"necessary expertise, extensive membership, and can ensure transparency," Amano called the IAEA the best venue for follow-up on the Fukushima accident.

*International Atomic Energy Agency*

## NIH mHealth Summer Program

The National Institutes of Health (NIH) announced on February 28 the creation of the first NIH mHealth (or mobile health) Summer Institute. Scheduled for the summer of 2011, this week-long workshop will bring together leaders in mobile health technologies, behavioral science researchers, federal health officials, and members of the medical community to provide early career investigators with an opportunity to learn about mHealth research. The Office of Behavioral and Social Sciences Research, part of NIH, partnered with Qualcomm, a developer of wireless technologies, to cosponsor the course. The mHealth Summer Institute will provide an overview of the engineering, behavioral science, and clinical aspects of wireless research and will facilitate interaction between participants and experts from across the mHealth spectrum. The institute will cover the current state of the science in mobile technology and engineering, behavior change theory and clinical applications and will highlight the intersection of these areas for health-related research. Interdisciplinary teams of participants will develop potential mHealth research projects. Registration for the program filled within days of the announcement. More information is available at: http://obssr.od.nih.gov/training_and_education/mhealth/index.aspx.

*National Institutes of Health*

# 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. 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

## Imaging Cellular Events in Angiogenesis

In an article e-published on March 8 ahead of print in *Stem Cells and Development*, Li and Stuhlmann from the Weill Medical College of Cornell University (New York, NY) reported on in vitro imaging of angiogenesis using embryonic stem (ES) cell–derived endothelial cells. The authors described the development of green fluorescence protein–expressing endothelial cells from a transgenic cell line. Aggregated ES cell–endothelial cells were embedded into a 3D collagen gel matrix, with subsequent migration and coalescence into a capillary network. Time-lapse microscope imaging showed migration of the cells, proliferation, and anastomosis to other capillary vessels, a process "reminiscent" of angiogenesis. These and additional studies led the authors to conclude that this ES model and imaging technique represent a high-resolution dynamic video-image system for visualizing the cellular events underlying angiogenic cascades." They also noted that the model can serve as "an image screening tool for the identification of pro-angiogenic and anti-angiogenic molecules."

*Stem Cells and Development*

## Molecular Targeting in Hepatocellular Carcinoma

Li et al. from Nanjing University (China) reported in the March 3 issue of the *Journal of Experimental and Clinical Cancer Research* (2011;30:25) on a study evaluating the targeting effects of antisperm protein 17 monoclonal antibody (anti-Sp17) on cancer in vivo and assessing its utility as a reagent for optical molecular imaging. Human sperm protein 17 is expressed in some malignant tumors. After verification of expression in a hepatocellular carcinoma cell line and corresponding tumor xenograft specimens, a near-infrared fluorescence dye was used to label anti-Sp17 for imaging. The labeled agent was injected into tumor-bearing mice through the caudal vein, and tumor targeting was evaluated by near-infrared imaging. Good targeting capability was demonstrated, as was tumor accumulation lasting for at least 7 d. The authors concluded that "anti-Sp17 antibody targeted and accumulated in Sp17 positive tumors in vivo, which demonstrated its capability of serving as a diagnostic reagent."

*Journal of Experimental and Clinical Cancer Research*

## Multimodal Imaging of Nanovaccine Carriers

In an article e-published on March 16 ahead of print in *Molecular Pharmaceutics*, Cruz et al. from the University Medical Centre (Nijmegen, The Netherlands) reported on a strategy to enhance immune response by targeting

delivery of nanovaccine particles to dendritic cells and to image that delivery using both MR and optical techniques. Carriers included both superparamagnetic iron oxide particles (SPIO) and fluorescently labeled antigens in a single particle. The authors coated the nanovaccine particles with antibodies recognizing a dendritic cell–specific receptor. The fluorescent label allowed for rapid analysis and quantification of uptake of targeted nanovaccine particles by dendritic cells compared to other blood cells. This imaging also showed that part of the encapsulated antigen reached the lysosomal compartment of dendritic cells within 24 h. The incorporated SPIO allowed tracking of the nanovaccine particles at the subcellular cell organel level using transmission electron microscopy, which tracked the particles to the endolysosomal compartments, where part of the SPIO was released by 24 h. Additional MR imaging studies confirmed efficient labeling and the ability to track particle migration. The authors concluded that "incorporation of 2 imaging agents within a single carrier allows tracking of targeted nanovaccines on a subcellular, cellular, and possibly organism level, thereby facilitating rational design of in vivo targeted vaccination strategies."

