

PET imaging results. In this clinical study, 97% of individuals with Lumipulse G  $\beta$ -amyloid Ratio (1-42/1-40)-positive results had amyloid-positive PET findings, and 84% with negative test results had negative PET findings. The FDA noted that the Lumipulse G  $\beta$ -amyloid Ratio (1-42/1-40) is not a standalone test and that other clinical evaluations or additional tests should be used for determining treatment options.

The Lumipulse G  $\beta$ -amyloid Ratio (1-42/1-40) was granted Breakthrough Device designation, a process designed to expedite the development and review of devices that may provide for more effective treatment or diagnosis of life-threatening or irreversibly debilitating diseases or conditions.

*U.S. Food and Drug Administration*

### Hearing on FIND Act Requested

On April 28, SNMMI and more than 70 organizations sent a letter to U.S. House Energy and Commerce and Ways and Means Committee leadership

requesting a hearing on the Facilitating Innovative Nuclear Diagnostics (FIND) Act. In July 2021, Reps. Scott Peters (CA), Bobby Rush (IL), Greg Murphy (NC), and Neal Dunn (FL) introduced the FIND Act (H.R. 4479), legislation that would significantly expand patient access to advanced nuclear diagnostic imaging technologies. The bill aims for a legislative fix to Centers for Medicare and Medicaid Services bundling of diagnostic radiopharmaceuticals in the hospital outpatient space after a 3-year passthrough period after U.S. Food and Drug Administration (FDA) approval. SNMMI and its coalition partners, the Medical Imaging & Technology Alliance and the Council on Radionuclides and Radiopharmaceuticals—in addition to dozens of patient advocacy organizations—praised the introduction.

The FIND Act addresses structural issues in the packaging methodology used in the Medicare outpatient hospital setting by directing the Department of Health and Human Services to pay

separately for all diagnostic radiopharmaceuticals with a cost threshold per day of \$500. If passed, this bill would give patients greater access to a wide range of diagnostic radiopharmaceuticals. This legislation would also help providers better manage costs while delivering more targeted and cost-efficient care. If passed, patients would not be responsible for the 20% drug copayment. The bill is also budget neutral. “This policy will safeguard Medicare beneficiary access to the most appropriate diagnostic radiopharmaceuticals and help spur continued innovations in nuclear imaging studies,” wrote the letter’s signatories. “To help advance this legislation, we again respectfully ask that your committees hold a hearing to consider the FIND Act and explore the potential of this policy to expand beneficiary access to care, improve health outcomes, create health care savings, and promote innovation and development in this space.”

*SNMMI*

## 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 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 radio-labels 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.*

### Preoperative PET and Long-Term Survival in Breast Cancer

Perrin et al. from CHU de Martiniq (Fort-de-France), Universitair Ziekenhuis Brussel (Belgium), Howard

University (Washington, DC), and Hackensack University Medical Center (NJ) reported on April 24 in the *World Journal of Clinical Oncology* (2022; 13[4]:287–302) on a study evaluating the predictive value of preoperative  $^{18}\text{F}$ -FDG PET for overall long-term survival in patients with breast cancer. In this retrospective study, 104 patients’ preoperative PET images were defined as positive or negative based on anatomic region-of-interest (ROI) findings for breast, axillary, sternal, and distant sites.  $\text{SUV}_{\text{max}}$  results in these ROIs were analyzed in the data from 36 of these patients. The follow-up period for the study was 15 y. PET positivity in axillary, sternal, and combined axillary/sternal nodes was predictive of poor overall survival. PET-positive axillary and combined axillary/sternal status were also predictive of poor disease-free survival. On additional analysis,  $\text{SUV}_{\text{max}}$  results for ipsilateral breast and axilla were significant covariate

predictors of long-term overall survival, with relative increases in risk of death of 25% and 54%, respectively, per  $\text{SUV}_{\text{max}}$  unit. The ratio of the ipsilateral axillary  $\text{SUV}_{\text{max}}$  to that of the contralateral axillary was the most significant predictor of overall survival, suggesting a 2-fold relative increase in mortality risk. The authors concluded that “preoperative PET is valuable for prediction of long-term survival” in patients with breast cancer, adding that “ipsilateral axillary  $\text{SUV}_{\text{max}}$  ratio over the uninvolved side represents a new prognostic finding that warrants further investigation.”

