

Each dose of Breyanzi is a customized treatment created using a patient's own T cells, which are collected and genetically modified to include a new gene that facilitates targeting and killing of the lymphoma cells. Once modified, the cells are infused into the patient. The safety and efficacy of Breyanzi were established in a multicenter clinical trial of >250 adults with refractory or relapsed large B-cell lymphoma (*Lancet*. 2020;396 [10254]:839–852). The complete remis-

sion rate after treatment was 54%. Because severe side effects include the risk of cytokine-release syndrome and neurologic toxicities, Breyanzi was approved with a risk evaluation and mitigation strategy, which includes elements to assure safe use. To further evaluate the long-term safety, the FDA is also requiring the manufacturer to conduct a post-marketing observational study.

The FDA granted Breyanzi Orphan Drug, Regenerative Medicine Advanced

Therapy (RMAT), and Breakthrough Therapy designations. Breyanzi is the first regenerative medicine therapy with RMAT designation to be licensed by the FDA. The Breyanzi application was reviewed using a coordinated, cross-agency approach, including both the Center for Biologics Evaluation and Research and the FDA Oncology Center of Excellence.

U.S. Food and Drug Administration

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.

DaTscan and PD Management in NSDD

Isaacson et al. from the Parkinson's Disease and Movement Disorders Center of Boca Raton (FL) reported on February 1 ahead of print in the *Journal of Parkinson's Disease* on the clinical impact of ^{123}I -ioflupane (DaTscan) SPECT brain imaging ordered for evaluation of nigrostriatal dopaminergic degeneration (NSDD) associated with movement disorders. The study included 201 patients with clinically questionable NSDD, their pre- and postscanning diagnoses, and any changes in management. Overall, DaTscan was abnormal in 58.7%, inconclusive in 3.5%, and normal in the remaining patients. DaTscan imag-

ing changed clinical diagnoses in 39.8% of patients and resulted in medication therapy changes in 70.1%. The authors concluded that DaTscan imaging can be useful in determining the presence of NSDD in several relevant clinical scenarios, including in patients with early subtle symptoms, suboptimal response to levodopa, prominent action tremor, drug-induced parkinsonism, and/or with lower extremity or other less common parkinsonism clinical symptoms. Imaging was also useful in identifying underlying NSDD in patients who had been diagnosed with Parkinson disease 3–5 y previously without clinical progression or development of motor fluctuations.

Journal of Parkinson's Disease

^{177}Lu -PSMA-617 vs Cabazitaxel in MCRPC

In an article published on February 11 ahead of print in the *Lancet*, Hofman and multiple collaborators from the TheraP Trial Investigators and the Australian and New Zealand Urogenital and Prostate Cancer Trials Group reported on a multicenter randomized phase 2 trial comparing ^{177}Lu -prostate-specific membrane antigen (PSMA)-617 therapy with cabazitaxel treatment in patients with metastatic castration-resistant prostate cancer. The study included individuals from 11 centers in Australia in whom cabazitaxel had been considered the next appropriate standard treatment. All participants underwent ^{68}Ga -PSMA-11 and ^{18}F -FDG PET imaging and were

determined eligible for the trial with PSMA-positive disease and no sites of metastatic disease with discordant ^{18}F -FDG-positive and PSMA-negative findings. Participants were randomly assigned to treatment with ^{177}Lu -PSMA-617 ($n = 98$) or cabazitaxel ($n = 85$). The primary endpoint was prostate-specific antigen (PSA) response defined by a reduction of at least 50% from baseline. Responses in PSA levels were more frequent in the ^{177}Lu -PSMA-617 group than the cabazitaxel group (65 and 37 responses, respectively). Grade 3–4 adverse events occurred in 32 (33%) ^{177}Lu -PSMA-617 patients and in 45 (53%) in the cabazitaxel group. These and other data from the study led the authors to conclude that ^{177}Lu -PSMA-617 “is a new and effective class of therapy and a potential alternative to cabazitaxel.”

Lancet

PSMA PET Post-RT PCa Biochemical Recurrence

Rowe et al. from the National Cancer Institute (Bethesda, MD), Cross Cancer Institute (Edmonton, Canada), the Frederick National Laboratory for Cancer Research (MD), and the Walter Reed National Military Medical Center (Bethesda, MD) reported in the February 10 issue of *Radiation Oncology* on a study using PET and multiparametric MR imaging to identify patterns of failure in a group of patients who received adjuvant or salvage radiation therapy after prostatectomy and later experienced biochemical recurrence.

