

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 recently 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 both 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.

DIAGNOSIS

PET and Moderate Alcohol Consumption

In an article e-published on February 14 ahead of print in *Psychiatry Research*, Volkow and colleagues from the National Institute on Drug Abuse (Bethesda, MD), National Institute on Alcohol Abuse and Alcoholism (Bethesda), and Brookhaven National Laboratory (Upton, NY) reported on the use of PET in assessing the effects of alcohol on patterns of brain activity and cerebral differentiation. The study included 20 healthy controls who underwent ^{18}F -FDG PET for assessment of brain glucose metabolism at baseline and during alcohol intoxication (0.75 g/kg). Changes in brain metabolic homogeneity were assessed using the coefficient of variation, which served as a metric for cerebral differentiation. Alcohol was found to decrease the coefficient of variation in the brain, a re-

sult independent of decreases in overall glucose metabolism. The study showed marked disruption in brain activity during alcohol intoxication, including decreases in global and regional brain differentiation, loss of right-versus-left brain metabolic laterality, and a shift in the predominance of activity from cortical to limbic brain regions—disruptions in functional organization that occurred at even moderate levels of consumption. The authors concluded that the widespread nature of the changes induced by a moderate dose of alcohol is “likely to contribute to the marked disruption of alcohol on behavior, mood, cognition, and motor activity.”

Psychiatry Research

Mapping Selective Neuronal Loss

Giffard et al. from the INSERM at the University of Caen (France) and from the University of Cambridge (UK) reported on January 31 ahead of print in *Stroke* on an in vivo study of the feasibility of PET and MR imaging for mapping selective neuronal loss after focal ischemia and reperfusion. The study included 5 young adult baboons that underwent ^{15}O PET imaging to assess cerebral blood flow, cerebral oxygen consumption, and oxygen extraction fraction mapping at baseline and during and after a 20-h period of temporary middle cerebral artery occlusion. These images documented moderately severe acute ischemia followed by reperfusion. Thirty d after occlusion, each animal underwent ^{11}C -flumazenil (^{11}C -FMZ) PET to assess selective neuronal loss and also underwent structural MR-based infarct mapping. Brains were then perfused and fixed. The researchers performed a voxel-level analysis to determine reduced and specific tracer binding in noninfarcted cortical middle cerebral artery areas. Visual inspection of the PET images showed reduced late ^{11}C -FMZ uptake in the affected cortical territory, extending well beyond the infarct. The voxel analysis

showed mild but significantly reduced tracer uptake and specific binding. Histopathology indicated only mild neuronal changes in or near the affected areas. The findings suggested moderate but definite late ^{11}C -FMZ binding reductions in noninfarcted cortical areas in the baboons, results that were consistent with previous studies in rat models and in humans. The authors noted that in the baboons these reductions were acutely characterized by moderate ischemia followed by reperfusion, consistent with neuronal damage from ischemic or reperfusion injury in salvaged at-risk tissue. The fact that only mild histopathologic changes accompanied these alterations in binding suggested the action of more subtle processes, such as isolated dendrite or synapse loss. They concluded that additional studies should focus on whether these changes affect clinical outcomes and on neuroprotective measures that might be developed to target specific neuronal loss.

Stroke

PET Metrics vs RECIST in Sarcoma Response

Evilevitch et al. from the University of Freiburg (Germany) and from the University of California at Los Angeles reported in the February 1 issue of *Clinical Cancer Research* (2008;14:715–720) on a study designed to determine whether ^{18}F -FDG PET imaging in patients with soft-tissue sarcomas facilitates a more accurate evaluation of histopathologic response to neoadjuvant therapy than the more conventional metric of change in tumor size as classified by the Response Evaluation Criteria in Solid Tumors (RECIST). The study included 42 patients with resectable, biopsy-proven, high-grade soft-tissue sarcoma who underwent PET/CT before and after neoadjuvant therapy. Relative changes in tumor ^{18}F -FDG uptake and size from the first to the second scan were calculated, as was the accuracy of PET

in the assessment of histopathologic response (defined as $\geq 95\%$ tumor necrosis). Reductions in tumor ^{18}F -FDG uptake were significantly greater in the 8 histopathologic responders than in the 34 nonresponders, but no significant differences were found for tumor size in these 2 groups. When a 60% decrease in tumor tracer uptake was designated as a threshold, the resulting sensitivity and specificity for PET assessment of histologic response were 100% and 71%, respectively. Comparative figures for RECIST were 25% and 100%, respectively. Given these results indicating that quantitative ^{18}F -FDG PET is significantly more accurate than size-based criteria at assessing histopathologic response to neoadjuvant therapy, the authors concluded that PET should be “considered as a modality to monitor treatment response in patients with high-grade soft-tissue sarcoma.”

