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.

^{124}I PET/CT in DTC

Gulec et al. from Florida International University (Miami) and a consortium of Miami area researchers reported on February 9 ahead of print in *Thyroid* on a study designed to assess the imaging characteristics and feasibility of routine ^{124}I PET/CT in ^{131}I therapy in patients with confirmed differentiated thyroid cancer. The study included 15 patients (6 women, 9 men; ages 29–91 y; mean age, 57 y) who were administered 2 mCi ^{124}I in liquid form and then underwent whole-body PET/CT at 2–4, 24 ± 6, 48 ± 6, 72 ± 6, and 96 ± 6 h after administration. Each patient then underwent ^{131}I treatment (100–300 mCi). Planar ^{131}I posttreatment images were acquired 5–7 d after treatment. ^{124}I PET/CT identified 46 lesions in the 15 patients, with a sensitivity of 92.5%. ^{124}I PET/CT also identified 22.5% more foci of ^{131}I-avid lesions than the ^{131}I posttreatment images. The study also provided results documenting different kinetic profiles for normal thyroid remnants (peak, 24 h with monoexponential clearance), salivary glands (peak, 4 h with biexponential clearance), and metastatic lesions (protracted retention) and documented individual variations in cumulated activities. The authors concluded that ^{124}I PET/CT is "a valuable clinical imaging tool/agent, in both determining the extent of disease in the setting of metastatic differentiated thyroid cancer and the functional volumetric and kinetic evaluation of target lesions."

Thyroid

^{68}Ga-PSMA PET/CT and Mesorectal LN Mets

In a study e-published on February 16 ahead of print in *Prostate*, Hijazi et al. from University Medical Center Göttingen (Germany) reported on the utility of ^{68}Ga–prostate-specific membrane antigen (^{68}Ga-PSMA) PET/CT in detecting prostate cancer metastatic to mesorectal lymph nodes. The study included a retrospective review of records from 76 patients, 61 with biochemical recurrence after curative treatment and 15 with high-risk prostate cancer before primary therapy. Each patient had undergone ^{68}Ga-PSMA PET/CT imaging. PET-positive lesions were detected on imaging in 66 (87%) patients, with nodal disease detected in 47 (71%) of these 66. PET-positive mesorectal nodal lesions were identified in 12 (15.8%) of the 76 patients, with a median number of 1 PET-positive node per patient. Seven of the 12 patients experienced disease recurrence after radical prostatectomy, with a median prostate-specific antigen (PSA) value of 1.84 ng/mL (range, 0.31–13 ng/mL). Five of the 12 patients had untreated first-diagnosed high-risk disease, with median PSA value of 90 ng/mL (range, 4.6–93 ng/mL) at PET/CT. PET-positive mesorectal nodal lesions correlated well with CT findings. PET/CT provided valuable information in directing subsequent treatment strategies in a subset of patients with recurrent disease and with high-risk disease. The authors concluded that "^{68}Ga-PSMA PET/CT seems to improve the detection of nodal metastasis in prostate cancer, especially concerning mesorectal lymph nodes."

Prostate

PET/CT and Joint Destruction in RA

Suto et al. from Gunma University Graduate School (Japan) and the Warren Alpert Medical School of Brown University/Rhode Island Hospital (Providence, RI) reported in the February issue of *Medicine (Baltimore)* (2016;95: e2841) on the utility of ^{18}F-FDG PET/CT in assessing status and monitoring biologic therapy in large joint destruction associated with rheumatoid arthritis. The study included 23 patients (6 men, 17 women; mean age, 66.9 ± 7.9 y) with rheumatoid arthritis and focused on a total of 264 large joints (shoulder, elbow, wrist, hip, knee, and ankle). Each patient underwent ^{18}F-FDG PET/CT at the start of the study and 6 mo after initiation of biologic therapy. Radiographs of each of the 12 large joints per patient were acquired at the start of the study and 2 y later. Radiographic progression of joint destruction was detected in 33 of the total 264 large joints. ^{18}F-FDG uptake in joints with destruction was higher than in joints without destruction. SUV_{max} at baseline and 6 mo and disease activity score 28-erythrocyte sedimentation rate at 6, 12, and 24 mo were found to be significantly higher in patients with progressive joint destruction at 2 y.