The study characterized lesions from 2 prospective trials of first- and second-generation ^{18}F -PSMA PET agents (^{18}F -DCFBC and ^{18}F -DCFpyL), with postimaging fusion with multiparametric MR imaging where available. The primary aim was to identify the location of lesions relative to previous radiation therapy fields and doses. The study included 35 participants, 32 of whom were found to have ^{18}F -PSMA-avid lesions. Seventeen (43.1%) of these patients had metastatic disease, 8 (25.0%) had locoregional recurrence, and 7 (21.9%) had local failure in the prostate fossa. Of this last group, 6 (86%) experienced in-field failures that had been encompassed by 100% isodose lines. The seventh patient experienced marginal failure encompassed by the 49-Gy isodose. In all, ~1 of 5 patients with unremarkable conventional imaging findings had detectable in-field failure despite postoperative radiotherapy, and 1 in 3 had oligometastatic disease. The authors concluded that these findings emphasize “the importance of future research in tailoring radiotherapy target delineation, investigating radiation dose escalation, or use of systemic treatment concomitantly with radiotherapy to optimize local control and improve metastasis-free survival in these patients.”

Radiation Oncology

Automated PET Mapping and AD Conversion Prediction

In an article published on February 12 ahead of print in *Current Alzheimer Research* Garibotto et al. from the University of Geneva/University Hospitals of Geneva (Switzerland), the University of Côte d’Azur (Nice, France), the IRCCS Fondazione Stella Maris (Pisa, Italy), the IRCCS Fatebenefratelli (Brescia, Italy), IRCCS AOU San Martino-IST (Italy), Ludwig-Maximilians-Universität München (Germany), Aix-Marseille Université (France), the Technische Universität (Münich, Germany), and VU University Medical Center (Amsterdam, The Netherlands) reported on a study evaluating 2 clinically validated tools for analysis of

cortical hypometabolism on ^{18}F -FDG PET in identification of individuals with mild cognitive impairment (MCI) likely to progress to Alzheimer disease (AD). The 2 automated mapping tools, SPMGrid and BRASS, were assessed using PET imaging data from 131 individuals with MCI and healthy elderly controls from the European Alzheimer’s Disease Consortium PET dataset. Three experienced readers blindly assigned diagnoses based on the 2 resulting map sets, and these data were compared against subsequent clinical conversion to AD among the subjects. BRASS showed significantly higher sensitivity than SPMGrid (82% and 59%, respectively), although good correlation was shown between mapping in the z and t maps between the respective systems. The 2 tools, however, showed significant differences, with maps that showed limited overlap in hypermetabolic patterns. The authors concluded that “these results underline the urgency for standardization across FDG-PET analysis methods for their use in clinical practice.”

Current Alzheimer Research

SPECT/CT and Lymphatic Drainage in Penile Cancer

Jakobsen et al. from Aarhus University/Aarhus University Hospital (Denmark) reported on February 11 ahead of print in the *Scandinavian Journal of Urology* on a study using SPECT/CT to assess lymphatic drainage in invasive penile cancer and the utility of resulting information for inguinal lymph node dissection. The study included data from 62 men in the Danish National Penile Cancer Quality database with uni- or bilateral clinical lymph node-negative (cN0) status. Participants underwent SPECT/CT to evaluate 122 cN0 inguinal basins, with regions divided into 10 Daseler zones. Surgeons completed a corresponding categorization at sentinel node biopsy, with histopathologic follow-up by zones. SPECT/CT visualized lymphatic drainage in 116 inguinal basins (95.1%). The large majority of sentinel nodes and all metastatic nodes were found in central and superior inguinal zones, including 6 metastatic

nodes in lateral superior zones. Minimal lymphatic drainage was seen in the inferior Daseler zones, with no metastatic deposits in these. No direct pelvic drainage was seen. The authors encouraged those using modified inguinal lymph node dissection as a standard in cN0 patients to include all the superior and central Daseler zones, whereas the inferior zones can be omitted. In summary, the study “confirms the absence of lymphatic drainage directly to the pelvic region and supports the practice of omitting pelvic nodes from sentinel node biopsy.”

