

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.

⁶⁸Ga-MAA Perfusion 4D PET/CT

In an article e-published on January 9 ahead of print in *Technology in Cancer Research & Treatment*, Siva et al. from the University of Melbourne (Parkville, Australia) and the Peter MacCallum Cancer Centre (East Melbourne, Australia) reported on the use of ⁶⁸Ga-macroaggregated albumin (⁶⁸Ga-MAA) PET/CT for functional adaptation of definitive radiotherapy plans in patients with non-small cell lung cancer (NSCLC). The study included 14 patients with NSCLC scheduled for definitive 3D conformal radiation therapy (to 60 Gy in 30 fractions) who underwent pretreatment respiratory-gated ⁶⁸Ga-MAA PET/CT. The researchers defined a “perfused lung volume” on the images as the entire lung parenchyma with tracer uptake. A “well perfused” volume was then contoured using a visually adapted threshold of 30% maximum standardized uptake value. Alternate 3D conformal plans were created to optimize avoidance of the identified perfused and well-perfused volumes. Conventional anatomic lung volumes were then compared with functional dose volumetrics on the basis of mean lung dose, V5 (volume receiving ≥ 5 Gy), V10, V20, V30, V40, V50, and

V60. Following the original treatment plan, the average mean lung dose with conventional anatomic lung volumes (12.11 Gy) was similar to the dose to perfused (12.15 Gy) and well-perfused functional lung volumes (12.67 Gy). Plans optimized for well-perfused lung volumes improved functional V30, V40, V50, and V60 values, with functional mean lung dose of well-perfused lung improved by a median of 0.86 Gy. Plans optimized for perfused lung showed significant improvement only in the functional V60 dose, with a worse functional V5. The authors concluded that these data suggest that 4D perfusion PET/CT may contribute to functional lung avoidance during radiation treatment planning in NSCLC.

Technology in Cancer Research & Treatment

¹⁸F-Fluorocholine PET/CT in Recurrent Prostate Cancer

Simone et al. from the Regina Elena National Cancer Institute (Rome, Italy) reported on January 11 ahead of print in the *World Journal of Urology* on a novel imaging acquisition protocol for ¹⁸F-fluorocholine PET/CT in patients with biochemical recurrence after radical prostatectomy. The study included 146 men with prostate-specific antigen (PSA) levels 0.2–1 ng/mL with negative conventional imaging who had not undergone salvage treatment. For the imaging protocol an early dynamic phase (at 1–8 min after injection) was followed by a conventional whole-body phase (10–20 min) and a late phase (30–40 min). The researchers analyzed the predictive capabilities of each of the elements in this technique. ¹⁸F-fluorocholine PET/CT was positive in 111 of 146 patients (76%); of these, 80 (72.1%) were positive only in the early dynamic phase imaging. Overall sensitivity, specificity, positive and negative predictive values, and accuracy were 78.9%, 76.9%, 97.2%, 26.3%, and 78.7 %, respectively. Trigger PSA ≥ 0.6 ng/mL and median PSA velocity ≥ 0.04 ng/mL/mo

were found to be independent predictors of positive PET/CT. The authors concluded that “increased sensitivity, thanks to the early imaging acquisition protocol, makes ¹⁸F-fluorocholine PET/CT an attractive tool to detect prostate cancer recurrences in patients with a PSA level <1 ng/mL,” but noted that the low negative predictive value remains a limitation of this protocol.

