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 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

EPO and Gray Matter Loss in Schizophrenia

In an article e-published on May 18 ahead of print in *Molecular Psychiatry*, Wüstenberg et al. from Georg-August University (Göttingen, Germany) reported on a study describing imaging assessment of weekly, high doses of hematopoietic growth factor erythropoietin (EPO) in individuals with schizophrenia. The researchers used voxel-based morphometry from MR imaging of 32 individuals, some on weekly high doses of EPO and some receiving placebos, to assess progressive cortical gray matter loss, an expected neurodegenerative process in schizophrenia. They found that after as short a time as 3 mo EPO administration halted progressive atrophy in brain areas usually affected in schizophrenia (hippocampus, amygdala, nucleus accumbens, and neocortex areas). They concluded that "a neuroprotective strategy is effective against common pathophysiological features of schizophrenic patients" and encouraged follow-up studies to optimize EPO treatment dose and duration. The authors cautioned, however, that schizophrenia is an etiologically heterogeneous and complex disease and that any treatments that might target neurodegeneration alone would not provide a complete therapeutic solution.

Molecular Psychiatry

Imaging Cellular Dynamics in HIV-1

In the May 10 issue of *Retrovirology* (2010;7:41), Miley et al. from McGill University (Montreal, Canada) reported on the use of bi- and trimolecular fluorescence complementation imaging to visualize live cell interactions between the HIV-1 Gag protein and the cellular RNA-binding protein Staufen1. The researchers identified where virus–host interactions between Gag and Staufen1 and Gag and IMP1 occur in cells and detected these interactions not only in the cytoplasm but in cholesterol-enriched GM1-containing lipid raft plasma membrane domains. The trimolecular fluorescence experiments showed that Gag and Staufen1 actively recruited protein partners when tethered to mRNA. The article is part of continued work by the group in developing detailed molecular imaging of both the intracellular trafficking of virus components and of virus–host protein complexes that can enhance understanding of HIV-1 pathogenesis.

Retrovirology

Switchable Fluorescent Probes

Mizusawa et al. from Kyoto University (Japan) reported on May 12 ahead of print in the *Journal of the American Chemical Society* on a study of "switchable" fluorescent probes, which induce changes in fluorescence properties only when the nanoparticles reach an intended target protein. The authors described a novel mechanism for generating protein-specific "turn on" fluorescent probes using an amphiphilic, self-assembling compound consisting of a fluorophore and a protein ligand. In aqueous solutions, the probe formed self-assembled aggregates and displayed almost no fluorescence, but emitted bright fluorescence in contact with the target protein. Using this technique, the authors developed 3 types of fluorescent probes specific to carbonic anhydrase, avidin, and trypsin. They concluded that "the present supramolecular approach may facilitate the development of new protein-specific switchable fluorescent probes that are useful for a wide range of applications, such as diagnosis and molecular imaging."

Journal of the American Chemical Society

PET and Intestinal Insulin Absorption

In an article e-published on May 10 ahead of print in the *Journal of Controlled Release,* Kamei et al. from Hoshi University (Tokyo, Japan) reported on the use of PET imaging to quantitatively analyze intestinal insulin absorption and subsequent distribution and to evaluate the effects of coadministration of cell-penetrating peptides. The study was conducted in rats. An unlabeled insulin solution containing tracer insulin (^{68}Ga-DOTA-insulin) was administered with or without cell-penetrating peptides into a rat ileal closed loop. Imaging results indicated that the cell-penetrating peptides significantly increased tracer insulin levels in the liver, kidney, and bloodstream. The increase in hepatic and renal tracer distribution with each peptide coadministration correlated with intestinal absorption, suggesting that increased accumulation of insulin in the liver and kidney induced by coadministration of cell-penetrating peptides was associated with increased intestinal absorption of insulin. The authors concluded that the ability of PET to enable quantitative analysis of the distribution of intestinally absorbed insulin in several organs "is

likely to be useful for developing effective drug delivery systems targeted to specific organs."

Journal of Controlled Release

DIAGNOSIS

Preoperative PET and PTMCs

In an article e-published on April 28 ahead of print in the *Journal of Clinical Endocrinology and Metabolism*, Yun and colleagues from the Yonsei University College of Internal Medicine (Seoul, Korea) and Brigham and Women's Hospital/Harvard Medical School (Boston, MA) reported on visually discernible ^{18}F-FDG uptake in papillary thyroid microcarcinoma (PTMC) as a potential risk factor that might be useful in management decisions. The retrospective study included 87 patients (17 men, 70 women; mean age, 51.2 y, range, 29–74 y) with unifocal PTMCs who underwent ^{18}F-FDG PET/CT before total thyroidectomy and central lymph node dissection. Variables considered in analysis were gender, age, tumor size, and tracer uptake in tumors. Histopathology confirmed extrathyroidal extension in 44 patients (51%) and central lymph node metastasis in 27 patients (31%). PET/CT demonstrated visually discernible tracer uptake in 46 PTMCs (53%), and this uptake was the only variable that correlated significantly with both extrathyroidal extension and central lymph node metastasis. The authors concluded that these results suggest that "visual FDG positivity in PTMCs is a potential risk factor that can be useful for preoperative risk stratification" and that additional studies should assess the long-term benefit and cost effectiveness of preoperative PET/CT.