*World Journal of Clinical Oncology*

### Predictive Value of SPECT/CT in Neck Pain Treatment

In an article published on May 7 ahead of print in the *Spine Journal*, Nolan et al. from the University of Vermont Medical Center/Robert Larner,

MD, College of Medicine (Burlington) reported on a study evaluating the utility of SPECT/CT in patients with axial neck pain for identifying specific facet joints that would benefit from steroid injections and/or medial branch block/radiofrequency ablation treatments. The retrospective study included data from 112 patients with neck pain who had undergone SPECT/CT and had no prior related treatment. All patients were treated with facet intervention by injection with steroid and local anesthetic or medial branch block with local anesthetic at sites determined by physicians based on clinical examination and image interpretation. Positive responses to the interventions were defined at both 50% and 80% thresholds for reduction in pain within 24 h and correlated with the focus of maximal uptake on SPECT/CT. Increased uptake was seen at the level of intervention in 89 patients. In the remaining 23, no uptake was seen at the level of intervention. Analysis of these results showed that intervention at a level concordant with SPECT/CT was significantly correlated with self-reported pain relief thresholds at 24 h. The authors concluded that facet interventions based on uptake on SPECT/CT were more successful in pain reduction than those that were not, suggesting “a role for SPECT/CT in diagnosing therapeutic targets for neck pain.”

*Spine Journal*

### **<sup>125</sup>I-BMIPP SPECT/CT vs PET/CT for BAT Imaging**

Frankl et al. from the University of Texas Southwestern Medical Center (Dallas), McGovern Medical School/University of Texas Health Science Center at Houston, Central Taiwan University of Science and Technology (Taichung City), and Texas Tech Health Sciences Center (El Paso) reported on April 28 in the *International Journal of Molecular Sciences* (2022; 23[9]:4880) on a preclinical study comparing <sup>125</sup>I-β-methyl-*p*-iodophenylpentadecanoic acid (<sup>125</sup>I-BMIPP; a fatty acid analog) SPECT/CT and <sup>18</sup>F-FDG PET/CT in noninvasive evaluation of

metabolically active adipose tissue, including brown adipose tissue (BAT). Mice treated with either a BAT-stimulating drug or saline vehicle control were imaged with both <sup>125</sup>I-BMIPP SPECT/CT and <sup>18</sup>F-FDG PET/CT, and tracer uptake was assessed in interscapular BAT, inguinal white adipose tissue, and gonadal white adipose tissue. Uptake of both tracers increased in BAT and inguinal white adipose tissue after the BAT-stimulating drug, with SUV<sub>means</sub> correlating closely with the adipose tissue deposits. However, <sup>125</sup>I-BMIPP uptake in BAT and inguinal white adipose tissue more closely correlated with fold changes in metabolic rate as measured by an extracellular flux analyzer. The authors concluded that “imaging BAT with the radioiodinated fatty acid analogue BMIPP yields more physiologically relevant data than <sup>18</sup>F-FDG-PET/CT” and that its routine use “may be a pivotal tool for evaluating BAT in both mice and humans.”

*International Journal of Molecular Sciences*

### **PET/CT and Disease Extent in Kaposi Sarcoma**

Pesqué et al. from Saint Louis University Hospital/Assistance-Publique Hôpitaux de Paris, Université de Paris Cité, and Cochin University Hospital (all in Paris, France) reported on April 27 in *Cancers (Basel)* (2022;14[9]: 2189) on a study exploring the diagnostic accuracy of <sup>18</sup>F-FDG PET/CT in defining the extent of disease in patients with Kaposi sarcoma. The study included 75 patients who underwent PET/CT, for which the diagnostic accuracy for cutaneous and extracutaneous Kaposi sarcoma staging was assessed on a per lesion basis. These results were compared with conventional staging from clinical examination, standard imaging, endoscopy, and histologic analyses, as well as follow-up data. The sensitivity and specificity of PET/CT for overall detection of lesions were 71% and 98%, respectively (with corresponding percentages of 100% and 85% for lymph nodes, 87% and 98% for bone, 87% and 100% for lungs, and 100% and 100% for

muscle involvement). Sensitivity was only 17% in detecting digestive involvement. The sensitivity for diagnosing cutaneous involvement was increased from 73% to 88% when whole-body PET/CT was used. The authors concluded that these data suggest that <sup>18</sup>F-FDG could be used for staging patients with active Kaposi sarcoma.