Medicine (Baltimore)

MR, CT, and PET in Rectal Cancer Restaging

In an article in the March issue of *Diseases of the Colon and Rectum* (2016;59:179–186), Schneider et al. from the Peter MacCallum Cancer Centre (East Melbourne, Australia) reported on a study designed to investigate the relative value of restaging with ^{18}F-FDG PET, CT, or MR imaging after preoperative chemoradiation in patients with rectal cancer. This retrospective study looked at the records of 199 patients with rectal adenocarcinoma who had been staged with all 3 modalities and treated with neoadjuvant

chemoradiation (50.4 Gy and infusional 5-fluorouracil) and who were restaged 4 wk after chemoradiation and before surgery. Tumor stages as assessed on the 3 modalities were compared before and after chemoradiation, with an analysis of the resulting effect of restaging on management planning. Tumor staging elements (determined by pathology and imaging) at initial presentation for the study population were T2, 8.04%; T3, 65.33%; T4, 26.63%; N0, 17.09%; N1, 47.74%; N2, 34.67%; M0, 81.91%; and M1, 18.09%. Almost half of the patients ($n = 99$) had a change in disease staging after neoadjuvant chemoradiation. In 29 (15%) patients, management plans were changed. PET contributed to changes in management in 11% of patients, whereas CT and MR imaging contributed to management changes in only 4% of patients each. In patients with metastatic disease at primary staging, the relative impacts of PET, CT, and MR imaging in changing management were 32%, 18%; and 6%, respectively. The authors concluded that given the fact that PET had "the most significant impact in the change of management overall. . .its use in restaging advanced rectal cancer should be further explored."

Diseases of the Colon and Rectum

PET and Bladder Metabolic Artifacts

Roman-Jimenez et al. from INSERM (Rennes, France), Université de Rennes (France), and Keosys Medical Imaging (Saint-Herblain, France) reported in the February issue of *Computers in Biology and Medicine* on a novel method for detection of ^{18}F-FDG bladder artifacts in PET based on a multifeature double-step classification approach. The approach was designed to overcome challenges in differentiating pelvic tumor uptake from physiologic bladder uptake. The method simultaneously accounts for SUVs on PET, Hounsfield units on CT, and distance to 2 manually defined seeds (tumor and bladder). The researchers described initial investigations using 52 PET/CT images from patients under treatment for locally advanced cervical cancer. Manual delineations of the bladder on CT images were used to evaluate bladder uptake detection capability. Using this method, tumor classification averages were 0.94 ± 0.09 sensitivity, 0.98 ± 0.01 specificity, and 0.98 ± 0.01 accuracy. The authors concluded that the results suggest that this approach "is able to detect most ^{18}F-FDG bladder metabolism artifacts while preserving tumor uptake and could thus be used as a preprocessing step" for further PET analyses.

Computers in Biology and Medicine

^{18}F-FET PET vs MR after Glioblastoma Resection

In an article e-published on February 15 ahead of print in *World Neurosurgery*, Buchmann et al. from the Technische Universität München (Germany) reported on a comparison of MR and ^{18}F-fluoroethyl-L-thyrosine (^{18}F-FET) PET imaging in detection of residual tumor after glioblastoma surgery. The study included 62 patients (63 total surgeries), each of whom underwent MR and ^{18}F-FET PET imaging before and after resection. PET imaging was performed within 72 h after resection in 43 surgeries and later than that time frame in 20 surgeries. Both imaging modalities confirmed complete resection in 44% and identified residual tumor in 37%. In 14% of patients/surgeries in which PET results identified residual tumor, MR imaging identified none. In 5% of patients/surgeries in which MR results identified residual tumor, PET identified none. The average residual tumor volume identified on PET was higher than that for MR (3.99 and 1.59 cm^3, respectively). Timing of PET after resection did not affect detection of residual tumors. The authors concluded by noting that ^{18}F-FET PET carries both advantages and disadvantages in this setting and that "the combination of the high-resolution MRI with high-sensitivity FET-PET could improve the postoperative planning of further therapies, such as radiation therapy, or even a further resection of tumor remnants."

