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.

Radiomic Features of PET/CT in NSCLC

Krarup et al. from the Rigshospitalet/Copenhagen University Hospital (Denmark) and King's College London/St. Thomas' Hospital (UK) reported on November 13 ahead of print in *Radiotherapy and Oncology* on a study assessing potentially prognostic radiomic features on ^{18}F-FDG PET/CT in patients with non–small cell lung cancer undergoing definitive chemoradiotherapy. The retrospective study included data from 233 such patients (145 men, 88 women; mean tumor volume, 129.873 cm^3) who had undergone PET/CT for radiation therapy planning. Preselected prognostic and reproducible PET texture and shape features were calculated. Correlations between radiomic features and metabolic active tumor volumes (MTVs), gross tumor volumes (GTVs), SUV$_{max}$, and SUV$_{mean}$ were derived to yield data on the predictive value of radiomic features. Texture and shape features were found to be more strongly correlated to MTV and GTV than to SUV$_{max}$ or SUV$_{mean}$. Four radiomic features predicted progression-free survival in univariate but not in multivariate analyses. The selected radiomic features also did not predict progression-free survival when combined with any of the other variables. The authors concluded that "These results might be due to variations in technical parameters. However, it is relevant to question whether radiomic features are stable enough to provide clinically useful information."

Radiotherapy and Oncology

Automated Quantitative Tools in AD Assessment

In an article in the November issue of *Medicine (Baltimore)* (2019;98[45]: e17824), Ferrari et al. from the Hospital Israelita Albert Einstein and the Universidade de São Paulo (both in São Paulo, Brazil) investigated the sensitivity and specificity of hippocampal volume and glucose metabolism in patients being evaluated for Alzheimer disease (AD), using automated quantitative tools. The study included 38 patients ≥45 y old with suspected AD, who had undergone ^{18}F-FDG PET/CT and MR imaging as part of clinical assessment. PET/CT images were analyzed qualitatively and with Scenium software. MR images were analyzed with NeuroQuant software. Final diagnoses after a mean follow-up period of 23 ± 11 mo were AD or high-risk mild cognitive impairment (MCI) for 16 patients (8 men, 8 women; average age, 69.38 ± 10.98 y). For the other 22 patients (14 women, 8 men; 67.50 ± 11.60 y), a diagnosis of AD was initially excluded but patients may have had low-risk MCI. Qualitative PET/CT analyses showed greater accuracy, sensitivity, and negative predictive value than quantitative PET analysis, hippocampal MR volumetry, or specificity. The positive predictive value of PET/CT was similar to that of MR imaging. The authors concluded that the fact that ^{18}F-FDG PET/CT qualitative analysis was significantly more effective than MR volumetry may, in part, "corroborate the sequential hypothesis of AD pathophysiology, which posits that functional changes (synaptic dysfunction) precede structural changes (atrophy)."

Medicine (Baltimore)

^{18}F-DOPA PET + MR in MTC Liver Staging

Puhr-Westerheide et al. from University Hospital/Ludwig Maximilians Universität München (Germany) reported in the November 14 issue of *Cancer Imaging* (2019;19:73) on the potential value of adding gadoxetic acid–enhanced MR imaging to ^{18}F-DOPA PET/CT for liver staging in medullary thyroid carcinoma (MTC). The retrospective study included 36 patients (14 women, 22 men; median age, 55 y) with histologically proven MTC who had undergone gadoxetic acid–enhanced liver MR and matching contrast-enhanced ^{18}F-DOPA PET/CT imaging within a 1-mo period. The imaging datasets were categorized on visual assessment for likelihood of metastases and differences in detection and characterization of lesions. Follow-up PET/CT and MR imaging were used as a reference standard. In all, 207 liver lesions (152 metastases, 37 benign cysts, 18 hemangiomas) were detected and analyzed (149 on ^{18}F-DOPA PET/CT, 207 on MR imaging). Of the 58 additional lesions detected by MR imaging, 54 were metastases (median diameter, 0.5 cm) not detected on ^{18}F-DOPA PET/CT. MR imaging allowed for definite lesion classification in 92% (190/207), compared with only 76% (113/149) for ^{18}F-DOPA-PET/CT. MR results also led to a change in category in 14% of lesions detected by PET/CT (21/149). The authors concluded that "gadoxetic acid–enhanced MRI allows for a more precise liver staging in MTC patients than ^{18}F-DOPA PET/CT alone, particularly for ^{18}F-DOPA–negative metastases and lesions <1 cm."