*Cancers (Basel)*

### **Postradiation PET in Cervical Cancer Management**

In an article published on May 7 ahead of print in *Gynecologic Oncology*, Mckinnish et al. from Washington University School of Medicine in St. Louis (MO), CoxHealth (Springfield, MO), and Dartmouth Hitchcock Medical Center (Lebanon, NH) detailed the effects of postradiation <sup>18</sup>F-FDG PET in management and outcomes in cervical cancer patients. The study included 81 women who showed a partial metabolic response on initial postradiation PET imaging. Thirty of these patients underwent cervical biopsy, of whom 14 (47%) had persistent cancer, with 9 undergoing treatment (surgery, 3; chemotherapy alone, 5; and chemotherapy and radiation; 1). Progression-free and overall survival were similar regardless of treatment type and with or without treatment. A second surveillance PET examination showed a positive-predictive value of 91% and negative-predictive value of 75% for progression and identified the 19% of patients with persistent extracervical disease. The results of cervical biopsy produced a higher positive-predictive value (100%) and lower negative-predictive value (62.5%) for progression. At the end of the study period, 46 (57%) patients had died, including all 8 with paraaortic or supraclavicular involvement. The authors concluded that if partial metabolic response is identified on 3-mo <sup>18</sup>F-FDG PET after completion of radiation for cervical cancer, “repeat FDG PET and/or biopsy are indicated to detect persistence and assist in counseling” and that “partial metabolic response predicts poor outcomes, particularly for those

with positive cervical biopsies and lymphatic involvement.”

*Gynecologic Oncology*

### **<sup>68</sup>Ga-PSMA PET and Locally Ablative RT in Prostate Cancer**

Hölscher et al. from the University Hospital Carl Gustav Carus/Technische Universität Dresden, National Center for Tumor Diseases (NCT) (Dresden), German Cancer Research Center (DKFZ) (Heidelberg), Klinikum Chemnitz GmbH/Medizin-campus Chemnitz der TU Dresden (Chemnitz), University Hospital Tübingen, RKH-Kliniken Ludwigsburg/Academic Hospital of University Heidelberg (Ludwigsburg), and the Helmholtz-Zentrum Dresden-Rossendorf/Institute of Radiooncology-OncoRay (Dresden, all in Germany) reported on April 21 in *Cancers (Basel)* (2022;14[9]:2073) on the results of a prospective clinical trial to evaluate local control and patterns of tumor progression in patients receiving <sup>68</sup>Ga-prostate-specific membrane antigen (<sup>68</sup>Ga-PSMA) PET-staged metastasis-directed local ablative radiation treatment (RT) for recurrent oligometastatic prostate cancer. The study included 63 patients who received ablative RT for 89 metastases (68 lymph node, 21 bony) with either 50 Gy in 2-Gy fractions (34 metastases) or 30 Gy in 10-Gy fractions (55 metastases). Mean gross tumor and planning target volumes were 2.2 and 14.9 mL, respectively. Over a median follow-up of 40.7 mo, local progression was identified in 7 metastases, for a 3-y local control rate of 93.5%. Local progression was not associated with treatment schedule, target volumes, or lesion types. Regional progression near lymph node metastases was observed in 19 of 47 patients with at least 1 lymph node metastasis, and distant progression was seen in 33 patients (52%). The overall median time to first tumor-related clinical event was 16.6 mo, with 22.2% of participants experiencing no tumor-related clinical event at 3 y after RT ablation. Fourteen patients (22%) underwent repeat RT ablation. The authors concluded that “local ablative RT in patients with PSMA PET–

staged oligometastatic prostate cancer may achieve local control, but regional or distant progression is common,” adding that additional studies are needed to define optimal target volumes in this setting.