Clinical Cancer Research

Imaging $\alpha_v\beta_3$ Integrin Expression After MI

In an article e-published on February 6 ahead of print in *Cardiovascular Research*, Higuchi et al. from the Technischen Universität München (Germany) reported on a new PET approach for imaging of $\alpha_v\beta_3$ integrin expression after myocardial infarction in a rat model. The study included male Wister rats that underwent 20 min of left coronary artery occlusion followed by reperfusion. Both autoradiography and PET imaging with an ^{18}F -labeled $\alpha_v\beta_3$ antagonist (^{18}F -galacto-RGD) were used to assess myocardial tracer uptake at different times after reperfusion. No significant focal myocardial uptake was seen immediately after and at 1 d after reperfusion. Focal accumulation was seen in the infarct area beginning at 3 d, peaking between 1 and 3 wk, and decreasing (but not to baseline levels) at 6 mo after reperfusion. Pretreatment with $\alpha_v\beta_3$ integrin antagonist c(-RGDfV-) significantly decreased tracer uptake, indicating the specificity of tracer uptake seen in the study. Immunohistochem-

ical analysis confirmed that the course of focal tracer uptake over time paralleled that of vascular density. The authors concluded that these results suggest that ^{18}F -galacto-RGD PET is “promising for the monitoring of myocardial repair processes.”

Cardiovascular Research

^{123}I -MIBG Cardiac Scintigraphy in MS

Lorberboym et al. from the Wolfson Medical Center (Holon, Israel) reported on February 20 ahead of print in the *Journal of Neurology* on a study assessing the ability of ^{123}I -MIBG cardiac scintigraphy to evaluate direct cardiac sympathetic denervation in patients with multiple sclerosis (MS) and comparing these results with routine electrophysiologic measures of autonomic dysfunction. The study included 10 individuals with MS (7 with relapsing–remitting and 3 with secondary progressive MS) and 7 age- and sex-matched controls. Neurologic deficit and disability stages of participants with MS were rated according to the Kurtzke Expanded Disability Status Scale, and autonomic tests included the relapsing–remitting interval, Valsalva ratio, and standup test. All participants underwent planar and ^{123}I -MIBG cardiac SPECT. A pathologic tracer cardiac washout rate was found in the 3 MS patients with secondary progressive disease; the remaining patients with MS had normal washout rates. No correlation was found between scans and individual parasympathetic autonomic test results. The authors concluded that these results suggest that ^{123}I -MIBG may detect direct disturbances of the sympathetic cardiac function in patients with MS, providing information incremental to parasympathetic dysfunction tests. The ability to determine the coexistence of autonomic dysfunction (especially cardiac sympathetic involvement in patients with the secondary progressive type of MS) “may aid in evaluation of disease severity and cardiac function follow-up.”

Journal of Neurology

PET-MR Fusion in Thyroid Cancer

Seiboth et al. from the Washington Hospital Center (DC) reported in the February issue of *Thyroid* (2008;18:103–111) on a study assessing the incremental clinical utility of fused PET and MR imaging of the neck in detection of recurrent or persistent thyroid cancer. The study included 34 patients treated for thyroid cancer who had previously undergone total or near-total thyroidectomy and laboratory studies, as well as neck sonography, ^{131}I scans, CT imaging, and/or MR imaging. Twenty-nine of these patients had received at least 1 ^{131}I treatment. For this study, each patient underwent both PET and MR imaging, and the resulting images were digitally fused. Images were reviewed separately and after fusion. Endocrinologists were asked to make 2 blind assessments: 1 based on all information in charts before PET and MR imaging and 1 supported by the added data. The endocrinologists categorized the PET-MR fusion results as: providing new information that altered the initial treatment plan (46%), providing new information that confirmed the initial treatment plan (36%), or providing no additional information (18%). The authors concluded that, given the overwhelming majority of patients in whom the combined structural and functional data from fused PET and MR provided additional information, that PET-MR fusion can be a “useful tool in surgical planning, radioactive iodine therapy decisions, and determining the level of follow-up necessary for each patient.”