World Neurosurgery

Antithyroid Drug–Induced Agranulocytosis

Yang et al. from the First Affiliated Hospital College of Medicine/Zhejiang University (Hangzhou, China) reported on February 11 ahead of print in *Thyroid* on a large-group study of the characteristics of antithyroid drug (ATD)–induced agranulocytosis in patients with hyperthyroidism referred for radioiodine treatment. In a retrospective record review of 9,690 patients referred for ^{131}I treatment, the authors identified 114 cases (104 women, 10 men; mean age, 41.7 ± 12.3 y) of agranulocytosis attributed to ATD. Average ATD doses at onset were 22.9 ± 8.0 mg/d for methimazole and 22.9 ± 8.0 mg/d for propylthiouracil. Onset of agranulocytosis was at 4, 8, and 12 wk after initiation of ATD therapy in 45.1%, 74.3%, and 88.5%, respectively, of patients. Mean recovery time was 13.41 ± 7.14 d. Recovery times did not differ among those treated or not treated with granulocyte-colony stimulating factor (G-CSF). Ninety-eight patients went on to ^{131}I treatment, which was successful in 87 (88.8%), with similar results for the 85 patients who had received methimazole (88.2%) and the 13 patients who had received propylthiouracil (92.3%). The authors summarized the results of this largest single-institution study in China: "ATD-induced agranulocytosis tends to occur within the first 12 wk after the onset of ATD therapy" and, in these patients, "G-CSF does not improve recovery time of agranulocytosis and ^{131}I is an optimal treatment approach."

Thyroid

PET/CT and MR in Salvage RT for Prostate Cancer

In an article in the February 3 issue of *Advances in Medical Sciences* (2016;61:212–218), Rischke et al. from the Albert-Ludwigs University Hospital of Freiburg (Germany) reported on a study investigating the feasibility of ^{11}C-choline PET/CT– and MR-directed extended salvage radiation therapy of involved lymph node regions in patients with nodal recurrent prostate cancer after primary therapy or previous

prostate fossa salvage radiotherapy. The study included 25 patients with nodal or nodal plus local recurrent prostate cancer as confirmed by ^{11}C-choline PET/CT and MR who were treated with extended salvage radiation therapy at the sites of recurrence. The mean follow-up period was 2.9 y. Based on PET/CT and MR findings, 84% (n = 21) of patients were treated to the pelvic area only, 12% (n = 3) to the retroperitoneal area only, and 4% (n = 1) to both the pelvic and retroperitoneal regions. Forty percent of patients (n = 10) also underwent irradiation of the prostatic fossa. Overall, the median time to prostate-specific antigen progression was 19.6 mo. For patients with 1–2 PET-positive lymph nodes (n = 15) this time period was 34.9 mo; for those with ≥3 PET-positive lymph nodes the corresponding interval was 12.7 mo. Observed acute and late toxicities were mild to moderate, with no grade 3 adverse events. The authors concluded that "PET/CT- and MR-directed extended salvage radiation therapy of nodal recurrent prostate cancer with or without local recurrence is feasible with low acute and late toxicity."

Advances in Medical Science

^{68}Ga-DOTATE PET and Tumor Growth

Sommerauer et al. from University Hospital Zurich (Switzerland) reported on February 9 ahead of print in *Neuro-Oncology* on a study assessing the ability of ^{68}Ga-DOTATE PET to predict tumor growth rate in meningiomas. The researchers looked at ^{68}Ga-DOTATATE PET findings in 64 meningiomas and calculated tumor growth rates from volumetric analysis of sequential MR images. SUV_{max} and tumor growth were well correlated in World Health Organization (WHO) grades I and II meningiomas. This correlation, as well as SUV_{max}, was significantly higher in transosseous than in intracranial meningiomas. No significant correlation of SUV_{max} and tumor growth was seen in anaplastic meningiomas. The authors concluded that "^{68}Ga-DOTATATE PET is a reliable predictor of tumor growth in WHO grades I and II meningiomas and provides additional information to conventional cross-sectional imaging modalities." This suggests that ^{68}Ga-DOTATATE PET can provide support for selection of time for treatment initiation. The authors added that because "meningiomas with fast tumor growth and transosseous expansion elicit the highest DOTATATE binding; therefore, they might be especially suited for DOTATATE-based therapy."