Cancer Imaging

PET/CT and Relapse Risk in GCA

In an article e-published ahead of print on November 12 in *Clinical Rheumatology*, Bellan et al. from the Università del Piemonte Orientale, Maggiore della Carità Hospital, and the Interdisciplinary Research Center of Autoimmune

Diseases (all in Novara, Italy) reported on the potential prognostic value of PET in stratification of relapse risk in patients with large-vessel giant cell arteritis (LV-GCA). The retrospective study included a review of 19 such patients (10 women, 9 men; median age, 74.0 y; 12 with typical cranial GCA and 7 with LV-GCA) who had undergone PET/CT imaging at diagnosis. Fifteen of the 19 patients were originally diagnosed with aortitis, including 8 with classical cranial GCA and 7 with LV-GCA. Over a follow-up of 15 mo (range, 4.5–26.5 mo), 4 relapses occurred. The only statistical difference between those who relapsed and those who did not was sex: all relapsers were male. In both sexes, aortitis was not more frequent among relapsers. The authors concluded that their study confirmed "PET as a valid tool in the identification of LV-GCA with no cranial involvement." They failed, however, to validate a role for PET in prognostic stratification of GCA, although male sex was a potential risk factor for GCA relapse.

Clinical Rheumatology

PET/CT After Hepatic Radioembolization from Breast Cancer

Deipolyi et al. from the Memorial Sloan Kettering Cancer Center (New York, NY) reported on November 15 ahead of print in *Cardiovascular and Interventional Radiology* on a study looking at PET/CT imaging characteristics in patients with metastatic breast cancer during follow-up after ^{90}Y radioembolization of hepatic metastases. The study included 30 patients who underwent 38 ^{90}Y-glass or -resin radioembolizations. PET/CT was performed (on average) 51 d before radioembolization, and 68 PET/CTs were acquired after treatment (6 at 0–30 d, 15 at 31–60 d, 9 at 61–90 d, 13 at 91–120 days, 14 at 121–180 d, and 11 at >180 d). Modified PERCIST were used in assessing response in the hepatic territory. An objective response was defined as a decrease in SUV$_{peak}$ by ≥30%. Twenty-five patients (83%) achieved objective response on at least

1 follow-up. Median survival was 15 mo after the first radioembolization. The highest responses were seen in those imaged at 30–90 d, with more than 75% of patients showing objective response at that time. After 180 d, objective response was seen in only 25% of patients, with a median time to progression of 169 d among responders. The authors concluded that "these results help to guide the timing of imaging and also to inform patients of expected outcomes after radioembolization."

Cardiovascular and Interventional Radiology

Amyloid PET AUC in a Memory Clinic

In an article e-published on October 6 ahead of print in *Alzheimer's and Dementia*, de Wilde et al. from the VU University (Amsterdam, The Netherlands), Lund University (Malmö, Sweden), University College London (UK), and University Medical Center Utrecht (The Netherlands) assessed the usefulness of appropriate use criteria (AUC) for amyloid PET imaging in an unselected memory clinic cohort. The study included 507 patients in whom the authors calculated the sensitivity and specificity of appropriate use (based on increased diagnostic confidence and management change), as defined by the Amyloid Imaging Taskforce and other clinical outcomes. The researchers also compared differences in post-PET diagnosis and management change between patients who were considered "AUC-consistent" (n = 250) and "AUC-inconsistent" (n =257) after PET diagnosis. In both groups post-PET diagnosis and management changes were significant. The Amyloid Imaging Taskforce's definition of appropriate use occurred in only 55 (13%) patients, detected by the AUC with a sensitivity of 93% and a specificity of 56%. Diagnostic changes were found to occur independently of AUC status. The authors concluded that "the current AUC are not sufficiently able to discriminate between patients who will benefit from amyloid PET and those who will not."

Alzheimer's and Dementia

PET/CT and Metabolic Activity in RA Therapies

Dam et al. from the Gunma University Graduate School of Medicine (Maebashi, Japan), the Bach Mai Hospital (Hanoi, Vietnam), and the Hanoi Medical University (Vietnam) reported on October 3 ahead of print in the *Scandinavian Journal of Rheumatology* on a study using ^{18}F-FDG PET/CT to evaluate the metabolic activity of axillary lymph nodes and effectiveness in clinical assessment of disease activity in rheumatoid arthritis patients treated with biologic therapies. The study included 64 patients with rheumatoid arthritis who underwent ^{18}F-FDG PET/CT imaging at baseline and after 6 mo of biologic therapy. SUV$_{max}$, metabolic active volume, and total lesion glycolysis data were used to assess glucose metabolism in the lymph nodes and 12 upper-limb joints. Clinical data included serum markers and a disease activity score based on 28-joint-count erythrocyte sedimentation rate (ESR). Results showed that changes in SUV$_{max}$ and total lesion glycolysis for the axillary lymph nodes correlated significantly with those in the ipsilateral wrist joints, as well as a positive correlation between changes in the 3 metabolic parameters of the axillary lymph nodes and changes in disease activity after treatment. After 6 mo of biologic therapy, all metabolic parameters for the axillary lymph nodes in patients with 28-joint-count ESR <3.2 were significantly lower than in those with corresponding rates ≥3.2. The authors concluded that "the metabolic activity and active volume of axillary lymph nodes may reflect the therapeutic response to the biologic treatment of rheumatoid arthritis."

