In the spring, the FDA approved two new PET imaging agents:

• **Axumin™** (18F-labeled fluciclovine injection) for detecting biochemical recurrence of prostate cancer: This is the first FDA-approved, 18F-labeled PET imaging agent for use in patients with suspected recurrent prostate cancer. Axumin will be commercially available through the national radiopharmacy network of Blue Earth Diagnostics’ exclusive U.S. commercial manufacturer and distributor, Siemens’ PETNET Solutions.

  PET imaging with the new agent may identify the location and extent of such recurrence. The agent was developed to enable visualization of the increased amino acid transport that occurs in many cancers, including prostate cancer.

  “Finding disease in men who have been treated for primary prostate cancer but present with a rising PSA has been a significant unmet need in medicine,” said SNMMI immediate past president Hossein Jadvar, MD, PhD, MPH, MBA, FACNM, FSNMMI. “We are excited to see that FDA has approved an agent that can facilitate the imaging evaluation of this large cohort of men with biochemical recurrence of prostate cancer. SNMMI has appreciated working with the FDA on bringing new molecular imaging drugs to approval. We applaud the FDA for recognizing the importance of this advanced imaging agent and granting priority review status.”

  The FDA-approved prescribing information provides summaries from two clinical studies of Axumin, including an evaluation of images from 105 patients by three independent readers who were unaware of the clinical details of each patient or whether the biopsy of the prostate gland was positive or negative for cancer.

  “An imaging agent with sufficient diagnostic performance to adequately detect and localize recurrent prostate cancer can provide referring physicians with actionable information to guide biopsy and inform management decisions for their patients,” said David M. Schuster, MD, associate professor of radiology and imaging sciences and director of the Division of Nuclear Medicine and Molecular Imaging at Emory University School of Medicine. “The fluciclovine molecule in Axumin was originally developed at Emory by Mark Goodman, PhD, and detects the upregulation of amino acid transport that occurs in prostate cancer and can potentially identify recurrent prostate cancer.”

  It seems likely that this trend will continue. For instance, 68Ga-DOT-ATATE offers superior image quality, superior lesion detection sensitivity and (Continued on page 6. See PET Agents.)
PET in the News

The international literature on PET, PET/CT and PET/MR continues to grow at a pace that challenges both researchers and clinicians. The media has recognized the value of these modalities and regularly features advances in research and technology in the news. In each issue, the PET CoE Newsletter presents a tomographic slice of the breadth of PET media coverage that appears in publications around the world. Additional news articles can be found online at www.snmmi.org under “MI: Making a Difference.”

Researchers develop noninvasive PET technique to diagnose and monitor depression
DOTmed

New PET scan tracer allows first imaging of the epigenetics of the human brain
Science Daily

PET imaging features linked to EGFR mutations in NSCLC
Healio

PET/CT calcium scores reveal chemo’s damage to the heart
Aunt Minnie

Old Versus New Neuroendocrine Tumor Imaging Agents
Medscape

PET imaging may measure risk for suicidal ideation, attempts, death
Healio

PET detector delivers ultrahigh performance medicalphysicsweb

PET with tau agent sheds light on Alzheimer’s disease
Aunt Minnie

New technique opens window into how brain cells communicate
AP

PET/MRI technique shows promise for prostate cancer
Aunt Minnie

Bone marrow biopsy does not add value to PET/CT staging of DLBCL
Healio

A Duel of Dual-Modality Imaging in Lung Cancer Detection
Medscape

PET CoE News

The PET Center of Excellence Peter E. Valk, MD, Memorial Lectureship and Award

Congratulations to Richard L. Wahl, MD, chair, Department of Radiology, and director, Mallinckrodt Institute of Radiology, at Washington University School of Medicine, who received the 2016 Peter E. Valk, MD, Memorial Award at the SNMMI Annual Meeting in San Diego, California! He gave a presentation titled “From Genome to Phenome using PET…‘PERCISTence’ Pays.”

(Continued on page 4. See PET CoE News.)
Combining PET imaging with multi-parametric MR improves the accuracy of targeted prostate biopsies.

A University of Michigan study published in the July issue of The Journal of Nuclear Medicine reports that the addition of molecular imaging based on F-18-choline positron emission tomography (PET) improves the identification of significant prostate cancer over multi-parametric prostate magnetic resonance imaging (mpMRI) alone for targeted transrectal prostate biopsies. MRI-guided biopsies already outperform standard, non-targeted biopsies. The addition of PET promises to improve targeted biopsies even further.

According to the National Cancer Institute, approximately 14 percent of men will be diagnosed with prostate cancer at some point during their lifetime. More than 2.5 million men are estimated to be living with prostate cancer in the United States.

Morand Piert, MD, professor of radiology in the Division of Nuclear Medicine at the University of Michigan, points out, “Our positive results suggest that in the future, PET/MRI may become a one-stop imaging test for men with suspected but undetected prostate cancer or for patients undergoing surveillance for known low-risk prostate cancer.” He explains, “Since prostate cancer is often multi-focal and presents with multiple lesions of varying risk, it is important to identify the lesions that harbour the greatest malignant potential. Accurate identification of clinically significant cancer and avoidance of clinically insignificant cancer is the centrepiece of modern prostate cancer diagnosis.”