Neuro-Oncology

Myocardial Metabolic Flexibility and Diabetes

Mather et al. from the Indiana University School of Medicine (Indianapolis) reported on January 5 ahead of print in the *American Journal of Physiology. Endocrinology and Metabolism* on a study investigating myocardial fuel selection and metabolic flexibility in human type 2 diabetes using rates of myocardial fatty acid oxidation as assessed by 16-^{18}F-fluoro-4-thia-palmitate (16-^{18}F-FTP) PET and myocardial perfusion and total oxidation as assessed by ^{11}C-acetate PET. The study included 10 lean controls and 8 glycemically controlled individuals with type 2 diabetes who underwent paired studies under fasting conditions, comparing 3-h insulin + glucose euglycemic clamp conditions with 3-h saline infusion. In both groups, insulin raised heart rate, blood pressure, stroke index, myocardial oxygen consumption, and myocardial perfusion. Insulin suppressed available nonesterified fatty acids in both groups, but fatty acid concentrations were higher in the diabetic group under both test conditions. Insulin also suppressed fatty acid oxidation in both groups, although fatty acid oxidation rates were higher in the diabetic group under both conditions. Myocardial work efficiency was lower in diabetes, with decreases induced by insulin in both groups. The authors speculated on observed shifts away from fatty acid metabolism with insulin in the diabetic participants, concluding that "these observations suggest that improved fatty acid suppression, or reductions in myocardial fatty acid uptake and retention, could be therapeutic targets to improve myocardial ischemia tolerance in type 2 diabetes."

American Journal of Physiology. Endocrinology and Metabolism

Aerobic Glycolysis and Gray Matter

In an article e-published on January 11 ahead of print in the *Journal of Cerebral Blood Flow and Metabolism*, Hyder et al. from Yale University (New Haven, CT), Aarhus University/Aarhus University Hospital (Denmark), and the University of Copenhagen (Denmark) reported on a study exploring the extent to which aerobic glycolysis and oxidative phosphorylation affect brain networks as visualized in functional MR imaging by assessing quantitative differences between the oxygen-to-glucose index and the oxygen extraction fraction as measured by ^{15}O-H_2O, ^{15}O-O_2, and ^{18}F-FDG PET. The study included 13 healthy men who underwent PET and MR imaging in a resting state (awake, eyes closed). Results found uniform spatial agreement between oxygen delivery and glucose oxidation, suggesting that no specific regions have preferentially high aerobic glycolysis or low oxidative phosphorylation rates. Globally optimal maximum adenosine triphosphate turnover rates were in good agreement with ^{31}P and ^{13}C MR spectroscopy measurements. The authors concluded that this implies "that the intrinsic network activity in healthy human brain powers the entire gray matter with ubiquitously high rates of glucose oxidation" and that "reports of departures from normal brain-wide homogeny of oxygen extraction fraction and oxygen-to-glucose index" may be the result of artifacts from relative PET measurements.

Journal of Cerebral Blood Flow and Metabolism

PET and Medically Resistant Pediatric Epilepsy

Bansal et al. from Nicklaus Children's Hospital (Miami, FL) and the University of Miami (FL) reported on January 18 ahead of print in *Epilepsia*

on a retrospective study reviewing the incidence of hypermetabolic PET in medically resistant pediatric epilepsy and correlating this with data from electroencephalography (EEG), MR imaging, and surgical outcomes. Out of a total of 498 PET studies of patients with medically resistant childhood epilepsy, 33 (6.6%) had findings of focal PET hypermetabolism. The region of PET hypermetabolism correlated with an EEG spike count of ≥10/min in 26 of 32 patients who underwent concomitant scalp EEG studies and with 18 of 21 lesions seen on MR imaging. In the subset of 17 patients who underwent surgical resection, PET hypermetabolism correlated with regions showing almost continuous epileptiform discharges on the intracranial EEG and with malformed tissue at histopathology. At a median 33 mo after surgery in 14 patients, 7 had Engel's class I outcome, 4 had class II, 2 had class III, and 1 was unchanged. At the most recent follow-up, 5 of 7 patients with focal PET hypermetabolism alone were seizure free, compared with 3 of 8 patients with PET hypometabolism. The authors concluded that "these observations indicate that focal PET hypermetabolism is an important marker of the epileptogenic zone and may represent its epicenter."