Scandinavian Journal of Urology

PSMA PET and Status After Radical Prostatectomy

In an article published online on February 4 ahead of print in the *Journal of Urology*, Amiel et al. from the Technical University of Munich (Germany), University of Montréal Health Center (Canada), University Hospital Frankfurt (Frankfurt am Main, Germany), and University Hospital Hamburg-Eppendorf (Hamburg, Germany) reported on the correlation of ^{68}Ga -PSMA-11 PET findings before radical prostatectomy and pelvic lymph node dissection at biochemical recurrence and time to adjuvant or salvage treatment. The retrospective study included 64 intermediate- and 166 high-risk prostate cancer patients who underwent PET followed by surgery and lymph node dissection. The overall sensitivity, specificity, and positive- and negative-predictive values of ^{68}Ga -PSMA-11 PET for pN1 disease were 48.5%, 95.7%, 82.1%, and 82.2%, respectively. Over a median follow-up of 30.2 mo, biochemical recurrence was seen in 116 patients (50.4%), and 107 (46.5%) patients underwent adjuvant or salvage therapy. The lowest rates of biochemical recurrence-free and therapy-free survival were in patients with pN1 disease with PET-positive lymph nodes, followed by patients with pN1 disease without PET-positive lymph nodes and patients with no evidence of lymph node metastasis on histology and PET (median biochemical recurrence-free

survival: 1.7, 7.5, and >36 mo, respectively; median therapy-free survival: 2.6, 8.9, and >36 mo, respectively). The authors concluded that patients with positive lymph nodes on ^{68}Ga -PSMA-11 PET before radical prostatectomy should expect early biochemical recurrence and adjuvant/salvage therapy, despite thorough pelvic lymph node dissection. They recommended that PET results be used for patient consultation, more stringent follow-up, and planning of neo- and adjuvant therapy.

Journal of Urology

Machine Learning Methods for PET in AD

In an article published on February 11 ahead of print in the *Journal of Alzheimer's Disease*, Ma et al. from Simon Fraser University (Vancouver, Canada), Northwestern University (Chicago, IL), and Jewish General Hospital (Montréal, Canada) reported on investigations comparing 2 advanced machine-learning methods for using ^{18}F -FDG PET neuroimaging-derived features to discriminate between dementia of Alzheimer type (DAT) and non-DAT control subjects. Using clinical data, PET-based dementia scores were generated and analyzed with a feature-engineered approach (multikernel probability classifier) and a non-feature-engineered approach (3D convolutional neural network). Each of the approaches had been pretrained on individuals with DAT and on cognitively normal individuals. Analysis provided probabilistic dementia scores for the new clinical data, and the resulting classifiers were compared against a blinded evaluation by experienced nuclear physicians. Although both classifiers were able to differentiate DAT from non-DAT imaging results, the non-feature-engineered dementia score showed higher sensitivity in individuals in whom the 2 models showed agreement and the feature-engineered approach showed higher specificity in individuals in whom the 2 models were not in agreement. The authors concluded that these results “showed good generalizability for 2 machine-learning approaches, marking

an important step for the translation of pretrained machine-learning models into clinical practice.”

Journal of Alzheimer's Disease

Quantitative SPECT and Uninfected Nonunion

Oe et al. from the Kobe University Graduate School of Medicine (Japan) reported on February 10 in the *Journal of Orthopaedic Surgery and Research* (2021;16[1]:125) on a study evaluating quantitative $^{99\text{m}}\text{Tc}$ -labeled SPECT bone imaging of uninfected nonunion to compare hypertrophic nonunion and nonhypertrophic nonunion using volume-based parameters. The study included 23 patients with uninfected nonunion who underwent either $^{99\text{m}}\text{Tc}$ -hydroxymethylene diphosphonate or $^{99\text{m}}\text{Tc}$ -methylene diphosphonate SPECT imaging. The researchers performed voxel-based quantitative analysis using the GI-BONE software, with the contralateral limb as a control. For hypertrophic nonunion, quantitative parameters (high uptake area/low uptake area) for SUV_{max} control ratio were $12.13 \pm 4.95/6.44 \pm 4.71$, for SUV_{peak} control ratio were $11.65 \pm 4.58/6.45 \pm 4.64$, and for SUV_{mean} control ratio were $11.94 \pm 5.03/6.28 \pm 4.95$. These parameters were higher than the corresponding values for nonhypertrophic nonunion: $7.82 \pm 4.76/3.41 \pm 2.09$, $7.56 \pm 4.51/3.61 \pm 2.23$, and $7.59 \pm 5.18/3.05 \pm 1.91$. The authors concluded that these control ratios obtained from bone SPECT imaging “can quantitatively evaluate the biological activity of nonunions and may be an effective evaluation method for treatment decisions, especially the necessity of autologous bone grafting.”