World Journal of Urology

PSMA-Based Imaging and Clinical Management

In an article e-published on January 18 ahead of print in *Prostate*, Demirkol et al. from the Koc University School of Medicine and the VKF American Hospital (both in Istanbul, Turkey) reported on the effect of prostate-specific membrane antigen (PSMA)-based PET/CT imaging on clinical decision making in patients with prostate cancer. The retrospective study focused on the medical records of 22 men (median age, 68 y; range, 43–86 y) with a median serum prostate-specific antigen (PSA) level of 4.15 ng/mL (range, 0.2–191.5 ng/mL), each of whom underwent ⁶⁸Ga-PSMA PET/CT. Indications for imaging included eventually rising PSA after local \pm adjuvant treatment ($n = 11$), pretreatment staging and evaluation in high-risk prostate cancer ($n = 7$), failure to achieve PSA nadir after local treatment for curative intent ($n = 1$), staging and metastatic evaluation after initiation of definitive treatment ($n = 1$), rising PSA despite systemic therapy in a patient who presented with metastatic disease ($n = 1$), and symptomatic progression despite hormonal therapy in a patient with locally advanced high-risk prostate cancer ($n = 1$). Twenty patients had prostatic \pm extra-prostatic PSMA-positive lesions on imaging, with treatment strategies modified accordingly. Above a PSA level of 2 ng/mL, all of the PSMA-based nuclear imaging studies showed positive results. The authors concluded that the ability of PSMA-based nuclear imaging “to detect lesions even in low

PSA values seems fairly promising and deserves to be supplemented with further clinical studies."

Prostate

DAT SPECT in Movement Disorder Practice

Bega et al. from Northwestern University's Feinberg School of Medicine (Chicago, IL) reported on January 15 ahead of print in *Neuro-Degenerative Diseases* on a study of the potential role for dopamine transporter (DAT) SPECT imaging in medical practices treating movement disorders. The authors retrospectively analyzed indications for ordering DAT SPECT scans and the clinical impact of scan results in 83 patients seen by 4 specialist neurologists in a movement disorders practice. Imaging was most often ordered to differentiate Parkinson disease from essential tremor ($n = 18$; 21.7%) or from drug-induced parkinsonism ($n = 18$; 21.7%). Changes in clinical diagnosis or medication were seen in 49 patients (59%) within 1 visit after imaging. Among those in whom imaging was ordered to differentiate Parkinson disease from essential tremor, this figure was 72.2%. The authors concluded that "DAT SPECT has significant impact on clinical diagnosis and management even in the hands of movement disorders specialists" at a tertiary referral center.

Neuro-Degenerative Diseases

Evidence-Based Guideline Effects on ^{131}I Treatment

In an article e-published on January 10 ahead of print in *Thyroid*, Sacks et al. from Cedars-Sinai Medical Center (Los Angeles, CA) reported on a study designed to identify whether and how the introduction of evidence-based radioactive iodine (RAI) treatment guidelines for differentiated thyroid cancer (DTC) would affect subsequent RAI use at their institution. The study included data on 444 patients, of whom ~95% ($n = 423$) had papillary thyroid cancer and 65% ($n = 290$) were in the stage I risk group. Analysis of Kaplan-Meier curves for those in stages I-III showed that patients who did not undergo ^{131}I treatment had 100% disease-free survival. This result was better

than that achieved in patients receiving RAI, although the results were not statistically significant for the very small percentage of patients in stages II and III. Patients with stage I disease who underwent RAI were found to have a significantly increased incidence of recurrent disease compared with those who did not. Significant differences were found between treatment rates at the authors' institution and aggregate data from other institutions in the National Cancer Database. After the introduction of new evidence-based guidelines, ablation rates steadily decreased at the authors' institution, particularly among low-risk patients with stage I tumors. The authors advised that "prudent use of RAI treatment should be considered for low-risk patients" and concluded that "it is apparent from our data that physician practices can change with the implementation and dissemination of evidence-based guidelines for the treatment of DTC with RAI."

Thyroid

PET and Placental Glucose Avidity

Sawatzke et al. from the University of Iowa Carver College of Medicine (Iowa City) reported in the February issue of *Placenta* (2015;36:115-120) on a study using ^{18}F -FDG PET to define the kinetics of glucose transport from maternal blood into the placenta and fetus in a late-gestational rat model. CT was coregistered with PET to enhance anatomical detail. The researchers found that the tracer was rapidly taken up by the placenta and the fetus after material injection, with standardized uptake values approaching those of the maternal brain. In both anesthetized and awake mothers, fully one-fourth of the tracer ultimately localized in the fetus and placenta. Additional kinetic modeling confirmed the placenta was twice as high in ^{18}F -FDG avidity as either the fetus or the maternal brain. Placental expression of glucose transporter 1 exceeded that of all other tissues. These results suggest that fetal and placental tissues place a substantial glucose metabolic burden on the mother. The authors

concluded that because of the "tremendous capacity" of the placenta to uptake and transport glucose in these translational models, "PET/CT imaging is an ideal means to study metabolite transport kinetics in the fetoplacental unit."