*Molecular Pharmaceutics*

## THERAPY

### Combined Melanoma Imaging/Diagnosis

In an article e-published on March 21 ahead of print in the *Journal of Medicinal Chemistry*, Maisonial et al. from the Université d'Auvergne, INSERM, and the Centre Jean Perrin (all in Clermont-Ferrand, France) described a range of new multimodal fluorinated and iodinated radiotracers for SPECT/PET imaging and targeted radionuclide therapy of melanoma. The 14 tracers studied provide both early imaging with $^{123}$I, $^{124}$I, and $^{18}$F and systemic treatment with $^{131}$I. $^{125}$I-labeled versions of each tracer were evaluated with serial scintigraphy in a mouse model of melanoma. Biodistribution studies indicated that the tracer called $^{123}$I-56 had the highest specific tumor uptake and most promising kinetic profile. $^{18}$F-56 was synthesized for evaluation studies and provided excellent in vivo PET imaging of melanoma in the mouse models. When $^{131}$I-56 was administered to mice bearing subcutaneous melanoma tumors, a significant decrease in the rate of tumor growth was noted. The authors concluded that "these data support further development of 56 for PET imaging ($^{18}$F, $^{124}$I) and targeted radionuclide therapy ($^{131}$I) of melanoma using a single chemical structure."

*Journal of Medicinal Chemistry*

### Posttherapy PET and Cervical Cancer

Siva et al. from the Peter MacCallum Cancer Centre (Melbourne, Australia) reported on March 1 ahead of print in *Cancer* on posttherapy PET and prognostic stratification and monitoring after curative intent chemotherapy for cervical cancer. The study included 105 patients, each of whom underwent $^{18}$F-FDG PET imaging between 3 and 12 mo after treatment. Results on imaging were categorized as complete metabolic response, partial metabolic response, or progressive metabolic disease. Patients were followed for an average of 3 y to assess outcomes. At the time of posttherapy PET imaging, 73 (70%) patients were determined to have complete metabolic response, 10 (9%) had partial metabolic responses, and 22 (21%) had progressive metabolic disease. At 3-y follow-up, overall survival was 77%. Survival was 95% for those in the complete metabolic response group at posttherapy imaging. Complete metabolic response and pretreatment tumor volumes were found to be strong predictors for overall survival, and the number of involved lymph nodes as well as the International Federation of Gynecology and Obstetrics stage were found to be predictive of relapse-free survival. Women with complete metabolic response had a distant failure rate 36-fold less than those with partial metabolic response, and only 1 patient with a complete metabolic response relapsed without symptoms and was detected through physical examination. The authors concluded that "the presence of a complete metabolic response at posttherapy FDG-PET is a powerful predictor for survival after chemoradiation" and that "the very low rate of recurrence in patients with a complete metabolic response justifies a conservative follow-up approach for these patients, because relapse is usually symptomatic and not detected by routine clinical review."

*Cancer*

## DIAGNOSIS

### Inflammation and CFR

In an article in the March 15 issue of the *Journal of the American College of Cardiology* (2011;57:1271–1279), Vaccarino et al. from the Emory University Schools of Public Health and Medicine (Atlanta, GA) reported on a study examining the relationship between inflammation and coronary microvascular function in asymptomatic twins using PET assessment of coronary flow reserve (CFR).The study included 268 asymptomatic male monozygotic and dizygotic twins. Laboratory assessments were made of several plasma biomarkers of inflammation and endothelial cell activation, and each participant also underwent $^{13}$N-ammonia PET at rest and after adenosine stress for blood flow quantitation and calculation of CFR. Summed stress scores for visible perfusion defects were calculated.

All except 1 biomarker were higher in twins whose CFRs were lower than their brothers. This association persisted even after adjusting for summed stress score and coronary artery disease risk factors. The authors concluded that "even in asymptomatic subjects, a decrease in coronary microvascular function is accompanied by a systemic inflammatory response, independent of coronary artery disease risk factors"

and noted that these results "highlight the importance of coronary microvascular function in the early phases of coronary artery disease."

