{F}$ -FDOPA PET and were

examined by a movement disorders specialist. Regional specific uptake ( $K_i$ ) of the tracer was analyzed for each participant. Results showed that caudate  $K_i$ s were lower in asymptomatic welders than in control participants. The regional pattern of uptake in welders was most affected in the caudate, anterior putamen, and posterior putamen (in descending order). This uptake pattern was reversed in participants with idiopathic Parkinson disease. The reduced  $^{18}\text{F}$ -FDOPA uptake in welders with manganese exposure indicated dysfunction in the nigrostriatal dopamine system. The authors concluded that “the caudate  $K_i$  reduction in welders may represent an early (asymptomatic) marker of manganese neurotoxicity and appears to be distinct from the pattern of dysfunction found in symptomatic idiopathic Parkinson disease.”

*Neurology*

### $^{13}\text{N}$ - $\text{NH}_3$ PET and Brain Lesions

In an article e-published on April 19 ahead of print in the *Journal of Neuro-oncology*, Xiangsong et al. from Sun Yat-sen University (Guangzhou, China) reported on the utility of  $^{13}\text{N}$ - $\text{NH}_3$  PET in characterizing brain lesions that are hypometabolic on  $^{18}\text{F}$ -FDG PET. The study included 18 patients with brain lesions in whom  $^{13}\text{N}$ - $\text{NH}_3$  PET imaging (14 for initial diagnosis and 4 for detection of astrocytoma recurrence) was performed after hypometabolic findings on  $^{18}\text{F}$ -FDG PET. Final diagnoses, as established by histopathology or clinical follow-up, included 10 gliomas, 1 metastatic tumor, 1 dysembryoplastic neuroepithelial tumor, and 6 nonneoplastic lesions (including 3 patients with radiation necrosis, 2 with encephalitic foci, and 1 with an ischemic lesion). Seven of the 12 brain tumors showed increased  $^{13}\text{N}$ - $\text{NH}_3$  uptake despite hypometabolism on  $^{18}\text{F}$ -FDG PET. The 3 low-grade gliomas, 1 metastatic tumor, and 1 dysembryoplastic neuroepithelial tumor showed decreased  $^{13}\text{N}$ - $\text{NH}_3$  uptake. The mean uptake of  $^{13}\text{N}$ - $\text{NH}_3$  in tumors was significantly

higher than that of  $^{18}\text{F}$ -FDG. All non-neoplastic lesions showed decreased  $^{13}\text{N}$ - $\text{NH}_3$  uptake. The authors concluded that “the preliminary results of this study suggest that  $^{13}\text{N}$ - $\text{NH}_3$  PET may be helpful to detect and differentiate brain tumors which show hypometabolism on  $^{18}\text{F}$ -FDG PET from nonneoplastic lesions with high specificity, especially for cerebral astrocytomas, but the sensitivity is relatively limited.”

*Journal of Neuro-oncology*

## Sex Differences in Cardiac Hypertrophy

Foryst-Ludwig et al. from the Charité Universitätsmedizin (Berlin, Germany) reported ahead of print on April 8 in the *American Journal of Physiology. Heart and Circulatory Physiology* on a study exploring the reasons for sex-specific differences in exercise-induced cardiac hypertrophy. The authors looked at whether previously reported sex-dependent differences in cardiac hypertrophic response during exercise are associated with cardiac energy substrate availability/utilization. The study was conducted in female and male mice challenged daily with active treadmill running for 1.5 h/d for 4 wk. Mice underwent cardiac and metabolic analyses, includ-

ing echocardiography, small-animal PET imaging, periexercise indirect calorimetry, analysis of adipose tissue lipolysis, and cardiac gene expression. Female mice showed greater cardiac hypertrophic responses to exercise than male mice, as measured by echocardiography. This was found to be associated with increased plasma free fatty acid levels and augmented adipose tissue lipolysis in females after training. The respiratory quotient during exercise was found to be significantly lower in females. Cardiac genes involved in fatty acid uptake/oxidation were increased in females. The authors concluded that, collectively, these data demonstrate that “sex differences in exercise-induced cardiac hypertrophy are associated with changes in cardiac substrate availability and utilization.”

*American Journal of Physiology Heart and Circulatory Physiology*

## 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. In an article e-published in the April 1 issue of *Current Pharmaceutical Biotechnology* (2011;12:508–527), Sekar et al. from Stanford University (Palo Alto, CA) provided an overview of “Imaging cellular receptors in breast cancer.” Coles and Li, from the Emory University School of Medicine (Atlanta, GA) reviewed “Functional neuroimaging in the examination of effects of prenatal alcohol exposure” on April 12 ahead of print in the *Neuropsychology Review*. A meta-regression analysis of “Stem cell tracking in human trials” was presented by McColgan et al. from Imperial College Hospitals (London, UK) on April 8 ahead of print in *Stem Cell Reviews*. Santra and Malhotra, from the University of Central Florida (Orlando) reported on April 8 ahead of print in *Wiley Interdisciplinary Reviews: Nanomedicine and Nanobiotechnology* on “Fluorescent nanoparticle probes for imaging of cancer.” In a 3-part series published in the April issue of *Health Physics* (2011;100:359–416), Watson and Strom, from the Pacific Northwest National Laboratory (Richland, WA), reported on “Radiation doses to members of the U.S. population from ubiquitous radionuclides in the body.”

(Continued from page 20N)

provide some guidance and will help our young nuclear medicine physician trainees transition to the next step in their careers.

## REFERENCES

1. Harolds JA, Novelline RA, Guiberteau MJ, Metter D, Oates ME. Commentary: jobs and new initiatives in nuclear medicine education. *J Nucl Med*. 2011;52[2]:17N.
2. Cuocolo A, Milcinski M, Bischof Delaloye A. Syllabus for postgraduate specialisation in nuclear medicine: 2006/07 update. *Eur J Nucl Med Mol Imaging*. 2010;37:430–433.
3. Pons F. Questions about the common core curriculum. *Rev Esp Med Nucl*. 2010;29:99.
4. American Board of Medical Specialties. certiFACTS Web site. FAQs. Available at: [www.certifacts.org/faq.html#4](http://www.certifacts.org/faq.html#4). Accessed on February 28, 2011.
5. European Association of Nuclear Medicine. Certificate of fellowship of the European Board of Nuclear Medicine 2011 information. Available at: [http://uems.eanm.org/committees/fellowship\\_examination/ebnm\\_fellow\\_certificate.php?navId=401#can](http://uems.eanm.org/committees/fellowship_examination/ebnm_fellow_certificate.php?navId=401#can). Accessed on February 28, 2011.
6. Society of Nuclear Medicine. Young Professional Committee Newsletter. 2009. Available at: [http://interactive.snm.org/docs/YPC\\_Newsletter\\_060209.pdf](http://interactive.snm.org/docs/YPC_Newsletter_060209.pdf). Accessed on February 28, 2011.
7. Schelbert HR. Editorial. Comments and Perspectives. *J Nucl Med*. 2004;45:1273.
8. Ell PJ. Editorial. *Eur J Nucl Med*. 2000;27:1735–1736.

Syed Mahmood, MD

Jacobi Medical Center & North Central Bronx Hospital  
Bronx, NY

Sofía Rodríguez Martínez de Llano, MD, PhD  
Centro Oncológico de Galicia  
La Coruña, Spain