Placenta

Imaging Trends in Postdiagnosis Thyroid Cancer

In an article e-published on January 6 in *Cancer*, Wiebel et al. from the University of Michigan (Ann Arbor) assessed U.S. trends in imaging after diagnosis of differentiated thyroid cancer (DTC). Data from the Surveillance, Epidemiology, and End Results-Medicare database were used from a population of 23,669 patients diagnosed with localized, regional, or distant DTC and treated between 1991 and 2009. Medicare claims were then reviewed to identify those patients who underwent neck ultrasound, ^{131}I imaging, or PET imaging within 3 y after diagnosis. Patients diagnosed in the second half of the study period (2001–2009) were more likely to have localized disease and tumors <1 cm than those in the first half (1991–2000). In the later group, neck ultrasound and ^{131}I imaging increased in patients with localized disease, regional disease, and distant metastasis. PET imaging use increased 32.4-fold in the 2005–2009 period in patients with localized disease, 13.1-fold in regional disease, and 33.4-fold in distant DTC when compared with corresponding patients diagnosed from 1996 to 2004. The authors concluded that "despite an increase in the diagnosis of low-risk disease, the use of postdiagnosis imaging increased among patients with all stages of disease."

Cancer

$^{99\text{m}}\text{Tc}$ Alternative to ^{18}F -FMISO

Mallia et al. from the Bhabha Atomic Research Centre (Mumbai, India) reported on January 8 ahead of print in *Cancer Biotherapy & Radiopharmaceuticals* on a study investigating the potential of a $^{99\text{m}}\text{Tc}$ -labeled SPECT alternative to the PET radiopharmaceutical ^{18}F -fluoromisonidazole (^{18}F -FMISO) for

tumor hypoxia imaging. The researchers labeled a misonidazole analog with a ^{99m}Tc (CO)₃ core and compared the imaging efficacies and characteristics of this agent and ^{18}F -FMISO in mice with fibrosarcoma tumors. SPECT imaging with misonidazole- $^{99m}\text{Tc}(\text{CO})_3$ showed significant uptake and retention in tumor, as well as a slower clearance of the misonidazole complex from tumor than was seen with ^{18}F -FMISO PET. The maximum tumor-to-muscle ratio with misonidazole- $^{99m}\text{Tc}(\text{CO})_3$ was significantly higher than that of ^{18}F -FMISO.

Cancer Biotherapy & Radiopharmaceuticals

PET/CT and Carotid Plaque Inflammation

In an article e-published on January 15 ahead of print in the *International Journal of Stroke*, Skagen et al. from Oslo University Hospital and the University of Oslo (Norway) reported on a study assessing tracer uptake in carotid plaques on ^{18}F -FDG PET and correlating results with cerebrovascular symptoms, carotid plaque ultrasound echogenicity, and plaque inflammation histology. The study included 36 patients who were scheduled for carotid endarterectomy because of $\geq 70\%$ carotid stenosis and who underwent color duplex ultrasound, ^{18}F -FDG PET/CT imaging, and hematologic tests < 24 h before surgery. Patients were defined as symptomatic when plaques were associated with ipsilateral cerebral ischemic symptoms within a 30-d period before inclusion in the study. Tracer uptake on PET and the amount of inflammation identified at histology were significantly correlated, with ^{18}F -FDG uptake significantly higher in symptomatic (median maximum standardized uptake value [SUV_{\max}] = 1.75) than in nonsymptomatic (median SUV_{\max} = 1.43) patients. The amount of ^{18}F -FDG uptake also correlated positively with echolucency on Doppler ultrasound. The authors concluded that "these results support the use of ^{18}F -FDG PET/CT in the detection inflammation in carotid atherosclerosis, which may be of help in the detection of vulnerable plaques."