Journal of Clinical Endocrinology and Metabolism

SPECT Sensitivity in Hyperparathyroidism

Swanson and colleagues from St. Paul's Hospital and the University of British Columbia (Vancouver, Canada) reported in the May issue of the *American Journal of Surgery* (2010;199:614–620) on a study designed to evaluate the influence of patient and adenoma characteristics on ^{99m}Tc-methoxy isobutyl isonitrile (MIBI) scan performance in primary hyperparathyroidism. The retrospective study included records of 161 patients undergoing parathyroidectomy for primary hyperparathyroidism. The true-positive rate for ^{99m}Tc-MIBI SPECT in these patients was 56%. Adenomas of sizes 1.9–3.5 cm were more likely to have true-positive scans than were smaller (0.3–1.8 cm) adenomas. Scanning was more sensitive when preoperative ionized calcium levels were 1.49–1.72 mmol/L than when they were at lower levels (1.27–1.48 mmol/L). No single medication was shown to significantly affect true-positive rates. A decrease in sensitivity was observed for larger adenomas in patients on ≥1 medication. The authors concluded that in primary hyperparathyroidism, "^{99m}Tc-MIBI scan positivity is most related to adenoma size and preoperative ionized calcium level."

American Journal of Surgery

Brown Fat and Body Temperature

In an article e-published on May 6 ahead of print in *Obesity (Silver Spring)*, Yoneshiro et al. from Tenshi College (Sapporo, Japan) reported on a study that evaluated the relationship between brown adipose tissue (BAT), whole-body energy expenditure, and thermogenesis. The study included 13 healthy men (ages, 20–28, with similar body fat content and body mass index) who underwent ^{18}F-FDG PET imaging after 2-h of cold exposure (19°C) and intermittent leg contact with ice blocks. Six of the participants showed marked tracer uptake in adipose tissue of the supraclavicular and paraspinal regions (BAT-positive group). The other 7 showed no detectable uptake (BAT-negative group). Tests under warm conditions indicated that energy expenditures (estimated by indirect calorimetry) were similar in the 2 groups (1,434 ± 246 kcal/d). After the cold exposure, however, energy expenditures increased significantly in the BAT-positive group (by 410 ± 293 kcal/d) and only slightly in the BAT-negative group (by 42 ± 114 kcal/d). After cold exposure, skin temperature in the supraclavicular area close to BAT deposits dropped by 0.14°C in the BAT-positive group and even more markedly (by 0.60°C) in the BAT-negative group. The authors concluded that these results "suggest that BAT is involved in cold-induced increases in whole-body energy expenditure, and, thereby, the control of body temperature and adiposity in adult humans."

Obesity (Silver Spring)

PET in Pediatric Neurosurgery

Two articles by Pirotte et al. from the Université Libre de Bruxelles (Belgium) appearing in the May issue of the *Journal of Neurosurgery. Pediatrics* (2010;5:479–485 and 486–499) reported on the use of PET imaging in presurgical workup and during surgery in children with brain tumors. In the first article, the authors evaluated the impact of PET data on clinical management of newly diagnosed, incidental brain lesions. The study included 55 children in whom MR imaging proved to be limited in assessing the tumor, its evolving nature, and/or the malignant potential of the lesion. Thirteen children underwent ^{18}F-FDG PET imaging, and 42 underwent L-methyl-^{11}C-methionine (^{11}C-MET) PET. The PET and MR images were coregistered in image fusion navigation planning. Seventeen children had increased PET tracer uptake and underwent surgery, at which tumor diagnosis was confirmed in all cases (i.e., no false-positive PET findings). The remaining 28 children, with little or no tracer uptake, were treated conservatively, although surgically accessible lesions were resected in 16. Of these 16, histology showed no malignancy nor evolving tumor tissue but characterized 9 indolent tumors and 7 nontumoral lesions. The authors concluded that these results "confirmed the high sensitivity and specificity of PET to detect tumor as well as malignant tissue" and that in incidental brain lesions "PET findings enabled the authors to make more appropriate decisions regarding treatment than those made on MR imaging findings alone." As a result, the risk of surgically treating a nontumoral lesion was reduced, as was the risk of managing a malignant tumor too conservatively.

