

### High Amyloid Levels and Early-Stage AD

The National Institute on Aging (NIA) released a press statement on April 6 about the first published data from the Anti-Amyloid Treatment in Asymptomatic Alzheimer's Disease (AD) study, supporting the hypothesis that higher levels of amyloid protein in the brain represent an early stage of AD. The results were published as "Association of factors with elevated amyloid burden in clinically normal older individuals in the A4 study screening cohort" on the same day in *JAMA Neurology* by Sperling et al. from Brigham and Women's Hospital/Massachusetts General Hospital/Harvard Medical School (Boston, MA), the University of Southern California (San Diego), Eli Lilly & Co. (Indianapolis, IN), and Siemens Integration LLC (Zionsville, IN). Amyloid burden in clinically normal older adults in the study was associated with a family history of disease, lower cognitive test scores, and reports of declines in daily cognitive function.

With completion expected in late 2022, the A4 study is an ongoing prevention trial launched in 2014 to test whether the drug solanezumab, a monoclonal antibody, can slow cognitive decline associated with elevated brain amyloid if started before clinical symptoms appear. "A major issue for amyloid-targeting AD clinical trials, and one that is being addressed with the A4 study, is that previous trials may have been intervening too late in the disease process to be effective," said NIA Director, Richard J. Hodes, MD. "A4 is pioneering in the field because it targets amyloid accumulation in older adults at risk for developing dementia before the onset of symptoms."

After a complex and large-scale prescreening process, the A4 researchers included 4,486 cognitively normal participants (65–85 y) who underwent <sup>18</sup>F-florbetapir amyloid- $\beta$  PET imaging. This yielded a group of 1,323 individuals with

elevated amyloid levels who were eligible to continue in the A4 study. Those individuals with amyloid- $\beta$  positivity were slightly older than those who were amyloid- $\beta$  negative, but no differences were seen in sex, education, marital or retirement status, or self-reported lifestyle factors. Amyloid- $\beta$ -positive individuals were more likely to have family histories of dementia and at least 1 apolipoprotein  $\epsilon$ 4 allele. Amyloid- $\beta$ -positive individuals also had worse performance on cognitive screening assessments. The authors concluded that these results "demonstrate the feasibility of enrolling these high-risk participants in secondary prevention trials aimed at slowing cognitive decline during the preclinical stages of AD."

*JAMA Neurology*  
National Institute on Aging

### NLM Expands COVID-19 Literature Access

The National Library of Medicine (NLM), part of the National Institutes of Health, announced on March 25 that it would be expanding access to scientific papers on coronavirus for researchers, care providers, and the public, as well as for text-mining research. The effort makes use of NLM's PubMed Central (PMC), a digital archive of peer-reviewed biomedical and life sciences literature. PMC currently provides access to almost 6 million full-text journal articles. NLM stated in a press release that it had stepped up its collaboration with publishers and scholarly societies to increase the number of coronavirus-related journal articles freely available in PMC, along with available supporting data. Submitted publications will be made available in PMC as quickly as possible after publication, in formats and with needed permissions that support text mining.

To advance this initiative, NLM reported that standard procedures for depositing articles into PMC were being adapted to provide greater flexibility and ensure that coronavirus research remains readily available. NLM will also engage

with journals and publishers that do not currently participate in PMC but are in scope for the NLM Collection. Additional information, including a list of participating publishers and journals, is available at: <https://www.ncbi.nlm.nih.gov/pmc/about/covid-19>.

By making this collection of articles more readily available in machine-readable formats, NLM hopes to enable artificial intelligence researchers to develop and apply novel approaches to text mining to answer questions about coronavirus. NLM has already made more than 10,000 full-text scholarly articles from PMC related to the coronavirus available through the COVID-19 Open Research Dataset (CORD-19), representing the most extensive machine-readable coronavirus literature collection available for text mining.

*National Library of Medicine*

### IAEA Focus on <sup>68</sup>Ga

The International Atomic Energy Agency (IAEA) announced on April 8 the launch of a new Coordinated Research Project (CRP) advancing its commitment to international efforts in the production and application of theranostic radiopharmaceuticals. The new CRP will focus on direct cyclotron production of [<sup>68</sup>Ga]GaCl<sub>3</sub> and related radiopharmaceuticals. According to a press release at the launch, the CRP is intended to aid and share international experience on production and quality control of <sup>68</sup>Ga using the <sup>68</sup>Zn(p,n)<sup>68</sup>Ga route. It will also focus on radiopharmaceutical production, quality control, quality assurance, supply challenges, and regulatory aspects for <sup>68</sup>Ga use in clinical applications.

The most common method for obtaining <sup>68</sup>Ga is with a <sup>68</sup>Ge/<sup>68</sup>Ga generator. The eluted <sup>68</sup>Ga, in the form of [<sup>68</sup>Ga]GaCl<sub>3</sub>, can be used for labeling and has led to significant advances in targeted PET radiopharmaceuticals. A previous IAEA CRP on generator-based <sup>68</sup>Ga radiopharmaceuticals was completed in 2017.