International Journal of Stroke

PET/CT and Childhood Rhabdomyosarcoma

Norman et al. from the University of York (UK), Royal Marsden Hospital (London, UK), Great Ormond Street Hospital (London, UK) and Children's Hospital for Wales (Cardiff) reported on January 8 in *BMJ Open* (2015;5: e006030) on a systematic review of the diagnostic accuracy and clinical effectiveness of advanced functional imaging in pediatric rhabdomyosarcoma. The analysis included studies with ≥ 10 patients and which compared PET or PET/CT with conventional imaging at any treatment stage. Eight eligible studies (6 PET/CT, 2 PET) were identified with a total of 272 patients. Although the limited number of disparate studies did not provide robust data, evidence suggested that initial PET/CT results were predictive of survival. PET/CT resulted in changes in management for 7 of 40 patients in 1 study. Sensitivity and specificity of PET/CT for nodal involvement were 80%–100% and 89%–100%, respectively. Corresponding figures for distant metastatic involvement were 95%–100% and 80%–100%. The authors concluded that although these limited data indicate that PET and PET/CT may increase initial staging accuracy in pediatric rhabdomyosarcoma, "there is a need to further assess PET/CT for this population, ideally in a representative, unbiased, and transparently selected cohort of patients."

BMJ Open

PET and RT Response in ATC

In an article e-published on January 13 ahead of print in *Oral Oncology*, Levy et al. from the Institut Gustave Roussy at Paris Sud University (Villejuif, France) reported on the ability of ^{18}F -FDG PET/CT to evaluate and predict tumor response after radiation therapy in patients with anaplastic thyroid cancer (ATC). The study included 92 patients seen from 1987 to 2012, of whom 64 (70%) underwent aggressive multimodal treatment and 28 (30%) underwent palliative treatment. Multimodal treatment included curative-intention sur-

gery ($n = 35$; 55%), chemotherapy ($n = 59$; 92%), and radiation therapy ($n = 56$; 88%). Subsets of patients underwent ^{18}F -FDG PET imaging before any treatment ($n = 26$; 40%), before RT ($n = 19$; 30%), and after radiation therapy ($n = 25$; 39%), with maximum standardized uptake values (SUV_{\max}) assessed in tumor, nodes, and metastases. The median follow-up was 3.2 y, with a 1-y overall survival of 18% (median, 5.2 mo) for all 92 patients and 27% (median, 7 mo) for the group that underwent multimodal treatment. Radiation therapy, surgery, and preradiation chemotherapy independently predicted for overall survival. On PET, mean SUV_{\max} significantly decreased in tumors but not in nodes and metastases during the assessment period. The mean relative SUV_{\max} decrease in tumor was lower in the 4 patients with local relapse than in nonrelapsing patients. A relative SUV_{\max} decrease $< 20\%$ significantly predicted for local relapse. The authors concluded that although several of these results did not reach the level of statistical significance, " ^{18}F -FDG PET/CT could potentially serve as a surrogate marker of treatment response in ATC."

Oral Oncology

SLN Staging in Prostate Cancer

Van den Bergh et al. from the University Hospitals Leuven and KU Leuven (Belgium) reported on January 16 ahead of print in *Acta Oncologica* on a study investigating the reliability of a sentinel node procedure for nodal staging in patients with prostate cancer at high risk for lymph node involvement. The study included 74 men with localized prostate adenocarcinoma who were clinically node negative with a calculated risk of lymph node involvement $\geq 10\%$. After intraprostatic ^{99m}Tc -nanocolloid injection, all participants underwent planar scintigraphy and SPECT imaging and proceeded to surgery. An intraoperative gamma probe guided surgical removal of the sentinel node, followed by a superextended lymph node dissection and radical prostatectomy. A total of 470

sentinel nodes (median 6/pt) were detected, with 371 (median 4/pt) located by gamma probe and selectively removed. Histopathology analysis confirmed lymph node metastases in 37 (50%) patients with 106 affected lymph nodes (median 2/pt). Histology indicated that 28 patients were node positive, but the superextended lymph node dissection showed 9 additional node-positive patients. Fifteen of 37 patients (41%) were found to have metastases in the sentinel node and could have been spared superextended lymph node dissection to remove all affected nodes. The authors concluded that these results indicated "a relatively low sensitivity when addressing the sentinel node procedure for nodal staging in prostate cancer patients at high risk for lymph node involvement," adding that "only less than half of the node-positive patients could have been spared a superextended lymph node dissection to remove all affected lymphoid tissue."

