SCIENCE BRIEFS FROM THE SNMMI ANNUAL MEETING

Scientific studies reported at the 2016 SNMMI Annual Meeting in San Diego, CA, June 11–15, covered a broad range of topics in molecular imaging, therapy, instrumentation, and practice. A number of these studies were reported by national and international media. Following is a selection and brief overview of some of these presentations.

Theranostic RIT in CRC

Researchers from Memorial Sloan–Kettering Cancer Center (New York, NY) and the Massachusetts Institute of Technology (Cambridge, MA) reported on continuing small animal studies with curative theranostic pretargeted ^{177}Lu-DOTAT-Bn radioimmunotherapy (PRIT) in GPA33-expressing colorectal cancer. Mice with established SW1222 subcutaneous xenografts underwent treatment with ^{177}Lu-DOTAT-Bn alone, 3 cycles of PRIT with anti-GPA33 PRIT + 55 MBq of ^{177}Lu-DOTA-Bn per cycle, or no treatment. Serial nanoSPECT/CT in the group undergoing PRIT was used for dosimetry calculations. ^{177}Lu-DOTA-Bn PRIT induced complete tumor response in animals autopsied at 21 d after treatment, with tumor-free survival of all other PRIT animals at 100 d. Histopathology at 100 d showed no remarkable findings in kidney, liver, spleen, or bone/marrow in treated animals. Dosimetry calculations from imaging allowed the authors to estimate total ^{177}Lu radiation exposure to tumor following curative treatment (all 3 cycles) at 14,000 rads, with radiation doses to blood and kidney of 150 rads and 875 rads, respectively. The authors concluded that these theranostic PRIT regimens with a cumulative tumor radiation dose of ~14,000 rads and therapeutic indices of 93 for blood and 16 for kidneys are "safe and sufficient for cure of colorectal cancer." "If these results can be replicated in prospective human studies, this multiplatform approach could be used with an array of antibodies to treat a number of cancers, especially colorectal and ovarian cancers," said Sarah M. Cheal, PhD, first author of the study.

PET and Brain Changes in Alcohol Dependence

Researchers from University Hospital Gasthuisberg (Leuven, Belgium) and colleagues from the University of Leuven and University of Antwerp (Belgium) reported on a study using ^{18}F-FPEB PET imaging to evaluate the role of metabotropic glutamate receptor subtype 5 (mGluR5) signaling in the physiopathology of alcohol-dependent individuals. The study included 16 recently abstinent alcohol-dependent individuals (ages, 45 ± 8 y; range, 32–57 y) and 32 age-matched healthy controls. All participants underwent ^{18}F-FPEB PET imaging and arterial blood sampling. Alcohol use was clinically assessed with self-report questionnaires and ethyl glucuronide hair analysis. Image analyses showed decreased mGluR5 availability in alcoholics in the bilateral cingulate, caudate, and insular cortex, changes not associated with sex or smoking status. Additional analyses showed mean changes in total tracer distribution volumes of $-27\% \pm 4\%$ in the caudate, $-26\% \pm 4\%$ in the insula, $-23\% \pm 5\%$ in the anterior cingulate, and $-19\% \pm 5\%$ in the posterior cingulate in alcohol-dependent individuals compared with controls. mGluR5 binding was also negatively correlated with ethyl glucuronide hair levels in alcohol dependence. The authors concluded that "mGluR5 availability is decreased in the limbic system of alcohol-dependent subjects" and that these data imply "the functional role of mGluR5 in the physiopathology of alcohol addiction." "Collectively, these findings strongly substantiate the development of mGluR5-targeted therapies that heal or protect against the dysfunctional brain circuitry that characterizes alcohol addiction," said Gil Leurquin-Sterk, MD, first author of the study.