Thyroid

Targeting Receptor-Mediated Signal Transduction

Bhattacharjee et al. from the National Institutes of Health (Bethesda, MD) reported on February 15 ahead of print in *Psychopharmacology* (Berlin) on animal studies with PET designed to image apomorphine stimulation of brain arachidonic acid

signaling via D₂-like receptors. The study included unanesthetized adult rats that were administered apomorphine or saline (control), with or without pretreatment with raclopride, a D₂/D₃ receptor antagonist. ¹⁴C-labeled arachidonic acid was injected, and the incorporation coefficient, k* (brain radioactivity/integrated plasma radioactivity), for arachidonic acid was determined in 62 brain regions in each rat. Apomorphine was found to significantly elevate k* in 26 brain regions, including the frontal cortex, motor and somatosensory cortices, caudate-putamen, thalamic nuclei, and nucleus accumbens. Raclopride alone did not change baseline values of k*, but raclopride pretreatment prevented apomorphine-induced increases in k*. The authors concluded that because apomorphine, a mixed D₁/D₂ receptor agonist, increased the arachidonic acid signal by activating only D₂-like receptors in brain circuits containing regions with high D₂-like receptor densities, then apomorphine might be used with PET “to image brain D₂-like receptor-mediated arachidonic acid signaling in humans in health and disease.”

Psychopharmacology (Berlin)

Scintigraphy, Diabetes, and Nicotinamide Therapy

Chianelli et al. from the Regina Apostolorum Hospital (Albano Laziale, Italy) reported in the February issue of *Diabetes/Metabolism Research and Reviews* (2008;24:115–122) on the utility of ^{99m}Tc-interleukin-2 pancreatic scintigraphy to identify pancreatic inflammation at the time of diagnosis of type 1 diabetes and after 1 y of combined therapy. The study included 42 individuals newly diagnosed with type 1 diabetes who underwent imaging before and 1 y after treatment with nicotinamide in addition to intensive insulin therapy. Metabolic status was monitored every 3 mo over the course of the study period. The study also included 16 healthy individuals as controls. Scintigraphy at diagnosis identified significant pancreatic accumulation in 31% of the patients. At the

time of diagnosis, neither positive nor negative pancreatic accumulation of interleukin-2 scintigraphy was correlated with metabolic or immunologic findings. However, patients who had positive pancreatic accumulation at diagnosis showed higher C-peptide values at 3 mo and lower insulin requirements at 1 y, compared with patients with negative uptake at diagnosis. Patients who had positive ^{99m}Tc-interleukin-2 scintigraphy and were treated with nicotinamide at 25 mg/kg showed a significant reduction in insulin requirement at 1 y after diagnosis. At that time point, all patients originally positive for pancreatic inflammation showed a significant decrease in pancreatic uptake of ^{99m}Tc-interleukin-2. The authors concluded that not only is this imaging technique of potential use in identifying pancreatic inflammation but also ^{99m}Tc-interleukin-2 scintigraphy “may be of potential use for assessing the autoimmune phenomena in endocrine pancreas.”

Diabetes/Metabolism Research and Reviews

PET in Staging SCLC

Vinjamuri et al. from the West Virginia University Hospital (Morgantown) reported in the January issue of *Clinical Lung Cancer* (2008;9:30–34) on a study to determine the utility of PET in staging of small-cell lung cancer (SCLC). The study included the records of 51 patients who had undergone both CT and PET imaging during initial evaluation of a lung mass. All 51 patients had PET-positive results for malignancy. In 40 (78%) patients, PET staging correlated with that determined on CT. Two (4%) patients had disease that was accurately upstaged by PET, and PET accurately downstaged disease in 6 (12%) patients. PET detected additional sites of disease in 13 of 42 (32%) patients; of these, PET detected supraclavicular nodes in 4 (30%) and bone lesions in 4 (30%) patients. PET detected brain lesions in 5 of 11 (45%) patients in this series. Overall, in 8 of 51 (16%) patients, PET staging would have resulted in a change in disease management; 6 (12%) patients who would not

otherwise have proceeded to additional treatment would have been directed to radiation treatment by PET imaging. The authors concluded that “PET is potentially useful for accurate initial staging of SCLC and can ensure that a patient’s disease is not overstaged by CT scan, which might result in denied potentially curative treatment for limited-stage SCLC.” They added that PET can identify occult adrenal metastases and metastases to supraclavicular lymph nodes that are missed on DC but may not be suitable for assessment of brain lesions.