Acta Oncologica

PET MR in Ankylosing Spondylitis

In an article e-published on January 9 ahead of print in *Clinical and Experimental Rheumatology*, Lee et al. from Pusan National University School of Medicine and Hospital (Busan, South Korea) reported on a study using ¹⁸F-fluoride PET/MR to assess bone synthesis in inflammatory lesions and syndesmophytes in patients with ankylosing spondylitis. The study included 12 patients whose PET/MR images were assessed for increased tracer uptake on PET, for corner inflammatory lesions (CILs) on MR, and for syndesmophytes on radiographs at the anterior vertebral corners. A total of 67 type A and 37 type B CILs were identified, along with 58 increased PET tracer uptake lesions, out of 552 vertebral corners, as well as 57 syndesmophytes out of 288 vertebral corners. A type A or B CIL and a syndesmophyte were significantly associated with increased ¹⁸F-fluoride lesion uptake. These results suggest that "an inflammatory lesion as

well as a syndesmophyte is associated with active bone synthesis assessed by ¹⁸F-fluoride uptake in the spine of ankylosing spondylitis patients," so that "¹⁸F-fluoride PET/MRI may have the potential for investigating the pathogenesis of structural damage" in these patients.

Clinical and Experimental Rheumatology

Guideline Familiarity: H&N Cancer Imaging Surveillance

Roman, from the University of Pennsylvania (Philadelphia) and researchers from New York, California, and other parts of Pennsylvania reported in the January issue of the *Journal of the National Comprehensive Cancer Network* (2015;13:69–77) on a study of the effect of physician guideline familiarity on surveillance imaging with PET/CT in patients with head and neck squamous cell cancer. The study included 502 respondents, of whom 79% had used PET/CT for routine surveillance imaging and 39% were categorized as high imaging users (using PET/CT surveillance in >50% of asymptomatic patients). A total of 76% of respondents indicated that they were familiar with the National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology for Head and Neck Cancers, which recommend against PET/CT imaging for routine surveillance. Although familiarity with this recommendation was positively associated with lower imaging use, 31% of those familiar with the guidelines were high imaging users and 73% of those familiar with the guidelines reported ever using PET/CT imaging for surveillance. The authors concluded that although NCCN guideline familiarity appears to influence the choices of some practitioners, "given the observed variation and high levels of imaging even among physicians who are familiar with the guidelines, further research should examine the reasons physicians choose to use surveillance PET/CT scans."

Journal of the National Comprehensive Cancer Network

PET and Skeletal Muscle Inflammation

In an article e-published on January 12 in *BMJ Open*, Tateyama et al. from the Tohoku University School of Medicine (Sendai, Japan) detailed a study of the utility of ¹⁸F-FDG PET in evaluating muscle lesions in polymyositis and dermatomyositis (PM/DM) syndromes. The retrospective study included the records of 33 patients with PM or DM who had undergone ¹⁸F-FDG PET imaging. Tracer uptake was visually evaluated in 16 regions of the body and standardized maximum uptake values (SUV_{max}) were calculated in all 4 limbs of the patient group as well as in images of patients with amyotrophic lateral sclerosis (ALS) with similar disabilities. In 24 of the 33-patient target group, additional MR imaging was compared with PET findings. The researchers found that visual assessment identified tracer uptake in multiple muscle lesions and varying distributions in approximately two-thirds of patients with PM/DM. The number of visually positive regions was strongly correlated with the mean SUV_{max} in all 4 limbs, and histologic grades of biopsied muscles corresponded with both of these tracer assessments. On MR imaging inflamed muscles showed diffused, patchy, or marginal signal abnormalities, whereas ¹⁸F-FDG uptake on PET was most prominent inside the muscles. Mean SUV_{max} was significantly higher in patients with PM/DM than in those with ALS, with much more bilateral and symmetric involvement. The authors concluded that visual assessment of ¹⁸F-FDG uptake and calculation of SUV_{max} enabled comprehensive evaluation of skeletal muscle and that "this method can improve clinical practices and provide insights into pathomechanisms of PM/DM."

