FROM THE LITERATURE

CTA for Diagnosis and Prognosis

Bittner and colleagues from the Massachusetts General Hospital/Harvard Medical School (Boston, MA), Friedrich-Alexander University Erlangen-Nürnberg/University Hospital Erlangen (Germany), Oregon Health and Science University (Portland), and Duke University School of Medicine (Durham, NC) reported in the May issue of Current Cardiology Reports (2016;18[5]:40) on additional findings from the Prospective Multicenter Imaging Study for Evaluation of Chest Pain (PROMISE) trial, focusing on the comparative effectiveness of coronary CT angiography (CTA) and functional assessment (exercise electrocardiography, stress echocardiography, or nuclear perfusion stress testing) in initial diagnosis of patients with suspected stable coronary artery disease. The PROMISE study included data from more than 10,000 patients randomized at 193 sites. The study included a median follow-up of 25 mo after imaging/assessment, during which no significant differences were identified in major clinical events among the diagnostic approaches. The PROMISE group has already published results indicating significant differences in preassessment likelihood for obstructive coronary artery disease and subsequently observed incidence, as well as the enhanced effectiveness of CTA in selecting appropriate patients with obstructive coronary artery disease for invasive coronary angiography. The authors noted that radiation exposure with nuclear assessment was highest, followed by CTA. They concluded that “improvement of patient selection for diagnostic testing and risk stratification will be keys to increase efficacy and efficiency of management of patients with suspicion for stable coronary artery disease.”

Current Cardiology Reports

PET/CT and Prostate Node Distribution

In an article in the March 11 issue of Radiation Oncology (2016;11[1]:37), Hegemann and colleagues from the Ludwig-Maximilians University (Munich, Germany) analyzed 11C PET/CT localization of positive lymph node distribution in a group of patients and compared findings with published contouring recommendations to create a PET/CT atlas to assist in adequate definition of radiation portals. The study included data from 119 patients (32 high-risk, untreated patients who underwent PET/CT, median prostate-specific antigen [PSA] = 12.5 ng/mL; 87 patients who underwent PET/CT for staging after biochemical failure; median PSA = 3.12 ng/mL). In the untreated patients, PET identified 78 positive lymph nodes. The most common sites for these nodes were external iliac (32.1%), common iliac (23.1%), and paraaortic (19.2%). In the postoperative patients, PET identified 209 positive lymph nodes, with the most common sites being common iliac (24.9%), external iliac (23.0%), and paraaortic (20.1%). All 287 PET-positive lymph nodes were manually contoured in a “virtual” 3D patient dataset to create an atlas of cumulative PET-positive lymph node distribution. The locations and contours of PET-positive nodes were assessed in each patient and compared with Radiation Therapy Oncology Group (RTOG) contouring atlas data, as well as a preexisting SPECT sentinel lymph node atlas to identify PET-positive pelvic lymph nodes that would not have been treated adequately by RTOG or SPECT-based clinical target volume definitions. The authors found that 34 (43.6%) PET-detected lymph nodes in the untreated patients and 77 (36.8%) in the postoperative patients would not have been treated adequately using the RTOG-defined target volumes. 11C PET/CT distributions corresponded well to those of the preexisting SPECT atlas. The authors concluded that “to reduce geographical miss, image-based definition of an individual target volume is necessary.”

Radiation Oncology

Thyroid Nodules with Indeterminate Cytology

Piccardo et al. from the Ospedali Galliera (Genoa, Italy), the Oncology Institute of Southern Switzerland (Bellinzona), and the Ospedali Civili de Brescia (Italy) reported on March 10 ahead of print in the European Journal of Endocrinology on a study comparing the efficacy of 18F-FDG PET/CT, multiparametric neck ultrasonography, 99mTc-MIBI scintigraphy, and histology in predicting malignancy of thyroid nodules with indeterminate cytology. The study included data from 89 patients with such nodules scheduled for surgery. All patients underwent the 3 imaging procedures. Histopathology was the standard of reference, with 69 of 87 nodules determined to be benign and 18 to be malignant. The sensitivity, specificity, accuracy, and positive and negative predictive values of 18F-FDG PET/CT were 94%, 58%, 66%, 37%, and 98%, respectively. The sensitivity, accuracy, and negative predictive value of PET/CT were significantly higher than those of the other 2 imaging modalities. Combining data from PET/CT and ultrasonography provided lower sensitivity and negative predictive value than PET/CT alone but offered significantly higher specificity. On multivariate analysis, only PET plus scintigraphy was
significantly associated with histopathologic results.