Journal of Orthopaedic Surgery and Research

PET/CT in Advanced Epithelial Ovarian Cancer

In a study published on February 5 in the *Journal of Clinical Medicine* (2021;10[4]:602), Tardieu et al. from CHU Limoges, Tours University Hospital, Poissy-Saint-Germain-en-Laye Hospital Center, and Clermont Ferrand University Hospital (all in France) reported on a retrospective FRANCOGYN Group

study intended to evaluate the diagnostic performance of PET/CT in assessing lymph node involvement in advanced epithelial ovarian cancer. The reported results included ^{18}F -FDG PET/CT data from 63 patients with primary advanced epithelial ovarian cancer who had undergone PET/CT at the time of diagnosis or before cytoreduction surgery with pelvic or paraaortic lymphadenectomy. The sensitivity, specificity, and positive and negative predictive values of PET/CT for preoperative lymph node evaluation were 26.7%, 90.9%, 72.7%, and 57.7%, respectively. The accuracy rate was 60.3%, with a false-negative rate of 34.9%. For the 16 patients who underwent primary cytoreduction, sensitivity was 50%, specificity was 87.5%, positive predictive value was 80%, and negative predictive value was 63.6%. The accuracy rate was 68.8%, and the false-negative rate was 25%. After neoadjuvant chemotherapy ($n = 47$), PET/CT sensitivity, specificity, and positive- and negative-predictive values were 18.2%, 92%, 66.7%, and 56.1%, with an accuracy rate of 57.5% and false-negative rate of 38.3%. The authors concluded that because of its high sensitivity, a preoperative PET/CT scan “could contribute to the deescalation and reduction of lymphadenectomy in the surgical management of advanced epithelial ovarian cancer in a significant number of patients free of lymph node metastases.”

Journal of Clinical Medicine

Predicting Chemo Response in NSCLC

Zhao, Wang, et al. from Yantai Yuhuangding Hospital and Shandong Cancer Hospital and Institute/Shandong University (Jinan; all in China) reported on January 14 in *BMC Cancer* (2021;21[1]:66) on the predictive value of ^{18}F -FDG PET and blood inflammatory markers for chemosensitivity and survival in patients with stage IIIB non-small cell lung cancer (NSCLC) receiving first-line chemotherapy. The retrospective study included 149 such patients. The authors found that participants with $\text{SUV}_{\text{max}} > 11.6$ or lymphocyte-to-monocyte ratio ≤ 3.73

at baseline had significantly lower objective response rates to chemotherapy. These were identified as independent predictive factors for chemotherapeutic response and for progression-free survival. On the basis of these factors, a novel scoring system was applied to categorize participants into 3 subgroups with differing prognoses. The authors noted that the score derived from the 2 factors based on primary tumor metabolic activity and systemic inflammatory response “might provide a promising tool to predict chemosensitivity, recurrence, and survival” in advanced NSCLC.

BMC Cancer

^{99m}Tc- and Cy7-Labeled Fab(Tocilizumab) in Multiple Myeloma

Camacho et al. from the Universidad de la República (Montevideo, Uruguay), the Hospital das Clínicas da Faculdade de Medicina da Universidade de Sao Paulo (Brazil), and the Instituto de Investigaciones Biológicas Clemente Estable (Montevideo, Uruguay) reported on January 4 ahead of print in *Anticancer Agents in Medicinal Chemistry* on an evaluation of the potential of Fab(tocilizumab) labeled with ^{99m}Tc and/or cyanine-7 for targeting overexpression of interleukin-6 (IL-6) in multiple myeloma. In vitro studies with laser confocal microscopy confirmed distribution of IL-6 in multiple myeloma cell lines, and biodistribution of ^{99m}Tc-Fab(tocilizumab) was confirmed by SPECT/CT. Cyanine-7-labeled Fab(tocilizumab) provided targeted in vivo fluorescence imaging up to 72 h. Initial preclinical studies showed rapid blood clearance and significant renal and multiple myeloma-engrafted tumor uptake. The authors concluded that these studies show a potential dual use for Fab(tocilizumab): with SPECT/CT “in the clinical setting for staging and follow up of multiple myeloma through radioactive whole-body IL-6R expression visualization in vivo” and with fluorescent labeling “for tissue sample evaluation and to guide surgical excision if necessary.”