The current CRP focuses on building knowledge sharing among research-oriented facilities using cyclotron-based approaches to expand  $^{68}\text{Ga}$  availability for preclinical and human use. Specific goals include: transfer of technology and expertise for optimal cyclotron production of  $^{68}\text{Ga}$  using solid and/or liquid targets; transfer of expertise and methods for the separation and purification of cyclotron-produced  $^{68}\text{Ga}[\text{GaCl}_3]$ ; provision of guidance for quality control and quality assurance of cyclotron-produced  $^{68}\text{Ga}[\text{GaCl}_3]$ ; provision of radiosynthetic procedures for preparation of widely used  $^{68}\text{Ga}$  radiopharmaceuticals (i.e., somatostatin-receptor and prostate-specific membrane antigen ligands) using cyclotron-produced  $^{68}\text{Ga}[\text{GaCl}_3]$ , including quality control tests; development of guidance for regulatory approval for human use of radiopharmaceuticals using cyclotron-produced  $^{68}\text{Ga}[\text{GaCl}_3]$  for investigational and routine clinical applications; and adaptation of methods

developed for production of  $^{68}\text{Ga}[\text{GaCl}_3]$  using liquid and solid targets to other radionuclides accessible through this technology.

Facilities can join the CRP if they meet minimal criteria necessitated by the short half-life of  $^{68}\text{Ga}$ : they must have an existing operational cyclotron with a proton beam energy  $>12$  MeV; a solid target station or a dedicated liquid target system (not in use for routine production of  $^{18}\text{F}$ ); and a dedicated synthesis module for radiometals.

Proposals to join the CRP are due no later than July 31. More information is available at <https://www.iaea.org/projects/crp/f22073>.

*International Atomic Energy Agency*

### Imaging Volumes Down During Pandemic

Volumes for imaging procedures after nationwide lockdowns remained markedly low in late April but, accord-

ing to one source, appeared to be stabilizing across the United States. Quinsite, LLC (Chapel Hill, NC), a health care analytics and consulting firm, releases daily updated reports on the effect of the COVID-19 pandemic on radiology practices. As of April 27, the website indicated that the estimated lost revenue in radiology practices was \$37,000 per full-time employee since a designated pandemic effect start date of March 16. The work Relative Value Unit impact was  $-45.1\%$ . The greatest effects were seen in the western states, where imaging volumes were off  $46.8\%$ , with comparable figures of  $42.6\%$  in the east and  $45.5\%$  in the middle states. The data are also broken down by weekly changes, with the drop in average daily volumes in the April 27 report at  $48.2\%$ , not quite as precipitous as that in previous weeks. Mammography has experienced the greatest drop in average daily volume,  $78.8\%$  since March.

*Quinsite LLC*

## 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.*

### $^{18}\text{F}$ -FDG Uptake and Atrial Arrhythmia in Cardiac Sarcoidosis

In an article e-published on April 19 ahead of print in the *International Journal of Cardiology*, Yodogawa

et al. from the Nippon Medical School (Tokyo, Japan) and the Chiba Hokusou Hospital (Japan) reported on an investigation of the presence of atrial  $^{18}\text{F}$ -FDG uptake on PET/CT in patients with cardiac sarcoidosis and the relationship with atrial arrhythmia. The retrospective study included 62 patients with cardiac sarcoidosis who underwent PET/CT imaging and echocardiography, as well as serum studies. Twenty-five patients ( $40.3\%$ ) had atrial arrhythmia (2 with atrial tachycardia and 23 with atrial fibrillation). Eighteen of the 25 patients with atrial arrhythmia were found to have atrial uptake on PET/CT ( $72.0\%$ ), and 14 of the 37 ( $37.8\%$ ) without atrial arrhythmia had atrial uptake. A significant association was found between atrial arrhythmia and age, atrial  $^{18}\text{F}$ -FDG uptake, and left atrial diameter. Sex, serum tests, and left ventricular ejection fraction were not found to have significant associations with atrial arrhythmia.

*International Journal of Cardiology*

### PET/CT and CE-CT Discrepancy in Inflammatory Breast Cancer

Jacene et al. from the Dana-Farber Cancer Institute/Brigham and Women's Hospital (Boston, MA) reported on April 21 ahead of print in *Breast Cancer Research and Treatment* on a study comparing contrast-enhanced CT (CE-CT) with  $^{18}\text{F}$ -FDG PET/CT in initial staging of inflammatory breast cancer, looking at resulting discrepancies in imaging results and potential effects on patient management. The study included 81 women with inflammatory breast cancer who underwent both PET/CT and CE-CT before treatment. Images were independently interpreted for locoregional and distant metastases, with findings classified by anatomic site as negative, equivocal, or positive for breast cancer involvement. Paired imaging findings were then reviewed as concordant or discordant. Discordant findings were characterized as related