*European Journal of Endocrinology*

**PET+MR vs. PET/CT in Mesothelioma Staging**

In an article in the April issue of *Lung Cancer* (2016;94:40-45), Martini et al. from the University Hospital Zurich/University of Zurich (Switzerland) reported on a study comparing the diagnostic accuracy of sequential coregistered PET and MR imaging with that of PET/CT for local staging of malignant pleural mesothelioma. The study included 34 patients (median age, 66 y; range, 40–79 y) with known malignant pleural mesothelioma who underwent both PET/CT and sequential PET plus MR imaging for staging or restaging/follow-up. Histopathology was available as a standard of reference in 26 patients. Images were evaluated for quality, T and N stage, confidence level, and interobserver agreement. Interobserver agreement for evaluation of T and N stage in PET/CT was better than that for PET plus MR, although both were good. The interclass correlation coefficients between PET/CT and PET plus MR for assessing T and N stage were excellent. Reviewers reported diagnostic confidence to be significantly higher with PET plus MR than for PET/CT. The authors concluded that diagnostic accuracy of PET+MR is comparable to PET/CT for local staging of malignant pleural mesothelioma, whereas radiologists felt significantly more confident staging PET+MR compared to PET/CT images using dedicated sequences.”

*Radiation Oncology*

**PET-Based Dose Painting in HNSCC**

In an article e-published on March 15 ahead of print in *Radiotherapy and Oncology*, Rasmussen and colleagues from the University of Copenhagen (Denmark) and the University of Maryland School of Medicine (Baltimore) reported on the safety of 18F-FDG PET-guided dose escalation in patients receiving accelerated chemoradiation for locally advanced head and neck squamous cell carcinoma. The report was part of the larger Conventional vs. Tumor Recurrence Adapted Specification of Target Dose (CONTRAST) phase I trial. The focus group for this report included 15 patients with primary squamous cell carcinoma of the oral cavity, oropharynx, hypopharynx, or larynx who were candidates for chemoradiation and had p16-negative or -positive tumors with smoking histories >10 pack year. Gross tumor volumes (GTVs) were assessed on PET, and anatomic GTVs were defined by CT. Dose escalation was in 2 steps. First a dose to the PET-defined GTV was escalated to a uniform prescription of 82 Gy (equivalent dose in 2 fractions). All patients then received accelerated radiation therapy (6 fractions/wk) delivering 34 fractions of 2.34 Gy to the PET-defined GTV, as well as weekly cisplatin. Over a median follow-up period of 18 mo (range, 7–21 mo) after completion of treatment, no incidents of early grade 4+ toxicity were noted. Four patients had ulceration at 2 mo, with 2 subsequently healing and 2 persisting. The authors concluded that “FDG PET–based dose escalation to 82 Gy passed the protocol-defined criterion for dose escalation.” However, the 2 cases of persistent ulceration raised concerns about late outcomes, leading the authors “to refrain from further dose escalation and proceed with the current dose level in a larger comparative effectiveness trial.”

*Radiotherapy and Oncology*

**SPECT/MR and Epilepsy Surgery**

Jalota and colleagues from Rush University Medical Center (Chicago, IL) reported on March 18 ahead of print in the *Journal of Neurosurgery* on a study designed to assess the prognostic value of presurgical subtracted ictal SPECT coregistered with MR imaging in patients with lesional (MR-positive) and nonlesional (MR-negative) refractory extratemporal lobe epilepsy (ETLE) and temporal lobe epilepsy (TLE). The authors looked specifically at the ability of SPECT coregistered with MR data to predict long-term postsurgical outcomes after resection of the ictal onset zone that overlapped with 1 or more regions of ictal onset–associated transient hyperperfusion. The study included 44 patients with refractory ETLE or TLE who underwent presurgical evaluation using ictal SPECT coregistered with MR. Follow-up after surgery was >2 y in most patients. The SPECT plus MR technique was in agreement with electrocortigraphic results and overlapped the resection site in 32 (73%; 19 ETLE and 13 TLE) patients. After surgery, 20 (63%) of these 32 patients were seizure free. In all 19 ETLE patients with concordant imaging and
electrocorticographic results, the location of ictal onset on electrocorticography was completely resected; 11 (58%) of these patients became seizure free. In all 13 TLE patients with concordant imaging and electrocorticographic results, the indicated electrocorticographic focus was completely resected; 9 (69%) of these patients became seizure free. In 7 of 34 patients (21%) the area of the combined imaging signal was partially resected; of these 7 patients, 5 (72%) were seizure free. In 16 of 34 patients (47%) the area of the combined imaging signal was completely resected; of these 16 patients, 10 (63%) were seizure free. In 16 of 34 patients (21%) the area of the combined imaging signal was completely resected; of these 16 patients, 10 (63%) were seizure free. In 7 of 34 patients (21%) the area of the combined imaging signal was partially resected; of these 7 patients, 5 (72%) were seizure free. In 16 of 34 patients (47%) the area of the combined imaging signal was completely resected; of these 16 patients, 10 (63%) were seizure free.