Anticancer Agents in Medicinal Chemistry

¹⁸F-FDG Avidity Factors in DTC

In an article published on January 7 in *Cancer Imaging* (2021;21[1]:8), Ha et al. from 108 Central Military Hospital (Hanoi, Vietnam), the Washington University School of Medicine (St. Louis, MO) and MRCCC Siloam Hospital (Jakarta, Indonesia) reported on an investigation of the relationships among clinicopathologic factors, BRAF V600E mutation status, and ¹⁸F-FDG avidity in patients with radioiodine-negative recurrence of metastatic differentiated thyroid cancer (DTC). The retrospective study included data from 63 patients (55 female, 8 male; median age, 48 y; range, 17–81 y), most with the BRAF V600E mutation ($n = 55$, 87.3%) and classical subtype ($n = 45$, 71.4%). Patients had received a median of 3 previous radioiodine treatments before suspected recurrence. All patients underwent ¹⁸F-FDG PET/CT, biopsy of lesions identified on imaging, and BRAF V600E mutation testing by immunohistochemistry and real-time polymerase chain reaction. Multiple resulting variables were correlated with the SUV_{max} of the highest hypermetabolic lesion on PET/CT. Of the 63 patients, 54 (85.7%) had local recurrence, and PET/CT showed FDG-avid disease in 58 (92.1%). Tumor size, aggressive histopathology, and distant metastases were found to be significant factors in predicting tracer uptake on PET/CT.

¹⁸F-FDG uptake in lesions with the BRAF V600E mutation was greater than in those without, although this difference was not statistically significant. The authors concluded that “the majority of recurrent or metastatic radioactive iodine-negative DTC have BRAF V600E mutation and detectable disease on FDG PET/CT” and that the “FDG avidity of the recurrent or metastatic radioactive iodine-negative DTC is independently associated with the aggressive histopathologic features.”

Cancer Imaging

¹¹C-Raclopride PET and fMRI in Autism

Zürcher et al. from the Massachusetts General Hospital/Harvard Medical School

(Boston), the University of North Carolina at Chapel Hill/University of North Carolina School of Medicine, North Carolina State University (Raleigh), and the McLean Hospital (Belmont, MA) reported on January 11 in *Translational Psychiatry* (2021;11[1]:33) on a study including molecular imaging in evaluation of striatal dopamine functioning in response to rewards in autism spectrum disorder. The investigation was part of an effort to expand on clinical understanding of the “social motivation hypothesis,” which suggests impaired dopamine function in specific behaviors. The authors used simultaneous ¹¹C-raclopride PET and functional MR imaging to assess striatal function in a monetary incentive challenge in 10 individuals with autism spectrum disorder and 12 controls. Differences between groups in voxel-wise binding potential on PET were used as seeds in whole-brain fMRI connectivity analyses. The autism spectrum group showed decreased phasic dopamine release in response to challenge incentives in the bilateral putamen and left caudate, in addition to increased functional connectivity between a PET-derived right putamen seed and the precuneus and insula. Decreased phasic dopamine release in the putamen was related to poorer theory-of-mind skills in the autism spectrum group. The authors concluded that “our findings that autism spectrum disorder is characterized by impaired striatal phasic dopamine release to incentives provide support for the social motivation hypothesis of autism” and that “PET-fMRI may be a suitable tool to evaluate novel autism spectrum disorder therapeutics targeting the striatal dopamine system.”

