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.

225Ac-PSMA-617 After 177Lu-PSMA in mCRPC

Feuerecker et al. from the Technical University of Munich/German Cancer Consortium (DKTK), the German Cancer Research Center (DKFZ) (Heidelberg), the European Commission, Joint Research Centre (Karlsruhe), and University Hospital Heidelberg (all in Germany) reported on December 5 ahead of print in *European Urology* on a retrospective study of the safety of 225Ac–prostate-specific membrane antigen (PSMA)–617 radioligand therapy in metastatic castrate-resistant prostate cancer (mCRPC) in men experiencing disease progression after 177Lu-PSMA therapy. The study included 26 patients with a median of 6 previous treatment regimens, who were scheduled to receive 225Ac-PSMA-617 every 8 wk until progression or intolerance resulting from toxicities/side effects. The participants received a median number of 2 cycles at a median activity of 9 MBq. In 17 patients, a ≥50% drop in prostate-specific antigen (PSA) was seen. The median PSA progression-free survival, clinical progression-free survival, and overall survival periods for all participants were 3.5, 4.1, and 7.7 mo, respectively. Hematologic grade 3 and 4 toxicities included anemia (35% of

participants), leukopenia (27%), and thrombocytopenia (19%), with all patients experiencing grade 1 or 2 xerostomia. The study was halted for 2 patients as a result of hematologic toxicities and for 6 as a result of xerostomia. Liver metastases were associated with shorter progression times and overall survival. The authors concluded that "225Ac-PSMA-617 showed measurable antitumor effect after 177Lu-PSMA failure in late-stage mCRPC," with side effects and toxicities (including xerostomia) limiting study length in about a third of patients.

European Urology

Outcomes and Molecular Profiling with 225Ac-PSMA-617

In an article published on December 19 ahead of print in *Urologic Oncology*, van der Doelen et al. from Radboud University Medical Center/Radboud University Medical Center (Nijmegen, The Netherlands), the European Commission, Joint Research Centre (Karlsruhe, Germany), University Hospital Heidelberg (Germany), and the Technical University of Munich (Germany) reported on the efficacy, quality of life considerations, and pretherapeutic biomarkers associated with 225Ac–prostate-specific membrane antigen–617 (225Ac-PSMA-617) treatment in metastatic castrate-resistant prostate cancer (mCRPC). Thirteen men were included in the trial. Median overall survival was 8.5 mo but was 1.3 mo for those who had previously undergone 177Lu-PSMA therapy and 12.6 mo for those who had not. Prostate-specific antigen level decreases of ≥90% were seen in 6 (46%) patients and ≥50% in 9 (69%) patients. Of the 6 patients who were evaluable by CT, 50% showed partial responses. 68Ga-PSMA-11 PET/CT imaging was available in 7 patients, with 6 (86%) showing partial responses according to PERCIST and all 7 showing >90% total tumor volume reduction. No grade 3 or 4 toxicities were observed, but all participants experienced varying degrees of xerostomia, which persisted in

follow-up. Patients reported clinically relevant decreases in pain as well as quality of life improvement. Biopsies from several patients were analyzed with immunohistochemistry and next-generation sequencing, with results indicating that individuals with higher tissue PSMA expression or DNA damage repair alterations (potential predictive biomarkers) tended to have longer overall survival. The authors summarized their findings that targeted α therapy with 225Ac-PSMA-617 resulted in "remarkable survival and biochemical responses in advanced mCRPC patients."

Urologic Oncology

Reduced PET/CT Scan Times in Lymphoma

Weber et al. from the University of Duisburg–Essen/University Hospital Essen, the German Cancer Consortium (DKTK) (Essen), and Siemens Medical Solutions USA, Inc. (Erlangen, all in Germany) reported on January 14 in *BMC Cancer* (2021;21[1]:62) on a study assessing the feasibility of reduced scanning times in evaluation of lymphoma, where the superior accuracy and sensitivity of 18F-FDG PET/CT in comparison to morphologic imaging alone leads to an upstaging in up to 30% of patients. The study included data from 20 lymphoma patients (indications: initial staging, 6; after systemic treatment, 12; and for suspicion of recurrence, 2) who underwent imaging on a Siemens Biograph Vision using continuous bed motion with total scan times of 15 minutes (for reference acquisition data) and 5 minutes (for the reduced acquisition protocol). The resulting datasets were reconstructed in multiple ways for lesion detectability by blinded assessment, lesion image quantification, and image noise. No changes in staging were observed between data acquired at different scan times, with all defined regions correctly classified in the images. Lesion quantification was acceptable. Image noise increased in the shorter scans from 7.1% to 11.0% (reconstructed with 4 iterations) and from 4.7% to 7.2% (reconstructed with 2 iterations). The authors concluded