**Pre-SCT PET in Refractory/Relapsed HL**

Adams and Kwee from University Medical Center Utrecht (The Netherlands) reported on March 2 ahead of print in *Annals of Hematology* on a systematic review and metaanalysis of the prognostic value of pretransplant 18F-FDG PET in refractory/relapsed Hodgkin lymphoma treated with autologous stem cell transplantation (SCT). A total of 11 studies met the analysis inclusion criteria, with 745 patients with refractory/relapsed Hodgkin lymphoma who underwent PET imaging before autologous SCT. In these studies, the percentages of patients who had positive findings on pretransplant PET imaging ranged from 25% to 65.2%. Progression-free survival was reported at 0–52% for patients who were pretransplant PET positive and 55%–85% for those who were pretransplant PET negative. Overall survival was reported at 17%–77% for patients who were pretransplant PET positive and between 78%–100% in patients who were pretransplant PET negative. In a subset of studies with sufficient data for metaanalyses, the pooled sensitivity and specificity of pretransplant 18F-FDG PET in predicting treatment failure (progressive, residual, or relapsed disease) were 67.2% and 70.7%, respectively. Pooling sensitivity and specificity of pretransplant PET in predicting death during follow-up were 74.4% and 58.0%, respectively. The authors concluded that despite the fact that “a considerable proportion of pretransplant FDG PET–positive patients remains disease free and a considerable proportion of pretransplant FDG PET–negative patients develops disease relapse after autologous SCT,” evidence from the systematic review suggests that pretransplant 18F-FDG PET has “value in predicting outcome in refractory/relapsed Hodgkin lymphoma patients treated with autologous SCT.”

*Annals of Hematology*

**18F-AV-1451 PET Correlations with Braak Tau Staging**

In a study e-published on March 2 ahead of print in *Brain*, Schwarz and colleagues from Eli Lilly and Company (Indianapolis, IN) and Avid Radiopharmaceuticals (Philadelphia, PA) reported on a study designed to determine whether PET imaging with 18F-AV-1451 can be used to correlate with and predict post-mortem Braak staging of neurofibrillary tau tangle topographic distribution. The study included imaging and clinical data from 187 individuals (14 young reference individuals, ages 21–39 y; 173 older individuals, ages 50–95 y [42 amyloid-negative cognitively normal, 47 clinically diagnosed amyloid-positive with mild cognitive impairment, 40 clinically diagnosed amyloid-negative with mild cognitive impairment, 28 amyloid-positive with Alzheimer disease, 16 amyloid-negative with Alzheimer disease]). All participants underwent 18F-AV-1451 PET imaging, and standardized uptake value ratio images were calculated. The authors defined 7 regions of interest in anterior temporal lobe and occipital lobe sections that corresponded closely to those used as decision points in Braak staging and applied an algorithm that estimated Braak stages directly from individual PET region-of-interest profiles. Resulting image analyses yielded region-of-interest and voxel-level profiles that mirrored key features of tau progression and were consistent with Braak stages. With the use of a set of decision rules, Braak stages corresponding to typical progression patterns could be estimated in 149 (86%) of the individuals studied. The authors summarized their results: “The estimated Braak stage was significantly associated with amyloid status, diagnostic category, and measures...
of global cognition” and noted that “in vivo 18F-AV-1451 PET images across the Alzheimer’s disease spectrum could be classified into patterns similar to those prescribed by Braak neuropathological staging of tau pathology.”

**PET at Diagnosis in Sarcoma**

Kubo et al. from Hiroshima University (Japan) reported in the March 15 issue of the *European Journal of Cancer* (2016;58:104–111) on a systematic review and metaanalysis designed to assess the utility of baseline 18F-FDG PET in predicting survival in patients with soft tissue sarcoma and bone sarcoma. A total of 6 studies (overall quality rated as adequate) with 514 patients with soft tissue sarcoma and/or bone sarcoma were included in the metaanalysis, which compared pooled hazard ratios of overall survival in patients with high and low SUVmax. The pooled hazard ratio for overall survival was 1.22 (95% CI, 1.03–1.46), indicating that higher SUVmax corresponded to shorter overall survival. This predictive ability held true in patients with soft tissue sarcoma alone. The authors concluded that “18F-FDG PET at diagnosis provides a very useful predictive tool for patients with soft tissue sarcoma and bone sarcoma.”