Translational Psychiatry

Tocilizumab, ¹⁸F-FDG PET, and Takayasu Arteritis

In an article published on January 13 ahead of print in the *Journal of Cardiology*, Isobe et al. from the Sakakibara Heart Institute and Tokyo Medical and Dental University (both in Tokyo, Japan) reported on the potential of ¹⁸F-FDG PET/CT for detection of recurrence of

inflammation during tocilizumab treatment for steroid-resistant Takayasu arteritis. The study was motivated by difficulties in diagnosing disease recurrence, because tocilizumab suppresses inflammatory biomarkers. The study included 17 patients under treatment with tocilizumab. Treatment resulted in abatement of arteritis symptoms and corresponding reduction of glucocorticoid dosage in 12 patients (remission induction rate, 70.6%; dosage reduced from 16.1 ± 10.2 to 3.8 ± 1.7 mg at 1 y). In the remaining 5 patients, glucocorticoid tapering was not successful, and dosages were raised. Results from ^{18}F -FDG PET imaging closely matched the clinical course in these 5 patients, even during tocilizumab treatment, and was negative in the 12 patients experiencing remission. The authors concluded that “tocilizumab injection provides robust steroid-sparing effect and improvement of inflammation without significant adverse effects” in Takayasu arteritis and that “recurrence of inflammation can be detected by FDG PET even during tocilizumab treatment.”

Journal of Cardiology

^{18}F -FDG PET/CT in Retroperitoneal Sarcomas

Subramaniam et al. from the Peter MacCallum Cancer Centre (Melbourne, Australia), St. Vincents Hospital (Melbourne, Australia), Amsterdam University Medical Center/University of Amsterdam (The Netherlands), The Netherlands Cancer Institute/Antoni van Leeuwenhoek (Amsterdam), and the University of Southern California (Los Angeles) reported on January 14 ahead of print in the *Journal of Surgical Oncology* on a study evaluating correlations between ^{18}F -FDG SUV_{max} on PET/CT and pathologic tumor grade in surgical specimens of primary retroperitoneal dedifferentiated liposarcoma (DDLPS) and leiomyosarcoma (LMS). The study included 58 patients (final pathologic subtypes: DDLPS, $n = 44$ [75.9%]; LMS, $n = 14$ [24.1%]) who had undergone preoperative PET/CT. Mean SUV_{max} was 8.7 (median, 7.1;

range, 2.2–33.9). Grades I, II, and III tumors were identified in 6 (10.3%), 35 (60.3%), and 17 (29.3%) patients, respectively. Higher histologic grade was correlated with higher SUV_{max} , and increasing SUV_{max} was associated with worse recurrence-free and overall survival. The authors concluded that ^{18}F -FDG SUV_{max} on PET/CT provides “a preoperative noninvasive surrogate marker of tumor grade and biological behavior.”

Journal of Surgical Oncology

Longitudinal Assessment in Autosomal-Dominant AD

Sanchez et al. from the Massachusetts General Hospital/Harvard Medical School (Boston), Universidad de Antioquia (Medellín, Colombia), Brigham and Women’s Hospital (Boston, MA), Hospital Pablo Tobón Uribe (Medellín, Colombia), Maastricht University (The Netherlands), and Banner Alzheimer’s Institute (Phoenix, AZ) reported on January 15 in *Alzheimer’s Research & Therapy* (2021;13[1]:27) on a study looking at the use of PET with ^{11}C -Pittsburgh compound B and ^{18}F -flortaucipir in longitudinal assessment of amyloid- β and tau accumulation, respectively, in individuals with autosomal-dominant Alzheimer disease (AD). The study included 14 autosomal-dominant AD mutation carriers (presenilin-1 E280A) and 15 age-matched noncarriers from the Colombia–Boston (COLBOS) kindred biomarker study. Each participant underwent 2–3 sessions of ^{11}C -Pittsburgh compound B and ^{18}F -flortaucipir PET and structural MR imaging, as well as neuropsychological evaluation over a 2–4-year follow-up. Longitudinal measurements were found to be consistent with the known sequence of autosomal-dominant AD-related changes, beginning with amyloid- β accumulation (16 y before expected symptom onset), then tau accumulation in the entorhinal cortex (9 y before expected symptom onset), neocortical tau (6 y before expected symptom onset), hippocampal atrophy (6 y before expected symptom onset), and cognitive decline (4 y before expected symptom onset). Rates of tau accumulation among carriers were most rapid in the parietal

neocortex, at $\sim 9\%/y$. PET identification of tau in the entorhinal cortex at baseline was a significant predictor of subsequent neocortical tau accumulation and cognitive decline in carriers. The authors concluded that these results “are consistent with the sequence of biological changes in autosomal-dominant AD implied by cross-sectional studies and highlight the importance of entorhinal cortex tau as an early biomarker and a potential link between amyloid- β burden and neocortical tau accumulation” in this disease setting.