BMJ Open

PET/CT and Epithelial Ovarian Cancer Relapse

Kim et al. from the Kyungpook National University School of Medicine/Hospital (Daegu, Republic of Korea) reported on December 31 ahead of print in *Gynecologic Oncology* on a study evaluating the prognostic value of quantitative metabolic parameters measured

on ^{18}F -FDG PET/CT at time of first relapse in patients with epithelial ovarian cancer. The retrospective study included the records of 56 women with relapsed epithelial ovarian cancer who underwent PET/CT imaging at the time of first relapse. Over the follow-up period of the study, 32 patients died from disease (median, 46.2 mo). Significant factors in postrelapse survival were found to include platinum-free interval, type of second-line treatment, whole-body metabolic tumor volume, and whole-body total lesion glycolysis. A subgroup of women who were platinum sensitive with low whole-body metabolic tumor volume on PET/CT had better survival than other subgroups. Patients treated with secondary cytoreductive surgery followed by second-line chemotherapy had significantly longer duration of postrelapse survival than those treated with second-line chemotherapy alone (61 and 36 mo, respectively). The authors concluded that these results suggest that “quantitative metabolic parameters measured on FDG PET/CT at the time of the first relapse have significant predictive values for post-relapse survival” and that “incorporating quantitative metabolic parameters and conventional clinical parameters has a superior prognostic discrimination compared with conventional clinical parameters alone.”

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 December and January. On January 2, ahead of print in *Progress in Cardiovascular Diseases*, Petretta et al. from the University Federico II (Naples, Italy), the IRCCS Regional Cancer Hospital CROB (Rionero in Vulture, Italy), and the National Council of Research (Naples, Italy) reported on “Quantitative assessment of myocardial blood flow with SPECT.” Isobe and Tezuka from the Tokyo Medical and Dental University (Japan) reviewed “Early cardiac sarcoidosis: clinical characteristics, diagnosis and treatment” on December 23 ahead of print in the *International Journal of Cardiology*. In an article in the January 16 issue of the *Journal of Orthopaedic Surgery and Research* (2015;10:5), Adesanya et al. from University Hospitals of Coventry and Warwickshire and the University of Warwick (Coventry, UK) published a “Review of the role of dynamic ^{18}F -NaF PET in diagnosing and distinguishing between septic and aseptic loosening in hip prosthesis.” Howes et al. from the Hammersmith Hospital and King’s College London (London, UK) provided an overview of “Glutamate and dopamine in schizophrenia: an update for the 21st century” in an article published online on January 13 ahead of print

in the *Journal of Psychopharmacology (Oxford)*. On December 27, ahead of print in *Neuro-Oncology*, Hutterer et al. from University Hospital and Medical School (Regensburg, Germany), University Hospital Bonn (Germany), and Ostbayerische Technische Hochschule Regensburg (Germany) described “Current standards and new concepts in MRI and PET response assessment of antiangiogenic therapies in high-grade glioma patients.” Alonso et al. from the University of Heidelberg (Germany) reported on “Molecular imaging of carotid plaque vulnerability” in the December 24 issue of *Cerebrovascular Diseases (Basel)* (2014;39:5–12). On December 24, ahead of print in *Stem Cell Reviews*, Wolfs et al. from KU Leuven (Belgium) provided an overview of “Radiolabeling strategies for radionuclide imaging of stem cells.” Piccinelli and Garcia from the Emory University School of Medicine (Atlanta, GA) reported on “Advances in software for faster procedure and lower radio-tracer dose myocardial perfusion imaging” on December 31 ahead of print in *Progress in Cardiovascular Diseases*. In an article e-published on January 5 ahead of print in *The Oncologist*, Humbert et al. from the Université de Bourgogne (Dijon, France) reviewed the “Role of positron emission tomography for the monitoring of response to therapy in breast cancer.”