*Cancers (Basel)*

### **Experience with Lenvatinib for Advanced Thyroid Cancer**

Hamidi et al. from the Centre Hospitalier de l'Université de Montréal (Canada) reported on March 23 ahead of print in the *Journal of the Endocrine Society* on their institution's experience with lenvatinib in treatment of advanced radioiodine-refractory differentiated thyroid carcinomas, with a focus on adverse events of the type reported in clinical trials. The study included 27 patients, whose records were reviewed retrospectively. Twenty-four of the patient records included evaluation of tumor response during treatment. Their overall response rate was 37.0%, and the disease control rate was 85.2%. For all patients, median progression-free survival was 12 mo. Adverse events noted were hypertension (77.8%), fatigue (55.6%), and weight loss (51.9%). Twenty-five patients (92.6%) experienced at least 1 grade  $\geq 3$  adverse event, with 59.3% experiencing hypertension. Lenvatinib administration was discontinued because of adverse events in 13 patients (48.1%). One patient experienced a grade 4 posterior reversible encephalopathy syndrome, and 1 patient developed a Takotsubo cardiomyopathy. These findings, as well as survival statistics, were similar to those from clinical trials of lenvatinib. The authors concluded that “rigorous blood pressure control is essential to avoid discontinuing therapy” in this setting.

*Journal of the Endocrine Society*

### **Reducing Motion-Related Inaccuracies in <sup>99m</sup>Tc-MAA SPECT/CT SIRT Planning**

In an article published on May 5 in *Physica Medica* (2002;98:98–112) Santoro et al. from the IRCCS Azienda Ospedaliero-Universitaria di Bologna

(Italy) reported on development of a data-driven solution to correct for respiratory motion in <sup>99m</sup>Tc-macroaggregated albumin (<sup>99m</sup>Tc-MAA) SPECT/CT pretreatment planning for <sup>90</sup>Y selective internal radiation therapy (SIRT) in primary and secondary hepatic lesions. The resulting tool realigns the functional centers of SPECT projection images and shifts them to derive a close registration with attenuation maps. The authors describe validation of the technique using a modified dynamic phantom with varied breathing patterns. The tool was applied and analyzed in 12 patients undergoing SIRT. Significant improvements over conventional techniques were noted. The authors concluded that “the proposed tool allowed the correction of <sup>99m</sup>Tc-MAA SPECT/CT images, improving the accuracy of the absorbed dose distribution.”

*Physica Medica*

### **Additional Value of SPECT in CCTA**

Javaid et al. from the University of Nevada Las Vegas School of Medicine, the Houston Methodist DeBakey Heart and Vascular Center (Texas), and Texas A&M College of Medicine (Bryan) reported on April 15 ahead of print in the *International Journal of Cardiology* on an exploration of the incremental prognostic role of SPECT physiologic assessment to coronary computed tomographic angiography (CCTA) in patients with suspected coronary artery disease. The study included 956 patients (mean age, 61.1  $\pm$  14.2 y; 54% men, 46% women; 89% with hypertension, 81% with diabetes, and 84% with dyslipidemia) with suspected coronary artery disease who underwent clinically indicated CCTA within 180 d of SPECT imaging. Patients were followed for major adverse cardiovascular events (all-cause death, nonfatal myocardial infarction, and percutaneous coronary intervention or coronary artery bypass grafting within 90 d after imaging). Obstructive stenosis was identified in 14% of patients, scar (fixed perfusion defect) in 17%, ischemia in 14%, and left ventricular ejection fraction <40% in 9%. Additional analyses

showed that perfusion and left ventricular function when added to a model with CCTA obstructive stenosis significantly improved risk prediction and risk reclassification on a continuous scale. The authors concluded that these data indicated that “a combined assessment of perfusion burden and left ventricular function added incremental value over and above a CCTA-based anatomic assessment in patients with suspected coronary artery disease.”