Clinical Lung Cancer

THERAPY

Single-Dose ²¹¹At RIT in Experimental Breast Tumor

Robinson et al. from the Fox Chase Cancer Center (Philadelphia, PA) reported in the February 1 issue of *Clinical Cancer Research* (2008;14:875–882) on a study to determine whether the C6.5 diabody, a noncovalent anti-HER2 single-chain Friend virus dimer, would be a suitable radioisotope carrier for radioimmunotherapy (RIT) of established tumors using the short-lived α -emitting radioisotope ²¹¹At in a mouse model of human breast cancer tumors. The study was conducted in immunodeficient nude mice bearing established HER2/neu-positive MDA-MB-361/DYT2 tumors treated with *N*-succinimidyl *N*-(4-²¹¹At-astatophenethyl)succinamate (²¹¹At-SAPS) C6.5 diabody. Additional groups of mice were treated with 2 other ²¹¹At-SAPS-labeled diabodies. The authors found that a single 20- μ Ci intravenous injection of the ²¹¹At-SAPS C6.5 diabody led to a 30-d delay in tumor growth and that a 45- μ Ci injection led to a 57-d delay in tumor growth (resulting in 60% of mice tumor free after 1 y). Results with the other diabodies labeled with ²¹¹At in the study suggested the specificity of the therapeutic effects achieved with the ²¹¹At-SAPS C6.5 diabody. The authors concluded that these findings “indicate that diabody molecules can be effective

agents for targeted RIT of solid tumors using powerful, short-lived α -emitting radioisotopes.”

Clinical Cancer Research

MAB RIT of Human Synovial Sarcoma

In an article in the February issue of *Cancer Science* (2008;99:452–440), Fukukawa et al. from the University of Tokyo (Japan) built on previous work with Frizzled homolog 10 (FZD10), a promising therapeutic target for synovial sarcomas, by reporting on the development of a murine monoclonal antibody (MAb) with specific binding activity against native FZD10 product expressed in synovial sarcoma cell lines. Immunohistochemical analyses conducted by the team indicated an absence or negligible levels of FZD10 in normal human organs. Both radioisotope and fluorescent imaging techniques were used to confirm specific binding of MAb 92-13 injected into mice carrying synovial sarcoma xenografts. MAb 92-13 was effectively internalized into the synovial sarcoma cells after binding to FZD10 on the cell surface. A single intravenous injection of ^{90}Y -labeled MAb 92-13 significantly suppressed tumor growth in mice with no accompanying severe toxicity. Median times to tumor progression were 58 d for mice treated with ^{90}Y -MAb 92-13 and 9 d for untreated mice and mice treated with nonlabeled control antibodies. The authors concluded that these findings suggest that “MAb 92-13 could be utilized as a novel treatment modality for synovial sarcoma and other FZD10-positive tumors.”

Cancer Science

PET and NHL Response to Fractionated RIT

In an article e-published on February 11 ahead of print in *Haematologica*, Bodet-Milin et al. from University Hospital (Nantes, France) reported on a study designed to evaluate the efficacy of ^{18}F -FDG PET imaging in early prediction of response to radioimmunotherapy (RIT) in patients with non-Hodgkin's lymphoma (NHL). The study included 27

patients from an ongoing multicenter, phase I/II trial of fractionated anti-CD22 ^{90}Y -epratuzumab RIT. Each patient underwent ^{18}F -FDG PET imaging and conventional diagnostic assessments and therapy, including chemotherapy at baseline and 6 wk after RIT and every 3 mo until progression. Responses evaluated from conventional methods were classified as complete response, unconfirmed complete response, partial response, stable disease, or progression of disease. PET images were classified as complete response, partial response, or progression of disease. Results were compared with histology and follow-up. A total of 81 paired post-RIT studies were interpreted as complete response (34), partial response (24), and progression of disease (23) on PET and as complete response (12), unconfirmed complete response (31), partial response (15), stable disease (8), and progression of disease (15) with conventional methods. Of the 31 studies evaluated as unconfirmed complete responses with conventional methods, 20 (65%) were classified as complete responses (negative for disease) on PET; the remaining 11 (35%) were positive for disease (7 partial response and 4 progression of disease). Among 22 assessable PET images acquired 6 wk after RIT, mean time to progression was 15.6 mo when PET was evaluated as indicating complete response, compared with 5.4 mo when PET indicated partial response or progression of disease. Sensitivity, specificity, positive and negative predictive values, and accuracy of PET at 6 wk after RIT were 86%, 63%, 80%, 71%, and 77%, respectively. These figures were 36%, 87%, 83%, 44%, and 55% with conventional methods. The authors concluded that ^{18}F -FDG PET may provide a reliable early method to predict response to RIT in patients with NHL.

