Lawhn-Heath Named 2019 Henkin Fellow

SNMMI and the Education and Research Foundation for Nuclear Medicine and Molecular Imaging announced on April 23 that Courtney Lawhn-Heath, MD, is the recipient of the 2019 Robert E. Henkin Government Relations Fellowship. Each year, fellowship recipients travel to Washington, DC, and spend a week with SNMMI staff, visiting Congress, federal agencies, and other medical societies. Throughout the visit, fellows learn about ways in which federal legislative and regulatory processes affect nuclear medicine and molecular imaging. The program is designed for young professionals, defined as residents or fellows (physicians, scientists, or technologists) who have completed training within the last 10 years.

Dr. Lawhn-Heath is a graduate of the University of Chicago (IL) Pritzker School of Medicine. She is completing a dual American Board of Radiology/American Board of Nuclear Medicine radiology residency. Her research interests are in prostate cancer, head and neck imaging, and breast imaging. She has presented her research at national and international venues and is enthusiastic about advocating for both scientific innovation and patient safety in the field of nuclear medicine and molecular imaging. During a previous internship with the SNMMI Clinical Trials Network, Dr. Lawhn-Heath had the opportunity to interface with governmental regulatory agencies such as the U.S. Food and Drug Administration. "Working through the process of safely bringing new nuclear medicine agents from development to the patients who benefit from them sparked my interest," she said. During her time as the 2019 Robert E. Henkin fellow, she hopes to gain a deeper understanding of the policy goals of SNMMI. Dr. Lawhn-Heath believes that "nuclear medicine is the future of medicine—one that will revolutionize our ability to more precisely diagnose, prognosticate, and treat a host of human maladies."

Courtney Lawhn-Heath, MD

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NEWSBRIEFS

LATE: Guidelines for Newly Defined Alzheimer-Like Brain Disorder

A press release from the National Institutes of Health (NIH) on April 30 provided an overview of a recently recognized brain disorder that mimics clinical features of Alzheimer disease (AD) and highlighted an article defining recommended diagnostic criteria and other guidelines for advancing future research. Scientists from several NIH–funded institutions, in collaboration with international peers, described the newly named pathway to dementia, limbic-predominant age-related TDP-43 encephalopathy (LATE), in the widely covered article published on April 30 ahead of print in in the journal *Brain*.

"While we've certainly been making advances in AD research—such as new biomarker and genetic discoveries—we are still at times asking, 'When is AD not AD in older adults?'" said Richard J. Hodes, MD, director of the National Institute on Aging (NIA). "The guidance provided in this report, including the definition of LATE, is a crucial step toward increasing awareness and advancing research for both this disease and AD as well."

The consensus group study, under lead author Peter T. Nelson, MD, PhD (University of Kentucky, Lexington), addressed the clear need for further diagnostic differentiation of dementias in the large numbers of elderly patients with clinical symptoms of dementia but no later postmortem pathology findings. Misfolds in the transactive response DNA binding protein of 43 kDa (TDP-43) protein have been implicated in contributing to this phenomenon, especially in hippocampal sclerosis, with clinical symptoms of cognitive impairment similar to those of AD.

"Recent research and clinical trials in AD have taught us 2 things: First, not all of the people we thought had AD have it; second, it is very important to understand the other contributors to dementia," said Nina Silverberg, PhD, director of the Alzheimer's Disease Centers Program at NIA. Noting the trend in research implicating TDP-43 as a possible AD mimic, a group of experts convened an NIA workshop in Atlanta, GA, in October 2018 to provide a starting point for further research to advance understanding of contributors to late-life brain changes. The session was cochaired by Nelson and Silverberg, with scientists from the United States, Australia, Austria, Sweden, Japan, and the United Kingdom bringing expertise in clinical diagnosis, neuropathology, genetics, neuropsychology, and brain imaging. The resulting outcomes published in *Brain* included classification guidelines for diagnosis and staging of LATE, as well as recommendations for future research directions.