As part of an ongoing prospective clinical trial, researchers studied 36 men with rising prostate-specific antigen (PSA) to assess the value of fusion F-18-choline PET/MRI for image-guided (targeted) prostate biopsies to detect significant prostate cancer, compared to standard (non-targeted, systematic 12-core) biopsies. The biopsy procedures were performed after registration of real-time transrectal ultrasound (TRUS) and included image-guided cores plus standard cores. Histological results were determined from standard and targeted biopsy cores, as well as prostatectomy specimens.

Fifteen subjects were ultimately identified with significant prostate cancer (Gleason ≥ 3+4), of which targeted biopsy identified 12, while standard biopsy identified only five. The figure shows a Gleason 3+4 prostate cancer (arrows) as identified on T2-weighted (A) and diffusion-weighted (B) MRI, F-18-choline PET (C), as well as PET/MRI (D). A total of 52 lesions were identified by mpMRI (19 low, 18 intermediate, and 15 high risk), and mpMRI-assigned risk was a strong predictor of final pathology (area under the curve (AUC) = 0.81; P < 0.001). Using the mean F-18-choline target-to-background ratio, the addition of F-18-choline to mpMRI significantly improved the prediction of Gleason ≥ 3+4 cancers over mpMRI alone (AUC = 0.92; p<0.001).

The study concluded that fusion PET/MRI-TRUS image registration for targeted prostate biopsies is clinically feasible and accurate, and the addition of F-18-choline PET to mpMRI improves identification of significant prostate cancer.

Piert notes, “The use of advanced imaging to inform placement of biopsy needles promises to greatly minimize the uncertainty associated with prostate cancer care. Imaging may one day be performed prior to biopsy. (Continued on page 5. See Speaks Out.)
Medical historians often credit Georg von Hevesy’s key role in the development of radioactive tracers—for which he was awarded the Nobel Prize in 1944—with laying the foundation for the future of functional imaging.\(^1\) Decades later, Gordon Brownell, David Kuhl, Michael Phelps, Michel Ter-Pogossian and many others developed instruments capable of detecting the radiation emitted from radioactive tracers and translating this into tomographic images.\(^2,3\) In the late 1970s, Alfred Wolf, Joanna Fowler and colleagues at Brookhaven National Laboratory developed \(^{18}\)F-labeled fluorodeoxyglucose (\(^{18}\)F-FDG), which allowed metabolic processes in the brain that relied on glucose consumption to be tracked visually, thereby setting in motion significant clinical advances in positron emission tomography (PET).\(^4\)

Soon after PET scanners reached the clinics, PET images of the brain began to circulate in mass media. For example, in 1983, the popular fashion magazine *Vogue* published an article entitled “High-Tech Breakthrough in Medicine: New Seeing-Eye Machines… Look Inside Your Body, Can Save Your Life.”\(^5\) The cultural anthropologist Joseph Dumit wrote, “Brain-imaging technologies like PET offer[ed] researchers the potential to ask a question about almost any aspect of human nature, human behavior, or human kinds and design an experiment to look for the answer in the brain.”\(^4\) In the 1988 courtroom drama, *Rampage*, the medical doctor, as the expert witness, explained to the jury that “What you are seeing is a computer-enhanced image of the chemistry of the brain. And what it shows is a picture of madness.”\(^6\)

PET provides a way to image cerebral metabolism, but what does this really mean in terms of who we are, how we perceive the world and how the world perceives us? The use of PET in science and medicine versus the portrayal of what it can show us according to our literature, movies and social media has been the topic of controversial debate for decades. Indeed, while some have tried to make a career of imaging criminals, the scientific community, in general, is not in favor of PET for such uses. Regardless, imaging will likely continue to be used to characterize normal and abnormal personhood for many years to come. Popular culture’s conflation of anatomy and physiology with mental illness, among other medical issues, can have profound consequences for our conceptions of human nature and existence, experience and embodiment. At the end of the day, the tools we use in clinical nuclear medicine can have a profound influence on our concept of personhood through the cultural psyche. It would be wise for us to remember this and continue to educate the public about what the science really shows.

**References**

much shorter exam length (study complete in 2 hours rather than 2 days) when compared with $^{111}$In-pentetreotide, its single-photon equivalent. Another example is $^{18}$F-flurpiridaz, a myocardial perfusion imaging agent currently in phase 3 clinical trials: with the user-friendly half-life and wide distribution network afforded by $^{18}$F labeling, optimized image quality (with attenuation correction) and ability to measure coronary flow reserve, this agent has potential to induce a significant migration from SPECT to PET in the arena of myocardial perfusion imaging.

Single-photon imaging has not and probably will not disappear entirely. There are many studies (e.g., MUGA scans, HIDA scan, GI bleeding studies, gastric emptying studies, V/Q scans, etc.) for which PET seems unlikely to replace single-photon imaging. SPECT/CT is also a very capable modality that helps to extend the benefits of hybrid PET/CT imaging (namely, attenuation correction and anatomic localization) to those facilities without access to PET equipment.