Alzheimer’s Research & Therapy

Arterial Wall Inflammation in RA and OA

In an article published on January 14 ahead of print in *Rheumatology (Oxford)*, Agca et al. from VU University (Amsterdam, The Netherlands) reported on the use of ^{18}F -FDG PET/CT in a comparison of arterial wall inflammation in rheumatoid arthritis (RA) and osteoarthritis (OA) and the respective associations with markers of inflammation and cardiovascular risk factors. The study included 61 patients with RA and 28 with OA who underwent PET/CT, with secondary comparative analyses performed in the RA patient group (30 patients with early untreated RA and 31 with established RA under disease-modifying antirheumatic drug treatment). RA patients were found to have significantly higher ^{18}F -FDG uptake in the wall of the carotid arteries and aorta than OA patients, a difference that persisted after adjustment for traditional cardiovascular risk factors. The highest ^{18}F -FDG uptake on PET was seen in patients with early RA, followed by patients with established RA, and then by those with OA. Higher erythrocyte sedimentation rate and disease activity scores in 28 joints were associated with higher ^{18}F -tracer uptake in all arterial segments. The authors concluded that increased ^{18}F -FDG uptake in the arterial wall, as seen in patients with RA, is a possible marker of early atherosclerosis. The higher level of clinical disease activity and circulating inflammatory

markers associated with higher arterial ^{18}F -FDG uptake “may support a role of arterial wall inflammation in the pathogenesis of vascular complications in patients with RA.”

Rheumatology (Oxford)

Sestamibi SPECT/CT in Hyperparathyroidism

In an article published online on January 3 ahead of print in the *Journal of Endocrinological Investigation*, Yang et al. from the First Affiliated Hospital/Zhejiang University School of Medicine (Hangzhou, China) reported on clinicopathologic factors affecting the accuracy and potential limitations of $^{99\text{m}}\text{Tc}$ -sestamibi SPECT/CT in assessing abnormal parathyroid glands in patients with primary hyperparathyroidism. The study included 96 patients with primary hyperparathyroidism (mean age, 54 y; 63 women, 33 men), and discordance between SPECT/CT and intraoperative findings was noted in 17. Of these, 10 had major discordance, most in patients with multigland disease. Patients with intraoperative findings concordant with SPECT/CT when compared with discordant patients showed decreased frequencies of autoimmune thyroid disease (10.1% and 29.4%, respectively),

multigland disease (3.8% and 41.2%, respectively), higher parathyroid hormone levels (296 and 146 pg/mL, respectively), and lower phosphorus levels (0.90 and 0.77 mmol/L, respectively). Multigland disease, parathyroid lesion size ≤ 12 mm, and parathyroid hormone level > 192.5 pg/mL were independently associated with discordant CT results. The authors concluded that “surgeons should recognize these potential limitations, which may improve the preoperative procedure by encouraging further localization imaging and promptly facilitate intraoperative troubleshooting.”

Journal of Endocrinological Investigation

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 Newslines editor recommends several general reviews accessioned into the PubMed database in February and March. Morrison and Han, from Oregon Health and Science University (Portland) provided an overview of the status and state of the art of “Re-evaluation of sentinel lymph node biopsy for melanoma” in the February 9 issue

of *Current Treatment Options in Oncology* (2021;22[3]:22). In an article online on February 9 ahead of print in *NeuroOncology*, Barajas, also from the Oregon Health and Science University, and a large group of international researchers published “Consensus recommendations for MRI and PET imaging of primary central nervous system lymphoma: Guidelines statement from the International Primary CNS Lymphoma Collaborative Group (IPCG).” Cope et al. from the University of Cambridge/Cambridge University Hospitals NHS Foundation Trust (UK), University College London (UK), Otto-von-Guericke University Magdeburg (Germany), and Massachusetts General Hospital/Harvard Medical School (Boston) described “Advances in neuroimaging to support translational medicine in dementia” in the March issue of the *Journal of Neurology, Neurosurgery, and Psychiatry* (2021;92[3]:263–270). In an article online on February 11 ahead of print in the *International Brazilian Journal of Urology*, Matushita et al. from a consortium of Brazilian hospitals and clinical research sites published “ ^{68}Ga -prostate-specific membrane antigen (PSMA) PET in prostate cancer: A systematic review and metaanalysis.”