*European Journal of Cancer*

**SPECT/CT, 131I, and Lingual Thyroid Ectopia**

In an article e-published on March 15 ahead of print in *Thyroid*, Gandhi et al. from the University of Michigan (Ann Arbor) and the Department of Veterans Affairs Health System (Ann Arbor, MI) reported on experience using 131I radioablation to manage obstructive lingual thyroid tissue. Three patients with lingual thyroid ectopia were prepared with a low-iodine diet and levothyroxine withdrawal before treatment. Assessment of 24-h radioiodine uptake and 131I or 99mTc-pertechnetate SPECT/CT were used to identify the size and location of lingual thyroid tissue and to guide selection of 131I doses, which ranged from 10.7 to 15.4 mCi. No treatment complications were noted, and obstructive symptoms were resolved at follow-up. The authors concluded that “radioiodine therapy with 131I is an effective treatment modality for ablation of ectopic thyroid tissue as an alternative to surgery.”

*Thyroid*

**Tau PET Patterns in AD**

Ossenkoppele and colleagues from the University of California San Francisco, the University of California Berkeley, the VU University Medical Center (The Netherlands), the University of Gothenburg (Sweden), Lawrence Berkeley National Laboratory (CA), and the University of Colorado Denver Anschutz Medical Campus (Aurora, CO) reported on March 8 ahead of print in *Brain* on a study investigating the relationship of regional tau distribution on 18F-AV1451 PET to clinical symptomatology and patterns of glucose hypometabolism in Alzheimer disease (AD). The study included 20 patients with a range of clinical presentations and probable AD or mild cognitive impairment resulting from AD, as well as 15 cognitively normal individuals who were amyloid-β negative. All participants underwent PET imaging with 18F-AV1451, 11C-PiB, and 18F-FDG, as well as apolipoprotein-E (APOE) genotyping and neuropsychological testing. 18F-AV1451 and 18F-FDG patterns in the 7 patients with posterior cortical atrophy (visual variant of AD) specifically targeted clinically affected posterior brain regions, whereas 11C-PiB was found to bind diffusely throughout the neocortex. The 5 patients with amnestic-predominant clinical presentations showed highest 18F-AV1451 retention in medial temporal and lateral temporoparietal regions. Three of the 5 patients with logopenic variant primary progressive aphasia (language variant of AD) showed asymmetric 18F-AV1451 uptake (uptake higher in the left than right hemisphere). In patients with AD, a strong negative association was identified between 18F-AV1451 and 18F-FDG uptake on PET, with less pronounced positive associations between 11C-PiB and 18F-FDG and 18F-AV1451 and 11C-PiB. Across all patients in the study, younger age was associated with greater 18F-AV1451 uptake across the neocortex, whereas older age was associated with increased 18F-AV1451 uptake in the medial temporal lobe. APOE ε4 carriers had greater temporal and parietal 18F-AV1451 uptake.
than noncarriers. Worse performance on domain-specific neuropsychological tests was associated with greater or asymmetric 18F-AV1451 uptake in the medial temporal lobes, occipital and right temporo-parietal cortex, and temporo-parietal cortex. The authors concluded that “tau imaging, contrary to amyloid-β imaging, shows a strong regional association with clinical and anatomical heterogeneity in AD” and that, although preliminary, “these results are consistent with and expand upon findings from post-mortem, animal, and cerebrospinal fluid studies, and suggest that the pathological aggregation of tau is closely linked to patterns of neurodegeneration and clinical manifestations of AD.”  

**PET/CT and Cervical Cancer Recurrence**

Hong et al. from Korea University (Seoul), Dankook University College of Medicine (Yongin, Korea), and Hallym University Hangang Sacred Heart Hospital (Incheon, Korea) reported in the March issue of *Medicine (Baltimore)* (2016;95:e2992) on a study assessing optimal 18F-FDG PET/CT parameters for predicting cervical cancer recurrence. The study included 56 patients with International Federation of Gynecology and Obstetrics (FIGO) stage II-B–IVA cervical cancer who underwent 18F-FDG PET/CT before definitive chemoradiotherapy. Among PET results analyzed were SUV<sub>max</sub>, metabolic tumor volume (MTV), and total lesion glycolysis (TLG) for both primary tumor and pelvic and paraaortic lymph nodes. For the purposes of this analysis, the authors defined the following parameters: SUV<sub>max</sub>-S, the sum of the primary tumor SUV<sub>max</sub> and the higher SUV<sub>max</sub> of the pelvic or paraaortic lymph nodes; MTV-S, the sum of the MTV of the primary tumor and pelvic and paraaortic lymph nodes; and TLG-S, the sum of the TLG of the primary tumor and pelvic and paraaortic lymph nodes. Correlations between imaging results and recurrence-free survival were investigated. Higher FIGO stage, lymph node metastasis, primary tumor MTV > 47.81 cm, primary tumor TLG > 215.02, MTV-S > 215.02, MTV-S > 59.01 cm, and TLG-S > 224.15 were all associated with recurrence-free survival. In multivariate analysis, FIGO stage and MTV-S > 59.01 cm were identified as independent predictive factors for recurrence-free survival.

**Reviews**

Review articles offer an important way to stay up to date on the latest topics and approaches by providing valuable summaries of pertinent literature.