that "these results suggest that scan time duration or administered tracer activity can be reduced 3-fold without compromising diagnostic performance" and that larger trials are needed to confirm and elaborate on these results. They highlighted the potential benefits of shorter scan times and reduced tracer activity, including higher patient throughput, cost efficiency, and a reduction in radiation exposure in the large number of younger lymphoma patients.

BMC Cancer

PET/CT in Langerhans Cell Histiocytosis

Ferrell et al. from the University of Cincinnati College of Medicine and Cincinnati Children's Hospital Medical Center (both in OH) reported on January 14 ahead of print in *Pediatric Blood & Cancer* on a retrospective study of discrepancies between PET/CT and conventional imaging in patients with Langerhans cell histiocytosis (LCH). The study included 107 ^{18}F-FDG PET/CT images acquired in individuals with histopathologically confirmed LCH from a single institution over a 10-y period, as well as MR, CT, and other imaging acquired during clinical care. Discrepancies between PET/CT and conventional imaging were seen in 53 instances. In 13 instances, increased uptake on PET was not correlated with any identifiable lesion on conventional imaging. On 40 occasions, conventional imaging identified lesions where no increased uptake was seen on PET. The authors concluded that "^{18}F-FDG PET/CT is vital in the evaluation of LCH lesions given its ability to detect LCH lesions not detectable on conventional imaging modalities, as well as its ability to distinguish metabolically active from inactive disease" and thereby avoid unnecessary treatment. They noted that MRI and diagnostic CT remain useful adjunctive tests for identification of central nervous system and lung lesions.

Pediatric Blood & Cancer

PSMA-Targeting Ligands for Intraoperative Applications

In an article in the January 1 issue of *Theranostics* (2021;11[4]:1527-1541), Derks et al. from Radboud University Medical Center/Radboud University Nijmegen (Nijmegen, The Netherlands), Prosper Clinics (Nijmegen, The Netherlands), Canisius Wilhelmina Hospital (Nijmegen, The Netherlands), and University Hospital Bonn (Germany) reported on the development and characterization of photosensitizer-based multimodal ^{111}In-DOTA(GA)-IRDye700DX–prostate-specific membrane antigen (PSMA) ligands, with varying molecular composition, for use in intraoperative radiodetection, fluorescence imaging, and targeted photodynamic therapy of prostate cancer lesions. Initial studies in xenografted tumor models and human prostate cancer biopsies indicated the PSMA specificity of the ligand and allowed optimization with the addition of the IRDye700DX photosensitizer and other modifications to increase uptake in PSMA-expressing tumors. An additional incubation study on human tumor biopsies confirmed PSMA specificity. The authors highlighted the potential of this approach for reducing incomplete resection rates.

Theranostics

^{18}F-PSMA-1007 PET-Based Contouring Techniques

Spohn et al. from the Medical Center/University of Freiburg and the German Cancer Consortium (DKTK) Partner Site Freiburg (both in Germany) reported on December 7 in *Frontiers in Oncology* (2020;10:600690) on a study comparing manual and semiautomatic ^{18}F–prostate-specific membrane antigen (PSMA)–1007 PET-based contouring techniques for intraprostatic tumor delineation. The prospective study included 10 patients with primary prostate cancer who underwent ^{18}F-PSMA PET imaging before radical prostatectomy. The resulting images were contoured manually with PET scaling at $SUV_{min-max}$ of 0–10 performed by 3 teams with varying levels of reader experience; and semiautomatic contouring using SUV_{max} thresholds of 20%–50%. Coregistered histopathologic gross tumor volumes were used as standards of reference. Interobserver agreement on manual contouring was good, with derived volumes showing no statistical differences with the standard of reference as well as high sensitivities (median, 87%; range, 84%–90%) and specificities (median, 96%; range, 96%–100%). The best-performing semiautomatic contour (gross tumor volume, SUV_{max} 20%) achieved high sensitivity (median, 93%) and specificity (median, 96%). The authors concluded that both "manual contouring with PET scaling $SUV_{min-max}$ 0–10 and semiautomatic contouring applying a threshold of 20% of SUV_{max} achieved high sensitivities and very high specificities and are recommended for ^{18}F-PSMA-1007 PET-based focal therapy approaches." In addition, "semiautomatic approaches applying thresholds of 30%–40% of SUV_{max} are recommended for biopsy guidance."

