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.

MOLECULAR IMAGING

Protease Imaging of Human Atheromata

In an article e-published on January 7 ahead of print in *Arteriosclerosis, Thrombosis, and Vascular Biology*, Kim et al. from Dongguk University Ilsan Hospital (Goyang, Korea) and colleagues from the University of Texas M.D. Anderson Cancer Center (Houston), the Asan Medical Center (Seoul, Korea), and the Korea Institute of Science and Technology (Seoul) reported on a study correlating protease imaging of human atheromata with conventional imaging and with clinical and histopathologic data. The study included 52 patients who underwent carotid endarterectomy (41 atheromata) or carotid stenting (15 captured emboli) and were imaged with cathepsin-B or matrix metalloproteinase-2/matrix metalloproteinase-9 molecular optical probes. The protease-related fluorescent signal in carotid atheromata and emboli was closely correlated with pathophysiologic alterations of plaque inflammation and statin-mediated therapeutic effects on plaque inflammation. Inflammation-related fluorescent signal was noted in plaques, and plaques found to be unstable at histopathology also had high cathepsin-B–related fluorescent signal. Although patterns of cathepsin-B imaging differentiated between symptomatic and asymptomatic plaque groups, the degree of carotid stenosis or ultrasound echodensity was only weakly correlated with the inflammatory proteolytic enzyme–related signal. This suggested to the authors that "molecular imaging yields complementary new information not available to conventional imaging." They concluded that "These results could justify and facilitate clinical trials to evaluate the use of protease-sensing molecular optical imaging in human atherosclerosis patients."

Arteriosclerosis, Thrombosis, and Vascular Biology

Firefly Luciferase Imaging of Apoptosis

Hickson et al. from Abbot Laboratories (Abbott Park, IL) reported on January 8 ahead of print in *Cell Death and Differentiation* on the use of Z-DEVD-aminoluciferin, a modified luciferase substrate, for noninvasive in vivo molecular imaging of apoptosis. The authors described the in vivo characterization of the substrate and the process by which it generates luminescent signal in apoptotic cells. Initial mouse studies in 2 cancer models (SKOV3-luc and MDA-MB-231-luc-LN) included administration of Z-DEVD-aminoluciferin at 24, 48, and 72 h after treatment with docetaxel. Images were acquired at each injection time and several timepoints thereafter. Significantly more signal was detected at 24, 48, and 72 h in animals after docetaxel than in a nontreated control group. Immunohistochemistry confirmed caspase-3 activation at each time point in treated animals. Although significant differences in the 2 groups were detected with the luciferase substrate as early as 24 h after treatment, it was not until 4–5 d later that caliper measurements could detect any difference. The authors concluded that "these data show that in vivo imaging of apoptosis using Z-DEVD-aminoluciferin could provide a sensitive and rapid method for early detection of drug efficacy, which could potentially be used by numerous therapeutic programs."

Cell Death and Differentiation

^{11}C-PIB PET and Course of Dementia

Burack et al. from the University of Rochester (NY) reported in the January 5 issue of *Neurology* (2010;74:77–84) on a study designed to assess the specificity of in vivo amyloid imaging with ^{11}C-Pittsburgh Compound B (^{11}C-PIB) PET in Parkinson disease–associated dementia (PDD) by correlating imaging findings with post mortem pathology. The study included the records of 3 individuals with PDD who underwent ^{11}C-PIB PET within 15 mo of death. Images were compared with detailed neuropathologic examination results from autopsy and pathologic studies. All 3 decedents were found to have abundant cortical Lewy bodies and were categorized as low-probability for Alzheimer disease. Two of the individuals' in vivo PET images showed elevated cortical uptake of tracer. These individuals had abundant diffuse Aβ plaques, with only sparse neuritic plaques and intermediate neurofibrillary tangle pathology. The individual without elevated cortical uptake on PET had rare diffuse plaques, no neuritic plaques, and low neurofibrillary tangle burden. The authors concluded that these results suggest that ^{11}C-PIB PET is specific for fibrillar Aβ molecular pathology but not for pathologic diagnosis of comorbid

Alzheimer disease in individuals with PDD. They added that "The ability to specifically identify fibrillar Aβ amyloid in the setting of α-synucleinopathy makes ^{11}C-PIB PET a valuable tool for prospectively evaluating how the presence of Aβ amyloid influences the clinical course of dementia in patients with Lewy body disorders."

Neurology

THERAPY

^{211}At α-RIT and Renal Function

Bäck et al. from the University of Gothenburg (Sweden) reported in the December issue of *Cancer Biotherapy and Radiopharmaceuticals* (2009;24:649–658) on a small animal study of the effects of high-linear energy transfer (LET) radiation on the kidneys after α-radioimmunotherapy (α-RIT) with ^{211}At-labeled monoclonal antibodies (mAbs). Renal toxicity studies were conducted in non-tumor-bearing mice and mice with subcutaneous xenografts of OVCAR-3, the human ovarian cancer cell line, by assessing the glomerular filtration rate (GFR). Astatinated MX35-F(ab')$_2$ mAbs were injected intravenously at levels close to the therapeutic dose limits (0.4, 0.8, or 1.2 MBq) in 1–3 fractions, with mean absorbed doses to the kidneys of 1.5–15 Gy. Serial GFR measurements using plasma clearance of ^{51}Cr-ethylenediaminetetraacetic acid were acquired for up to 67 wk after the first RIT injection. GFR was found to be affected in a dose-dependent manner during the period 8–30 wk after RIT. Reduction in GFR in treated animals progressed over time, suggesting that radiation effects on the kidneys are evident late. These effects, however, were only minor to moderate, despite the fact that levels were close to the dose limit for severe myelotoxitiy. The authors concluded that "these results suggest that a mean absorbed dose to the kidneys of approximately 10 Gy is acceptable and that the kidneys would not be the primary dose-limiting organ in systemic α-RIT when using ^{211}At-MX35-F(ab')$_2$."