Haematologica

MOLECULAR IMAGING _____

Tracking Human Embryonic Stem Cells

Li et al. from Stanford University (CA) reported on January 24 ahead of

print in *Stem Cells* on a study comparing reporter gene and iron particle labeling and their respective imaging techniques for tracking the fate of human embryonic stem (hES) cells and differentiated endothelial cells in living animals. hES cells were stably transduced with a lentiviral vector carrying a double-fusion reporter (firefly luciferase and enhanced green fluorescence protein). hES cells and h-ES endothelial cells (hESC-ECs) were colabeled with superparamagnetic iron oxide particles before transplantation into a mouse model, followed by serial bioluminescent and MR imaging. MR signals from both cell populations persisted up to 4 wk. Bioluminescent imaging identified different patterns for the 2 cell populations, with hESC-ECs having significant signals at 2 d and decreasing over the next 4 wk and undifferentiated hESCs increasing significantly over the same period. Histology and immunohistochemistry confirmed teratoma formation after injection of undifferentiated hESCs but not after injection of hESC-ECs. These results led the authors to conclude that both types of labeling carry advantages: “the reporter gene is a better marker for monitoring cell viability, whereas iron particle labeling is a better marker for high-resolution detection of cell location by MR.” They added that transplantation of predifferentiated rather than undifferentiated hES cells would help to avoid teratoma formation.

Stem Cells

Imaging Transglutaminase Activity in Cardiac Healing

Nahrendorf et al. from the Massachusetts General Hospital and the Harvard Medical School (Boston, MA) reported in the February issue of the *European Heart Journal* (2008; 29:445–454) on the use of a novel molecular imaging technique in the assessment of the effects of transglutaminase-modulating therapies on healing and evolution of heart failure. The authors assessed healing in a murine model of myocardial infarction while

monitoring local transglutaminase factor XIII (FXIII) activity with SPECT/CT and serial MR imaging. The study included FXIII-treated mice, dalteparin-treated mice, and saline-treated controls. Local infarct tissue FXIII activity was found on SPECT/CT to be increased by 80% in FXIII-treated mice and decreased by 65% in dalteparin-treated mice. The dalteparin-treated mice were significantly more likely to die from infarct rupture. MR imaging indicated that left ventricular dilation after myocardial infarction was attenuated by FXIII treatment. Additional laboratory analyses showed that FXIII treatment induced a faster resolution of neutrophil response, enhanced macrophage recruitment, increased collagen content, and augmented angiogenesis in the healing infarct. The authors concluded that because FXIII levels in tissues are decreased in patients with insufficient healing, these results in mice suggest that molecular imaging of FXIII might be used to monitor and predict cardiac healing and aid in selection of appropriate management strategies.

European Heart Journal

PET Monitoring of VEGF Expression

In an article e-published on February 4 ahead of print in *Circulation*, Willmann et al. from the Stanford University School of Medicine (CA) and the University of California at San Francisco reported on the use of ^{64}Cu -labeled vascular endothelial growth factor 121 (^{64}Cu -VEGF121) PET for noninvasive spatial, temporal, and quantitative monitoring of the biologic response to hindlimb ischemia in a mouse model with and without treadmill exercise. The study included 58 mice that underwent ligation of the femoral artery and postoperative assessment of tissue ischemia. VEGFR2 expression was quantified by ^{64}Cu -VEGF121 PET imaging at 8, 15, 22, and 29 d after induced ischemia in both exercised and nonexercised mice and correlated with postmortem γ -counting, immunohistochemistry, and microves-

sel density measurements. Perfusion in ischemic hindlimbs was lowest at 9% of contralateral hindlimbs at 1 d after ischemia induction, recovering to 82% at 29 d. ^{64}Cu -VEGF121 uptake was significantly increased in exercised mice and correlated with rises in VEGFR2 levels. Microvessel density was also increased significantly in exercised mice. The authors concluded that ^{64}Cu -VEGF121 PET allows “longitudinal spatial and quantitative monitoring of VEGFR2 expression in murine hindlimb ischemia and indirectly visualizes enhanced angiogenesis stimulated by treadmill exercise training.”