Nevertheless, I think it’s clear that “the march (toward PET) is on,” and the nuclear medicine department of the future will likely look very different than it has in the past or does today. Historically, most departments have typically operated more gamma cameras than PET scanners, but this ratio may change in the future as our armamentarium of PET tracers increases. This is an exciting time for molecular imaging, and we will need to respond accordingly.

Authors of the article “$^{18}$F-choline PET/MRI: The Additional Value of PET for MRI-guided Transrectal Prostate Biopsies” include Morand Piert, Jeffrey Montgomery, Lakshmi Priya Kunju, Javed Siddiqui, Virginia Rogers, Thekkelnaycke Rajendiran, Timothy D. Johnson, Xia Shao, and Matthew S. Davenport, University of Michigan, Ann Arbor, Michigan.

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(President’s Report. Continued from page 1.)

(Peeks Out. Continued from page 3.)

and, if negative, no biopsy would be needed. To reach that future state, advanced imaging will need to have a superior negative predictive value that may not be obtainable with multi-parametric MRI alone.” He adds, “Although we used F-18-choline PET in this trial, it is likely that other radiotracers, which are more specific for prostate cancer—for example, those that target PSMA—may hold even greater promise.”

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Calendar of Events

**Nuclear Medicine & Molecular Imaging Week - Committed to Quality. Dedicated to Patients.**
October 2-8, 2016
http://www.snmmi.org/nmw

**2016 Southeastern Chapter SNMMI Annual Meeting**
October 7-9, 2016 • Chattanooga, Tennessee
http://www.secsnm.org

**EANM’16 - 29th Annual Congress of the European Association of Nuclear Medicine**
October 15-19, 2016 • Barcelona, Spain
www.eanm.org

**International Conference on Medical Imaging & Diagnosis**
October 20-21, 2016 • Chicago, Illinois
http://www.omicsonline.org

**Clinical Nuclear Medicine: PET-CT and PET-MRI Case Review**
October 20-22, 2016 • Boston, Massachusetts
www.radcme.harvard.edu

**2016 Western Region SNM Annual Meeting**
October 20-23, 2016 • Anaheim, California
http://www.wrsnm.org

**2016 IEEE Nuclear Science Symposium and Medical Imaging Conference**
October 29-November 6, 2016 • Strasbourg, France
http://ieee-npss.org

**2016 Northeast Regional Meeting**
November 4-6, 2016 • Stamford, Connecticut
mitch360@aol.com

**4th Theranostics World Congress**
November 7-9, 2016 • Melbourne, Australia
http://www.unicornfoundation.org.au

**13th Global Summit on Cancer Therapy**
November 17-19, 2016 • Dubai, UAE
http://www.omicsgroup.com
cancer more reliably than conventional imaging techniques. The product will be convenient for patients and imaging facilities, as it can be made widely available and the entire imaging procedure can typically be completed in less than 30 minutes.”

• **NETSPOT™** (68Ga-labeled DOTATATE injection) for the localization of somatostatin receptor–positive neuroendocrine tumors (NETs) in adult and pediatric patients: NETSPOT is the first approved imaging agent using gallium-68 as a positron emitter. AAA intends to commercialize the product in the U.S. in two forms: as a kit for reconstitution using a 68Ge/68Ga generator and as an injection. The injection will be a ready-to-use dose prepared at and delivered from a local radiopharmacy in selected metropolitan areas.

“Although neuroendocrine tumors (NETs) are relatively rare, they tend to affect younger patients, and the incidence of NETs is on the rise in the U.S.,” said Jadvar. “We are pleased to see that the FDA has approved an agent that can facilitate more accurate imaging evaluation of NETs, which may allow more appropriate patient management.”

NETSPOT dosing and imaging can be completed in one two-hour visit, as opposed to a 48-hour cycle with older agents. Additionally, radiation exposure is reduced with the new PET agent.

The FDA-approved labeling was based on three studies: a comparison of 68Ga DOTATATE images of NETs with an approved drug, a second comparing images to histopathology or clinical follow-up, and a third that evaluated NET recurrence with 68Ga DOTATATE imaging.

“SNMMI has appreciated working with the FDA on bringing new molecular imaging drugs to approval,” Jadvar commented. “We applaud the FDA for recognizing the importance of this advanced imaging agent and granting priority review status.” FDA grants priority review to applications for drugs that, if approved, would significantly improve safety or effectiveness in the treatment of a serious condition.

Both agents represent a targeted approach and a new path for PET/CT. These agents are seeking CMS reimbursement and pass-through status with expected distribution in the next 12 months. Not all areas of the country will have access to these agents initially. New regulatory requirements are being made with an NRC meeting held on August 10 to evaluate, plan and provide guidance for the safe handling and use of gallium generators, which are used to provide NETSPOT.

All interested parties are encouraged to provide comments to the respective companies to request access and more information regarding reimbursement, coding, billing and when/how the material will be available to them.