*Journal of the American College of Cardiology*

## Imaging Hypoxia in Atherosclerotic Plaques

Silvola et al. from the University of Turku (Finland) and the University of Kuopio (Finland) reported on March 3 ahead of print in *Arteriosclerosis, Thrombosis, and Vascular Biology* on an investigation of the ability of the tracer $^{18}$F-EF5 to detect hypoxia in atherosclerotic plaques in mice. The study included 2 types of atherosclerotic mice with different genetic backgrounds (low-density lipoprotein receptor$^{-/-}$ apolipoprotein B and insulin-like growth factor II/low-density lipoprotein receptor$^{-/-}$apolipoprotein B). After dietary induction of plaque development, both types of mice and control mice were injected with $^{18}$F-EF5. Mice were killed for biodistribution studies, autoradiography, histology, and immunohistochemistry. The researchers found that uptake of the tracer was significantly higher in aortas with large atherosclerotic plaques than in the aortas of controls. Autoradiography showed an average 2.0-fold higher tracer uptake in atherosclerotic plaques than in adjacent normal vessel walls. Histochemical studies verified hypoxia in plaques. The tracer was found to have relatively slow clearance, with blood radioactivity remaining relatively high up to 180 min after injection. Despite the slow clearance, the authors concluded that "plaque hypoxia is a potential target for identifying high-risk plaques noninvasively."

*Arteriosclerosis, Thrombosis, and Vascular Biology*

## Microcirculatory Dysfunction after Angioplasty

In an article e-published on March 7 ahead of print in the *International Journal of Cardiology*, Amaya et al. from the University of Fukui (Japan) reported on a $^{13}$N-ammonia PET study identifying relationships between the degree of resolution of the ST-segment elevation (ST segment resolution; STR) and the extent of microcirculatory dysfunction in infarct-related areas in patients with ST-segment elevation myocardial infarction (STEMI). The study included 33 patients with STEMI, each of whom had undergone successful reperfusion. Each participant underwent electrocardiography before and 100 min after reperfusion to calculate STR and $^{13}$N-ammonia PET 2 wk later to assess myocardial flow reserve. The summed defect score of $^{99m}$Tc-tetrofosmin myocardial perfusion imaging was used as an index of the severity of myocardial infarction. Changes in the left ventricular end diastolic volume indices were also calculated as markers of postinfarct left ventricular remodeling. The STR was found to be significantly correlated with the myocardial flow reserve in infarct-related areas. The summed defect score and the baseline ST-segment elevation were also correlated, but no correlation was found between the summed defect score and the STR. A significant inverse correlation was found between the STR and changes in the left ventricular end diastolic volume indices. The authors concluded that "these data indicate that STR after successful reperfusion in STEMI is closely related to the extent of microcirculatory disturbance; in other words, incomplete STR may be a marker of persistent microcirculatory dysfunction after reperfusion therapy."

*International Journal of Cardiology*

## Neurochemistry and Response to Dependence Treatment

Martinez et al. from Columbia University College of Physicians and Surgeons (New York, NY) reported on March 15 ahead of print in the *American Journal of Psychiatry* on the use of PET to elucidate relationships between neurochemistry and response to treatment in cocaine dependence. The researchers hypothesized that dopamine signaling in the limbic striatum could be correlated with response to a behavioral treatment approach based on positive reinforcement. The study included 25 cocaine-dependent adults and 24 controls matched for cigarette smoking, gender, and ethnicity. Cocaine-dependent individuals underwent: (1) initial screening; (2) 14 d of abstinence; (3) $^{11}$C-raclopride PET imaging before and after administration of a stimulant to measure striatal dopamine receptor binding and presynaptic dopamine release; (4) 12 wk of behavioral treatment; (5) repeat PET imaging; and (6) an additional 12 wk of treatment. The controls underwent repeated PET imaging at the same 12-wk interval. All participants also underwent MR imaging to identify regions of interest. Response to treatment was measured by clinical and behavioral metrics and correlated with the imaging results. Both striatal dopamine receptor binding and presynaptic dopamine release were found to be lower in the cocaine-dependent individuals who did not respond to treatment than in those who experienced a positive treatment response. The authors concluded that in addition to providing insight into the neurochemistry of treatment response, "these data suggest that the combination of behavioral treatment with methods that increase striatal dopamine signaling might serve as a therapeutic strategy for cocaine dependence."