Cancer Biotherapy and Radiopharmaceuticals

DIAGNOSIS

PET/CT and Primary Choroidal Melanoma

In the January issue of *Retina* (2010;30:146–151), McCannel et al. from the University of California, Los Angeles, reported on a study to evaluate the utility of PET/CT in primary choroidal melanoma with chromosome 3 loss. The study included the records of 37 patients with choroidal melanoma and known chromosome 3 status who underwent whole-body PET/CT imaging. In 13 (35%) patients, primary choroidal melanomas were found to have a loss of chromosome 3, and 7 of these 13 (54%) melanomas were positive for metabolic activity on PET/CT imaging. None of the 24 melanomas without chromosome 3 loss showed metabolic activity on PET/CT. Positive PET/CT and chromosome 3 loss were positively correlated, and positive PET/CT results were 54% sensitive and 100% specific for loss of chromosome 3. The authors concluded from these and other results that "Positive metabolic activity of choroidal melanoma identified by PET/CT imaging was statistically significantly associated with chromosome 3 loss and larger tumor size."

Retina

High-Dose ^{131}Iodine in Treated Papillary Thyroid Cancer

In an article e-published on January 15 ahead of print in the *Journal of Clinical Endocrinology and Metabolism*, Kim et al. from the University of Ulsan College of Medicine (Seoul) and Ulsan University Hospital (Ulsan, Korea) reported on the utility of empirical radioiodine therapy in patients with elevated stimulated serum thyroglobulin (Tg) levels but negative ultrasound and ^{18}F-FDG PET studies after initial therapy for papillary thyroid cancer. The study included 39 patients at 1 y after initial treatment who had elevated serum Tg, negative whole-body diagnostic scans, and negative ultrasound and PET findings. Fourteen patients received empirical radioiodine therapy, and 25 patients were followed without therapy. Five patients (36%) in the treatment group and 8 (32%) in the control group had recurrence during the median 37-mo follow-up period. None of the 14 patients in the treatment group showed iodine uptake on posttreatment whole-body scans. Changes in serum-stimulated Tg concentrations were not different in the 2 groups. The authors concluded that empirical radioiodine therapy and posttreatment whole-body scans were "not useful diagnostically or therapeutically in patients with positive serum stimulated Tg if such patients had negative ultrasonography and negative ^{18}F-FDG PET findings after initial treatment of papillary thyroid cancer."

Journal of Clinical Endocrinology and Metabolism

Multi-Imaging PET/CT in MTC

Marzola et al. from the Santa Maria della Misericordia Hospital (Rovigo, Italy) reported on January 23 ahead of print in the *European Journal of Surgical Oncology* on a study designed to compare multitracer imaging PET using ^{18}F-DOPA and ^{18}F-FDG with conventional imaging in recurrent medullary thyroid carcinoma (MTC). The study included 18 postthyroidectomy MTC patients who were found during follow-up to have elevated and rapidly increasing calcitonin levels. Conventional imaging indicated metastatic deposits in 9 patients, who were referred for ^{18}F-DOPA and ^{18}F-FDG PET/CT. At least 1 PET-positive lesion in each of these patients was confirmed for recurrent MTC by histopathology. Foci of abnormal uptake were observed in 15

patients with ^{18}F-DOPA and 11 with ^{18}F-FDG. Eight of these patients had the same numbers of positive lesions with each tracer. Maximum standard uptake values were higher for ^{18}F-FDG PET than ^{18}F-DOPA. Calcitonin was higher in PET-positive than PET-negative patients, with no significant differences in results between the 2 tracers. The authors concluded that in MTC patients with rapidly increasing calcitonin levels during follow-up, "^{18}F-DOPA has a good sensitivity and a complementary role with ^{18}F-FDG PET/CT in detecting metastatic deposits." In the experience of these researchers, the sensitivity of the combined tracer approach was greater than that of conventional imaging.

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program also has the potential to supply more than 50% of the U.S. demand for ^{99}Mo. "U.S. government support of this work is highly beneficial in helping the nation establish a more secure domestic source of medical isotopes without using HEU," said S. Robert Cochran, Babcock & Wilcox president. In January 2009, an agreement was announced combining Covidien's expertise in radiopharmaceutical production and global regulatory approvals with Babcock & Wilcox's patented liquid phase nuclear technology.

SNM leaders congratulated the 2 companies and praised the NNSA for this proactive stance on domestic radioisotope supply. "We are pleased by this development," said Michael M. Graham, PhD, MD, president of SNM. "The ongoing worldwide isotope shortage has long been a critical problem affecting the U.S. We are encouraged by the progress that has been made to date by the NNSA on this issue.

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for delivery to brain with molecular Trojan horses; Nora Volkow, MD, NIH/National Institute on Drug Abuse: PET and functional MR imaging of addiction; Michael Phelps, PhD, UCLA: Translating metabolic assays into molecular imaging diagnostics; Edward Neuwelt, MD, Oregon Health and Science University: Strategies to overcome the blood–brain barrier for treatment of brain tumors; and Jeffrey R. Petrella, MD, Duke University Medical Center: Imaging genetics of brain longevity and mental wellness.

Please consider joining us for this 2-d agenda addressing breakthrough advances and developments in this exciting field. You may wish to also pass this information along to colleagues who might be interested in attending this symposium. For more information on the program and the meeting, see www.snm.org/brain2010.

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