The authors wrote that LATE is an underrecognized condition with a very large impact on public health, emphasizing that the "oldest old" are at

greatest risk and stated their belief that the public health impact of LATE is at least as large as AD in this group. The clinical and neurocognitive features of LATE affect multiple areas of cognition, ultimately impairing activities of daily life. In addition, based on existing research, the authors suggested that LATE progresses more gradually than AD. However, LATE combined with AD—a common occurrence for these 2 highly prevalent brain diseases—appears to cause a more rapid decline than would either alone. "It is important to note that the disease itself is not new. LATE has been there all along, but we hope this report will enable more rapid advancement in research to help us better understand the causes and open new opportunities for treatment," said Silverberg.

A key recommendation in the report was for routine autopsy evaluation and classification of LATE. The researchers suggested a sampling and staging system for routine autopsy diagnosis to characterize the anatomic distribution of TDP-43 proteinopathy in stage 1, amygdala only; stage 2, amygdala and hippocampus; and stage 3, amygdala, hippocampus, and middle front gyrus. Additional recommendations included the need for development of biomarkers, more advanced pathologic studies, and generation of new animal models. Suggestions were provided for possible strategies to help guide future therapeutic interventions, including the importance of identification and removal of subjects with LATE from other clinical trials, which could significantly improve the chances of successful AD breakthroughs. The researchers also discussed the importance of more epidemiologic, clinical, neuroimaging, and genetic studies to better characterize LATE, as well as the need for research in diverse populations. They concluded by pointing to the importance of promoting awareness in multiple scientific areas and focusing on translational and interdisciplinary approaches.

National Institute on Aging
Brain

CMS Outlines Strategy for Transformative Medical Technologies

Speaking on May 2 at the Medical Device Manufacturers Association Annual Meeting in Washington, DC, Centers for Medicare & Medicaid Services (CMS) Administrator Seema Verma, MPH, provided an overview of the agency's new strategy to improve access to emerging technologies. "We are committed to removing government barriers and modernizing regulations around new technologies to ensure safe and effective treatments are readily accessible to beneficiaries without delaying patient care." Two specific actions were highlighted in Verma's remarks.

First, CMS is changing the current process of allowing only 1 opportunity per year to apply for new Level II Healthcare Common Procedure Coding System codes, moving to a process with quarterly opportunities to apply for drugs and semiannual opportunities to apply for devices. In a related press release, CMS noted that the agency "anticipates this will greatly improve the ability for technologies to move through the adoption curve, and additional details will be forthcoming on the updates to the process."

Second, for technologies with Current Procedural Terminology (CPT) Category III codes (temporary codes used for emerging technologies), CMS is clarifying that for technologies that do not fall under an existing Local Coverage Determination (LCD), Medicare contractors are required to follow the LCD process for every LCD, including reviewing evidence about technology. This clarification was part of a list of answers to commonly asked questions about the LCD process that the agency posted online in May.

CMS stated that these 2 elements are key components of a comprehensive CMS strategy to address barriers to medical innovation in the Medicare program. In late April, CMS proposed a number of rule changes to the Inpatient Prospective Payment System designed to advance innovation, including proposing to increase the new technology add-on payment that provides hospitals with additional payments for cases with high costs involving new technology. CMS also proposed to modernize payment policies for medical devices that meet the Food and Drug Administration's Breakthrough Devices designation. The agency's strategy is intended to "ensure predictable coverage pathways, enhance opportunities for coverage for transformative technologies, reduce wait times to apply for permanent codes, and modernize payment for innovative services."

Centers for Medicare & Medicaid Services

Roadmap for AI in Medical Imaging

A media advisory issued on April 18 by the National Institute of Biomedical Imaging and Bioengineering (NIBIB) highlighted a "foundational research roadmap for artificial intelligence [AI]" published on April 16 ahead of print in *Radiology*. The report was based on outcomes from an August 2018 meeting of experts who explored the future of AI in medical imaging at a workshop hosted at the National Institutes of Health (Bethesda, MD). The workshop was cosponsored by NIBIB, the Radiological Society of North America, the American College of Radiology, and the Academy for Radiology and Biomedical Imaging Research. The collaborative report, under lead author Curt Langlotz, MD, PhD (Stanford University, CA), underscored the need for standards bodies, professional societies, government agencies, and private industry to work together to accomplish a set of shared goals in service of patients who will benefit from the potential of AI to bring about innovative imaging technologies. The report described innovations that would help to produce more publicly available, validated, and reusable datasets against which to evaluate new algorithms and techniques, noting that to be useful for machine learning these datasets require methods to rapidly create labeled or annotated imaging data. Identified priorities for AI in medical imaging research included: (1) new