Epilepsia

MR vs PET/CT in Uterine Carcinosarcoma

In an article e-published on January 8 ahead of print in *Gynecologic Oncology*, Lee et al. from the University of Ulsan College of Medicine (Seoul, Republic of Korea) compared the utility of MR and ^{18}F-FDG PET/CT in preoperative evaluation of uterine carcinosarcoma, using pathologic analyses of primary tumor lesions and paraaortic and pelvic lymph node areas as gold standards. In detecting primary tumor lesions, the sensitivity, specificity, accuracy, and positive and negative predictive values for ^{18}F-FDG PET/CT were 98.1%, 33.3%, 94.6%, 96.3%, and 50%, respectively. The corresponding values for MR were 98.1%, 100%, 98.2%, 100%, and 75%, respectively. In detecting positive paraaortic lymph node areas, the sensitivity, specificity, accuracy, and positive and negative predictive values for ^{18}F-FDG PET/CT were 77.8%, 90.2%, 85.9%, 80.8%, and 88.5%, respectively. The corresponding values for MR were 51.9%, 100%, 83.3%, 100%, and 79.7%. In pelvic lymph nodes, the sensitivity, specificity, accuracy, and positive and negative predictive values for ^{18}F-FDG PET/CT were 61.1%, 86.8%, 78.6%, 68.8%, and 82.5%. The corresponding values for MR were 50%, 89.5%, 76.8%, 69.2%, and 79.1%. For extrauterine disease, corresponding patient-based values for ^{18}F-FDG PET/CT were 100%, 78.9%, 85.7%, 69.2%, and 100%. The authors concluded that although ^{18}F-FDG PET/CT is comparable to MR in detecting primary uterine lesions in patients with uterine carcinosarcoma, PET/CT may be insufficient for replacing lymphadenectomy or MR imaging in predicting lymph node metastases. However, ^{18}F-FDG PET/CT "might allow lymphadenectomy to be omitted" in poor surgical candidates and could also be useful in detecting extrauterine metastases.

Gynecologic Oncology

Reviews

Review articles provide an important way to stay up to date on the latest topics and approaches by providing valuable summaries of pertinent literature. The Newsline editor recommends several reviews accessioned into the PubMed database in February and March. Lindenberg et al. from the National Cancer Institute (Bethesda, MD) summarized current efforts in "Prostate cancer imaging with novel PET tracers" in the March issue of *Current Urology Reports* (2016;17:18). In an article e-published on February 17 ahead of print in the *European Journal of Trauma and Emergency Surgery*, Govaert and Glaudemans from University Medical Center Gröningen and University Medical Center Utrecht (both in The Netherlands) described "Nuclear medicine imaging of posttraumatic osteomyelitis." Leiblich et al. from the University of Oxford (UK) reviewed "The utility of molecular imaging in prostate cancer" in the March issue of *Current Urology Reports* (2016;17:26). In an article e-published on February 20 ahead of print in the *Journal of Neuro-Oncology*, Frosina, from the Azienda Ospedaliera Universitaria San Martino/IST Istituto Nazionale per la Ricerca sul Cancro (Genoa, Italy) provided an overview of "Positron emission tomography of high-grade gliomas." Bleumel et al. from University Hospital Würzburg (Germany), Technische Universität München (Germany), University of California Los Angeles, and the The Ohio State University (Columbus) published "3D scintigraphic imaging and navigation in radioguided surgery: freehand SPECT technology and its clinical applications" on February 15 ahead of print in *Expert Review of Medical Devices.*