Scandinavian Journal of Rheumatology

^{18}F-FDG PET/CT in LN Staging in Urothelial Carcinoma

In an article e-published on October 4 in *European Urology Oncology*, Voskuilen et al. from the Netherlands Cancer Institute–Antoni van Leeuwenhoek Hospital (Amsterdam, The Netherlands), Aarhus University Hospital (Denmark), UZ Leuven (Belgium), Fondazione

IRCCS Istituto Nazionale dei Tumori (Milan, Italy), the Moffitt Cancer Center (Tampa, FL), the IRCCS Ospedale San Raffaele/Vita-Salute San Raffaele University (Milan, Italy), the Medical University of Vienna (Austria), I.M. Sechenov First Moscow State Medical University (Russia), Bichat-Claude Bernard Hospital (Paris, France), Zealand University Hospital (Roskilde, Denmark), and Seoul National University Hospital (South Korea) reported on the diagnostic value of ^{18}F-FDG PET/CT for lymph node staging in patients with upper-tract urothelial carcinoma. The retrospective study included data from 117 such patients who underwent PET/CT before surgery in 8 centers (patients who received neoadjuvant chemotherapy were excluded). Imaging results were compared with those from histopathology in 62 patients after lymph node dissection. Analyses looked at differences in survival in groups with and without suspicious lymph nodes on presurgical PET/CT. At histopathology, lymph node metastases were identified in 17 patients. The sensitivity and specificity of ^{18}F-FDG PET/CT for diagnosis of lymph nodes metastases were 82% and 84%, respectively. Recurrence-free survival was significantly worse in patients with lymph node–positive PET/CT than in those with lymph node–negative imaging findings.

Cancer-specific and overall survival rates were similar in the 2 groups.

European Urology Oncology

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 October and early November. Luiting et al. from the Erasmus University Medical Center (Rotterdam, The Netherlands), The Netherlands Cancer Institute (Amsterdam), Amsterdam University Medical Centers (The Netherlands), the University of New South Wales (Sydney, Australia), St. Vincent's Prostate Cancer Centre (Darlinghurst, Australia), and Garvan Institute of Medical Research/Kinghorn Cancer Centre (Darlinghurst, Australia) published the "Use of ^{68}Ga-PSMA PET for detecting lymph node metastases in primary and recurrent prostate cancer and location of recurrence after radical prostatectomy: An overview of the current literature" ahead of print in the November 4 issue of *BJU International*. In an article released on November 5 ahead of print in the *International Journal of Molecular Sciences*, Frankl et al. from the University of Texas Southwestern Medical Center (Dallas)

reported on "Imaging metabolically active fat: A literature review and mechanistic insights." In an article e-published on October 11 in *Current Urology Reports,* Pozzessere et al. from the AUSL Toscana Centro San Giuseppe Hospital (Empoli, Italy), Lausanne University Hospital/University of Lausanne (Switzerland), San Camillo De Lellis Hospital (Rieti, Italy), and the Medical University of Vienna (Austria) presented "Renal cell carcinoma: The oncologist asks, can PSMA PET/CT answer?" Bélissant Benesty et al. from the Hôpital Tenon APHP/Sorbonne University (Paris), the Hôpital Cochin APHP/Paris Descartes University (Paris), the Hôpital Bicêtre APHP/Université Paris Sud (Bicêtre), and the Centre Hospitalo-Universitaire de Caen/Université de Caen Normandie (all in France) summarized the state of the art in "[68]Ga-DOTATOC PET/CT in detecting neuroendocrine tumours responsible for initial or recurrent paraneoplastic Cushing's syndrome" on October 3 ahead of print in *Endocrine*. Ahead of print on October 2 in the *International Journal of Molecular Sciences*, Van de Wiele et al. from AZ Groeninge (Kortrijk, Belgium), University Ghent (Belgium), the University of Pretoria (South Africa), and the University of Leuven (Belgium) published "PSMA-targeting positron emission agents for imaging solid tumors other than nonprostate carcinoma: A systematic review."