*American Journal of Psychiatry*

## PET Imaging in Down Syndrome Adults

Landt and a consortium of researchers from the University Cambridge (UK), the Cambridgeshire and Peterborough National Health Service Foundation Trust (UK), and INSERM (Paris, France) reported on March 14 ahead of print in the *Archives of Neurology* on a study designed to investigate the safety, acceptability, and feasibility of $^{11}$C-Pittsburgh compound B ($^{11}$C-PiB) PET imaging to measure cerebral β-amyloid

in adults with Down syndrome and to explore whether the technique differentiates between individuals with and without Alzheimer disease (AD). The study included 9 adults with Down syndrome (age range, 25–64 y; 5 of these individuals also had been diagnosed with AD) and 14 healthy volunteers without Down syndrome (age range, 33–69 y). All participants underwent $^{11}$C-PiB PET and MR imaging, and $^{11}$C-PiB binding in regions of interest associated with AD was assessed. No adverse events were noted in the imaging process. When compared with the group without Down syndrome, only Down syndrome participants who were >45 y old had significant $^{11}$C-PiB binding in regions of interest associated with AD, regardless of whether they had clinical evidence of dementia. The authors concluded that "dynamic $^{11}$C-PiB PET can be used successfully to measure cerebral β-amyloid deposition in Down syndrome" and that a clinical diagnosis of AD and age appear to be predictors of $^{11}$C-PiB binding in regions of interest in these individuals.

*Archives of Neurology*

## Animal PET of Behavior and Neurochemistry

In an article e-published on March 13 ahead of print in *Nature Methods*, Schulz et al. from the Brookhaven National Laboratory (Upton, NY) described a method for simultaneous assessment of rodent behavior and neurochemistry using small animal PET. The process overcomes the barrier previously posed by the need to anesthetize animals for PET imaging. The "rat conscious animal PET," or RatCAP, is a miniature portable PET scanner mounted onto the subject animal's head, combined with a mobility system that allows freedom of movement, a set of specific radiotracer administration techniques, and methods for quantifying behavior and correlating the 2 resulting datasets. The authors concluded that simultaneously acquiring PET and behavioral data "provides a multidimensional tool for studying the functions of different brain regions and their molecular constituents."

*Nature Methods*

## Age, Sex, and 5-HT$_4$ Receptors

Madsen et al. from the Copenhagen University Hospital Rigshospitalet (Denmark) reported on March 2 ahead of print in the *Journal of Cerebral Blood Flow and Metabolism* on a study investigating sex and age effects on 5-HT$_4$ receptor–binding potentials in striatum, the limbic system, and neocortex. 5-HT$_4$ receptor activation is reported to influence cognitive function, affective symptoms, and the development of Alzheimer's disease (AD). The study included 30 healthy individuals (14 men, 16 women; mean age, 44 y; range, 20–86 y) who underwent $^{11}$C-SB207145 PET brain imaging. Women were found to have 13% lower 5-HT$_4$ receptor binding in the limbic system, which the authors suggested "supports a role for 5-HT$_4$ receptors in the sex-specific differences in emotional control and might contribute to the higher prevalence of affective diseases and AD in women." Binding was found, however, to decline among both men and women only by about 1% per decade, which the authors noted contrasts with other subtypes of receptors, which generally decrease with aging.

*Journal of Cerebral Blood Flow and Metabolism*

## 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 March. In an article e-published on March 9 ahead of print in the *Proceedings of the National Academy of Sciences of the USA,* Volkow et al. from the National Institute on Drug Abuse (Bethesda, MD) provided an overview on "Addiction: beyond dopamine reward circuitry" as part of the Quantification of Behavior Sackler Colloquium. Wang et al. from the Case Western Reserve University (Cleveland OH) reviewed "Design, synthesis, and evaluation of coumarin-based molecular probes for imaging of myelination" on March 10, ahead of print in the *Journal of Medicinal Chemistry.* On March 7, ahead of print in *Urologic Oncology*, Krause et al. from the Technische Universität München (Germany) summarized the current state of research on "Imaging of prostate cancer with PET/CT and radioactively labeled choline derivatives." Welling et al. from the Leiden University Medical Center (The Netherlands) reviewed techniques for assessing "In vivo biodistribution of stem cells using molecular nuclear medicine imaging" in the online prepublication of material scheduled for the June issue of the *Journal of Cellular Physiology.* In an article in the April issue of *Seminars in Radiation Oncology* (2011;21:101–110), Bentzen and Gregoire offered an overview of and commentary on the literature on "Molecular imaging-based dose painting: a novel paradigm for radiation therapy prescription."