image reconstruction methods that efficiently produce images suitable for human interpretation from source data; (2) automated image labeling and annotation methods, including information extraction from imaging reports, electronic phenotyping, and prospective structured image reporting; (3) new machine learning methods for clinical imaging data, such as tailored pretrained model architectures and distributed machine learning methods; (4) machine learning methods that can explain the advice they provide to human users (so-called explainable AI); and (5) validated methods for image deidentification and data sharing to facilitate wide availability of clinical imaging datasets.

National Institute of Biomedical Imaging and Bioengineering

FROM THE LITERATURE

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. 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.

Amyloid PET: Semiquantification and Grading

Chincarini, from the Istituto Nazionale di Fisica Nucleare (Genova, Italy), and other members of the European Alzheimer's Disease Consortium (EADC) from Italy, Spain, Portugal, France, Belgium, Switzerland, and Germany reported on May 4 ahead of print in *Neuroimage. Clinical* on development of a model to compare and integrate visual reading of amyloid PET images using 2 independent semiquantification methods designed to yield tracer-independent multiparametric evaluation. The study included PET/CT imaging from 175 cognitively impaired patients from multiple EADC member institutions using ^{18}F-florbetaben (n = 53), ^{18}F-flutemetamol (n = 62), and ^{18}F-florbetapir (n = 60). Scans were first classified visually as positive or negative according to approved criteria. Additional classification by 5 independent readers unaware of clinical data assigned grades of negative, mild negative, borderline, mild positive, and positive. Scan quality was visually assessed and recorded. Semiquantified assessments were provided by SUV ratio and the ELBA method. The authors measured reader agreement and inconsistency in visual assessment as well as the relationship between discrepancies on grading and semiquantification. Their results showed that it is feasible to create a map between different tracers and different quantification methods without resorting to ad hoc acquired cases. The visual scale, combined with the mathematical model, delivered cutoffs and transition regions on all fluorinated tracers and were largely independent from the population. These tracers appeared to have the same contrast and discrimination ability with respect to the negative-to-positive grading. The authors concluded that validating the integration of both visual reading and different quantifiers in a more robust framework contributes to "bridging the gap between a binary and a user-independent continuous scale."

Neuroimage. Clinical

^{18}F-NaF PET/CT vs MR or CT in Spondyloarthritis

In an article published on May 14 in *Arthritis Research and Therapy* (2019; 21:119), Raynal et al. from the Centre Hospitalier Régional Universitaire Nancy (Vandóuvre-lès-Nancy, France) and the University of Alberta (Edmonton, Canada) reported on a study intended to assess increased sacroiliac joint uptake on ^{18}F-NaF PET/CT and compare data acquired to MR imaging for inflammation and to CT for structural damages. The study included 23 patients (ages, 18–45 y) with axial or mixed spondyloarthritis. All patients had undergone pelvic radiography, MR imaging and CT scanning of the sacroiliac joint, and ^{18}F-NaF PET/CT within a month. Images were analyzed by 3 readers unaware of clinical records. MR images were assessed according to the Assessment of Spondyloarthritis International Society (ASAS) criteria and the Spondyloarthritis Research Consortium of Canada Magnetic Resonance Imaging Index for Assessment of Spinal Inflammation (SPARCC) method. Erosion and ankylosis were quantified on CT images using the same methodology. Abnormal uptake on ^{18}F-NaF PET was assessed using a qualitative method inspired by the ASAS criteria and 2 quantitative approaches (the PET activity score according to the SPARCC method and SUV_{max}). Imaging results showed structural sacroiliitis on 7 radiographs and 10 CTs. MR imaging in 10 patients showed inflammatory sacroiliitis, whereas PET imaging was positive in 20 patients. Positive PET findings were not correlated with positive MR images nor with structural sacroiliitis on CT. Interreader agreement was good for PET activity scores and good to excellent for SUV_{max}. These PET metrics were correlated with SPARCC inflammation scores but not with erosion or ankylosis scores on CT scan. The authors concluded that "further studies with a control group and a larger sample are needed to evaluate the