Circulation

Monitoring $\alpha_4\beta_1$ Integrin

Peng et al. from the University of California Davis (UC–Davis) Cancer Center (Sacramento) reported in the February issue of *Molecular Cancer Therapeutics* (2008;7:432–437) on in vivo optical imaging of human lymphoma xenografts using a library-derived peptidomimetic against $\alpha_4\beta_1$ integrin. Exploration of the role of $\alpha_4\beta_1$ integrin, a cell adhesion molecule that has been suggested as a significant element in autoimmune diseases and cancer development, has been challenged by a lack of high-affinity targeting ligands. The UC–Davis group previously reported on the identification of the peptidomimetic, LLP2A, which preferentially binds to activated $\alpha_4\beta_1$ integrin (*Nat Chem Biol.* 2006;2:381–389). In the current study, an LLP2A-Cy5.5 conjugate was injected into the tail veins of mice bearing $\alpha_4\beta_1$ -positive Molt-4 T-leukemia cells. From 1 to 24 h after injection, subcutaneous tumors were clearly visualized on direct optical imaging. Confocal microscopy of excised tumors and organs confirmed LLP2A accumulation in tumor with little or no uptake in normal organs, with the exception of lymph nodes. Although kidney uptake was high over the whole organ, it was negative under confocal microscopy, suggesting that LLP2A bound loosely to the renal tubules. The authors concluded that these results indicate that LLP2A

shows promise for rapid development as an optical imaging probe for in vivo monitoring of activated $\alpha_4\beta_1$ integrin.

Molecular Cancer Therapeutics

Optical Imaging of *Staphylococcus Aureus*

A group of 9 researchers representing academic institutions across the United States and from China reported on February 9 ahead of print in *Bioconjugate Chemistry* on a study of optical imaging of *Staphylococcus aureus* infection in living mice. Leevy et al. described the development of a fluorescent imaging probe composed of a bacterial affinity group conjugated to a near-infrared dye. The affinity group, a synthetic zinc (II) coordination complex, targets the anionic surfaces of bacterial cells. The probe facilitated detection of *S. aureus* (5×10^7 cells) in a mouse model of leg infection using whole-animal near-infrared fluorescence imaging. Infected-to-uninfected leg signal ratios reached approximately 3.9 at 21 h after probe injection, with ex vivo imaging providing a ratio of 8. Immunohistochemistry confirmed that the probe targeted bacterial cells in infected tissue. The authors concluded that these results suggest “that near-infrared molecular probes are amenable to noninvasive optical imaging of localized *S. aureus* infection.”

Bioconjugate Chemistry

Receptor Binding and Predisposition to Alcoholism

Underwood et al. from the New York State Psychiatric Institute (New York, NY) reported on January 30 ahead of print in *Alcohol: Clinical and Experimental Research* on post mortem investigations to determine whether 5-HT_{2A} receptors are altered in the prefrontal cortex in alcoholics. The study included brain tissue collected at autopsy from 25 alcoholics and 19 controls. The diagnosis of DSM-IV alcoholism/abuse was confirmed in the alcoholic group and a determination of positive or negative

family history of alcohol abuse was made for all 44 participants. Quantitative autoradiography was used to measure specific binding to 5-HT_{2A} ³H-ketanserin receptors in the prefrontal cortex. 5-HT_{2A} binding was found to decrease with age across all subjects, and no overall differences

were identified in receptor binding between the alcoholic and control groups. However, those with a family history of alcoholism ($n = 23$), whether alcoholics or controls, had lower 5-HT_{2A} binding throughout the prefrontal cortex than those without ($n = 21$). These and other findings led

the authors to conclude that lower 5-HT_{2A} receptor binding in the prefrontal cortex of individuals with a family history of alcoholism “suggests a genetic predisposition to alcoholism.”

Alcohol: Clinical and Experimental Research

(Continued from page 17N)

technique, including new detector materials and improved lesion detectability in heavier patients. Compensation for respiratory motion is a major concern in PET/CT, because of the different acquisition times for the fast CT and slower PET components of the procedure. Sadek Nehmeh, PhD, from Memorial Sloan–Kettering Cancer Center (New York, NY), described various approaches to dealing with resulting image artifacts. Tinsu Pan, PhD, of the M.D. Anderson Cancer Center (Houston, TX), discussed the effects of advances in CT technology on PET/CT and also described methods to

correct for motion in cardiac and tumor imaging. An emerging technology for molecular imaging is the combination of PET and MR imaging into a single system capable of simultaneous imaging. Ciprian Catana, PhD, of Harvard Medical School (Boston, MA), discussed the challenges in designing these systems and showed promising results in systems for small animal studies and for clinical imaging in humans.

*Peter Herscovitch, MD
National Institutes of Health Clinical Center
Bethesda, MD*