In the second article, the authors evaluated the effect of PET information

on surgery. The study included 85 children referred for newly diagnosed brain lesions, 35 in whom MR imaging was unable to identify accurate biopsy targets and 50 in whom MR was unable to delineate tumors for optimal resection. All patients underwent either ^{18}F-FDG PET or ^{11}C-MET PET imaging. The PET data were found to influence surgical decisions or procedures in all cases and with a wide range of benefits. The authors concluded that "PET has a significant impact on the surgical decisions and procedures for managing pediatric brain tumors" and called for further studies to identify effects on outcomes.

Journal of Neurosurgery. Pediatrics

Verifying Remission in RA

Tishler and colleagues from the Assaf Harofe Medical Center (Zrifin, Israel) reported on April 28 ahead of print in *Clinical and Experimental Rheumatology* on a study comparing clinical data with results from ^{99m}Tc-nanocolloid joint scintigraphy in patients with rheumatoid arthritis (RA) who were considered to be in remission. The study included 40 patients (29 women, 11 men; mean age, 60.8 ± 13.5 y, range, 22–86 y) with RA who were determined to be in clinical remission according to conventional clinical criteria. The group had a mean disease duration of 13.4 ± 7.7 y (range, 2–23 y) and mean duration of remission of 22.2 ± 5.2 mo (range, 11–36 mo). Each patient underwent ^{99m}Tc-nanocolloid spot scanning of the skeleton, with SPECT/CT of the wrists and hands. Scanning was scored as positive when at least 1 hand joint showed tracer uptake. Scintigraphy results were negative in 14 (35%) and positive in 26 (65%) patients. Of the 14 negative patients, 1 was seronegative; of the 26 positive patients, 24 were seropositive. No correlation was identified between type of treatment used, time that elapsed in remission, or laboratory parameters and the scintigraphic results. The authors concluded that these results suggest that "the clinical criteria used for remission in RA are not consistent with the actual inflammatory activity in the joints," particularly in the subgroup of seropositive patients.

Clinical and Experimental Rheumatology

REVIEWS

Review articles provide an important way to stay up to date on the latest topics and approaches and provide valuable summaries of pertinent literature. The Newsline editor recommends several reviews accessioned into the PubMed database in late April and May. These include "Criteria for evaluation of disease extent by ^{123}I-metaiodobenzylguanidine scans in neuroblastoma: a report for the International Neuroblastoma Risk Group (INRG) Task Force" by a consortium of nuclear medicine physicians and oncologists, published in the April 27 issue of the *British Journal of Cancer* (2010;102:1319). After an extensive review of the literature and consensus development, the group concluded that "metaiodobenzylguanidine [mIBG] scans are the most sensitive and specific method of staging and response evaluation in neuroblastoma, particularly when used with a semiquantitative scoring method" and that "use of the optimal techniques for mIBG in staging and response, including a semiquantitative score, is essential for evaluation of the efficacy of new therapy." Other noteworthy reviews included "Nanoparticles as a potential cause of pleural and interstitial lung disease" by Bonner from North Carolina State University (Raleigh, NC), published in the *Proceedings of the American Thoracic Society* (2010;7:138–141); "Advances in cardiovascular molecular imaging for tracking stem cell therapy" by Ransohoff and Wu from the Stanford University School of Medicine (CA), e-published on May 10 ahead of print in *Thrombosis and Haemostasis*; "In vivo molecular imaging using nanomaterials: general in vivo characteristics of nano-sized reagents and applications for cancer diagnosis" by Rosenblume et al. from the National Cancer Institute (Bethesda, MD), e-published on May 10 ahead of print in *Molecular Membrane Biology*; and "Viral nanoparticles as platforms for next-generation therapeutics and imaging devices" by Steinmetz from the Scripps Research Institute (La Jolla, CA), e-published on April 27 ahead of print in *Nanomedicine: Nanotechnology, Biology, and Medicine.*

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nuclear medicine is a small but growing field, and internal dosimetry expertise is becoming increasingly important for these specialists. The consensus among the lecturers—also reflected in the participants' evaluation forms—was that the school successfully addressed the need to master internal dosimetry techniques. Many presentations will be available at www.ictp.it, and recorded lectures will be available on the IAEA Web resource for health professionals, to be launched in September 2010 (humanhealth.iaea.org).

Leaving the event proved to be challenging, with virtually all departure flights canceled because of volcanic ash. Many assisted in this situation, but in particular Suzie Radosic went much beyond her responsibilities as course secretary in assuring that all participants and lecturers were looked after until they could leave Trieste.

Each year, the Dosimetry and Medical Radiation Physics section of the IAEA organizes 1 or 2 joint IAEA–ICTP advanced schools on medical physics topics. Proposed for 2011 are a school on advanced radiotherapy techniques, with emphasis on imaging and treatment planning, and an advanced course on mammography. If prioritized, it may be possible to repeat this internal dosimetry course in the 2012–2013 time period.

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