*International Journal of Cardiology*

### Optimal Radioiodine Treatment in Hyperthyroidism

In an article published on April 25 in *Thyroid Research* (2022;15[1]:8) Nilsson et al. from the Karolinska Institutet/Karolinska University Hospital (Stockholm, Sweden) reported on a study addressing appropriate activity dosages and pretherapeutic measurements required for optimal radioiodine treatment of hyperthyroidism. The retrospective study included outcomes and treatment parameters for 904 patients treated for Graves disease (prescribed absorbed dose, 120 Gy), toxic multinodular goiter (200 Gy), or solitary toxic adenoma (300 Gy) from 2016 to 2020 at a single institution. Cure rates for hyperthyroidism after a single radioiodine administration were 79% for Graves disease, 94% for toxic multinodular goiter, and 98% for solitary toxic adenoma. Thyroid mass, uptake, and effective half-life were significantly associated with cure in Graves disease but not in toxic multinodular goiter. Therapy-induced hypothyroidism occurred in 20% and 29% of patients with toxic multinodular goiter and solitary toxic adenoma, respectively. In patients with toxic nodular goiters who received individualized effective half-

life assessments, cure rates and hypothyroidism rates were not improved over patients who did not have such assessments. Poor renal function was found to be associated with what the authors termed “dubious” iodine uptake measurements but did not correlate with worse outcomes. The authors concluded that “multiple measurements of individual iodine uptake for kinetics estimation may be unnecessary” in treatment of hyperthyroidism and that a population-based value may be used instead. Patients with renal impairment were found to have outcomes similar to those of other patients, despite a higher incidence of confounding uptake measurements.

*Thyroid Research*

### Reviews

Review articles provide an important way to stay up to date on the latest topics and approaches through valuable summaries of pertinent literature. The Newsline editor recommends several general reviews accessioned into the PubMed database in April and May. Borgheresi, from the University Politecnica delle Marche (Ancona, Italy), and colleagues from a consortium of research entities in Italy published “Lymph nodes evaluation in rectal cancer: Where do we stand and future perspective” on May 5 in the *Journal of Clinical Medicine* (2022;11[9]:2599). In an article published on April 28 ahead of print in *The Oncologist*, Wirth, from Harvard Medical School/Massachusetts General Hospital (Boston), and researchers from Sapienza University of Rome (Italy), Alfred Health/Monash University (Melbourne, Australia), the University of Western Ontario (London, Canada), Rabin Medical Center/Beilinson Hospital, Tel Aviv University (Israel), Kanagawa Cancer Center (Japan), University Hospital Marburg (Germany), Univer-

sity of Pisa (Italy), Gustave-Roussy Institut (Villejuif, France), the University of Paris-Saclay (Gif-sur-Yvette, France), and the National Cancer Center Hospital East (Kashiwa, Japan) reviewed “Lenvatinib for the treatment of radioiodine-refractory differentiated thyroid cancer: Treatment optimization for maximum clinical benefit.” Huan, from the First Affiliated Hospital of Dalian Medical University (China), and researchers from the Second Affiliated Hospital of Guangzhou University of Chinese Medicine (China), the University of West London (UK), Hainan General Hospital (Haikou, China), and Rutgers University (New Brunswick, NJ) published “Brain imaging changes in patients recovered from COVID-19: A narrative review” on April 22 in *Frontiers in Neuroscience* (2022;16:855868). “New advanced imaging parameters and biomarkers: A step forward in the diagnosis and prognosis of TTR cardiomyopathy” were summarized by Rimbas and colleagues from the University and Emergency Hospital and the University of Medicine and Pharmacy Carol Davila (both in Bucharest, Romania) on April 22 in the *Journal of Clinical Medicine* (2022; 11[9]:2360). Kaliszewski et al. from Wroclaw Medical University (Poland) reported in the April 17 issue of *Cancers (Basel)* (2022;14[8]:2028) on “Advances in the diagnosis and therapeutic management of gastroenteropancreatic neuroendocrine neoplasms.” In an article published on April 22 in *Endocrine-Related Cancer* (2022;29[5]:R57–R66), Karapanou et al. from the General Military Hospital of Athens, Alexandra Hospital/Athens University School of Medicine, and Evangelismos Athens General Hospital (all in Greece) reported on “Advanced RAI-refractory thyroid cancer: An update on treatment perspectives.”