PET and MS Neuroinflammation

Rosenberg and colleagues from the Washington University School of Medicine (St. Louis, MO) reported on preclinical studies with second-generation sphingosine 1–phosphate receptor 1 ($S1P_1$)–specific ^{18}F-labeled tracers for imaging in small animal models of multiple sclerosis (MS) and in normal nonhuman primates (NHPs). $S1P_1$ is highly expressed under specific neuroinflammatory conditions, particularly in MS lesions. After screening, 3 ligands with high potency and selectivity for $S1P_1$ were synthesized and radiolabeled with [18]F. Autoradiography, biodistribution, and PET imaging studies were then carried out in rodent models of MS and normal NHPs. Biodistribution in rodents showed acceptable brain uptake with peak uptake at 1 h postinjection. MicroPET studies of one of the ligands, ^{18}F-TZ43113, in an experimental autoimmune encephalomyelitis model of MS in rats showed a 31% increased uptake in the lumbar spinal cord when compared with sham-treated animals, which was confirmed on histology. Imaging with another ligand, ^{18}F-TZ35104, documented excellent brain uptake and washout in NHPs. The 3 ligands were shown to cross the blood–brain barrier, and PET successfully detected increases of $S1P_1$ expression in the rat model of MS. The authors concluded that "these compounds represent promising PET tracers for imaging MS as well as other neuroinflammatory diseases, and represent a step forward for $S1P_1$ imaging."

Predicting PRRT Success in NETs

Researchers from the Nuclear Medicine European Institute of Oncology (Milan, Italy), Erasmus Medical Center (Rotterdam, The Netherlands), IRST Cesena (Italy), IRST IRCCS (Meldola, Italy), Wren Laboratories (Branford, CT), Yale University School of Medicine (New Haven, CT), and the Zentralklinik Bad Berka (Germany) reported on a blood-based multitranscript test designed to predict the effectiveness of peptide receptor radionuclide therapy (PRRT) in neuroendocrine tumors (NETs). Called

NETest, the multigene algorithm–derived scale defines clinical disease status on a scale of 0 to 100%. The authors evaluated NETest in data from 72 patients with NETs treated with ^{177}Lu-based PRRT. A predictive response index was developed for PRRT efficacy based on transcript analysis incorporating gene clusters that define growth factor signaling and metabolism. Disease control was evaluated against Response Evaluation Criteria in Solid Tumors. Over all, PRRT resulted in a 68% disease control rate in the study population, with median progression-free survival not achieved over the median follow-up of 16 mo. Although low grade (G1/G2) was the only baseline clinical characteristic correlated with outcome, grade alone was not predictive (73% of low-grade and 50% of high-grade tumors responded). The NETest assessment, however, correlated with 87% accuracy, predicting 95% of responders and 90% of nonresponders. The authors concluded that the test serves as a predictive multimolecular biomarker for PRRT efficacy. Further assessment adding a progression response index (combining genes involved in signaling and metabolism genes with grading) provided a 94% accurate predictive biomarker, with results significantly better than those achieved with somatostatin receptor imaging. They added that "NET multigene measurement in blood can be used to predict tumors that are responsive to PRRT and to assess efficacy on a real-time basis during therapy." "This research shows that the molecular information obtained from a simple blood draw can be easily integrated with radiological and molecular imaging to provide a more accurate assessment of tumor behavior and response to therapy," said Lisa Bodei, MD, PhD, first author of the study.

and fellowship in nuclear medicine at Johns Hopkins Medical Institutions (Baltimore, MD), with an internship in the Department of Surgery at St. Luke's Hospital (New York, NY). Conti is board certified in both diagnostic radiology and nuclear medicine. He has served as director of the USC Molecular Imaging Center (previously the Positron Imaging Science Center and Clinic) since its launch in 1991.

Conti's research focuses on development of novel diagnostic imaging agents for oncology applications. He was among the pioneers of the use of PET imaging in the understanding and characterization of cancer metabolism and gene expression, and he has focused on the discovery and clinical translation of novel PET imaging agents for in vivo cancer diagnosis, evaluation of metastatic disease potential, and assessment of response to therapy. He has published more than 300 peer-reviewed scientific articles and abstracts in the field of molecular imaging.

Conti is board certified in both diagnostic radiology and nuclear medicine. He is a fellow of the American College of Radiology and the American College of Nuclear Medicine Physicians. At this year's SNMMI meeting he was among the first group to be named as SNMMI fellows. Conti is a past president of SNMMI and remains active in the society, including service on government and regulatory affairs committees supporting the development of molecular imaging technology and its applications in medicine.

"Dr. Conti's innovative research has advanced the field of nuclear medicine and molecular imaging," said Gary L. Dillehay, MD, chair of the SNMMI Committee on Awards and a past president of the society. "His research includes the development of specific PET radiopharmaceuticals for imaging cancers and other disease processes, as well as the development of radiotracers for gene therapy."