Frontiers in Oncology

Cerebral ^{99m}Tc-TRODAT-1 SPECT in PD

In an article published on December 23 in *Medical Science Monitor*, Ariona et al. from the Hospital Israelita Albert Einstein and the Federal University of São Paulo (both in São Paulo, Brazil) reported on the use of cerebral ^{99m}Tc-TRODAT-1 SPECT imaging of dopamine transporters in patients with suspected Parkinson disease (PD) or clinically unclear parkinsonism. The study also included a brief questionnaire from referring physicians (the majority of whom were neurologists) to assess the scans' utility in clinical management decisions. Among the indications for requested scans were evaluation or confirmation of dopaminergic denervation (69%), differentiation of PD from essential tremor (10%), and differentiation of degenerative from drug-induced parkinsonism (6%). Resulting analysis indicated that ^{99m}Tc-TRODAT-1 SPECT was useful in 85% of cases, changing management in 75% of patients. "Inappropriate use" of dopamine transporter imaging was identified in 5% of cases. The authors concluded that this study "demonstrated that brain scintigraphy with the dopamine transporter ligand ^{99m}Tc-TRODAT-1 may influence diagnostic or therapeutic interventions" and that Brazilian physicians who requested the exam were considering these results in clinical decision making.

Medical Science Monitor

Quantitative PET/CT Dynamic Perfusion and SABR in Lung Cancer

Yang et al. from the University of Western Ontario (London), Lawson Health Research Institute (London), London Regional Cancer Program, London Health Sciences Centre, and the Sunnybrook Health Sciences Centre (Toronto; all in Canada) reported on January 13 in *Radiation Oncology* (2021;16[1]:11) on a study designed to develop a predictive model for true pathologic complete response to stereotactic ablative radiation therapy (SABR) using imaging-based biomarkers from dynamic ^{18}F-FDG PET and CT perfusion. The study included 26 patients with early-stage non–small cell lung cancer treated with SABR before surgical resection. Dynamic ^{18}F-FDG PET and CT perfusion imaging was performed before and 8 wk after SABR. PET provided SUV_{max} and SUV_{mean} and kinetic parameters, and CT perfusion measured blood flow, blood volume, and vessel permeability surface product. A resulting predictive model incorporating these data was compared to RECIST and PERCIST. The model identified 3 response groups based on tumor blood volume before SABR (threshold = 9.3 mL/100 g) and change in SUV_{max} (threshold, –48.9% change). The highest true pathologic complete response rate of 92% was observed in the group with corresponding values of <9.3 mL/100 g and change in SUV_{max} <–48.9% after SABR. The model achieved excellent pathologic complete response prediction (concordance: 0.92), whereas the corresponding values for RECIST and PERCIST were poor (concordance: 0.54 and 0.58, respectively).

Radiation Oncology

Postdiurectic ^{68}Ga-PSMA-11 PET/CT in Indeterminate Lesions

In an article in the December issue of the *Asian Pacific Journal of Cancer Prevention* (2020;21[12]:3719-3723) Ghadanfer et al. from Kuwait University, the Kuwait Cancer Control Center, the Sheikh Jaber Al Ahmad Al Sabah for Nuclear Medicine and Molecular Imaging Center (Kuwait), and Government College University (Faisalabad, Pakistan) evaluated the effect of diuretic-assisted ^{68}Ga–prostate-specific membrane antigen (PSMA) PET/CT on image quality and clinical interpretation of indeterminate/equivocal lesions in pre-Lasix imaging of prostate cancer. The study included 45 men who underwent baseline ^{68}Ga-PSMA-11 imaging 45–60 min after tracer injection followed by a post-Lasix administration study at ±15 minutes. Image data were analyzed, and experienced physicians evaluated lesion detectability and features that could affect clinical interpretation. Imaging in 12 patients was negative and in 33 indicated metastases. Thirty-six percent of the metastatic scans included indeterminate/equivocal lesions. Of these, the post-diuretic study produced false-negative findings in 7 (16%), better delineation of lesions in 10 (22%), and better confidence in reporting lesions as abnormal in 5 (11%), with an overall 11 (24%) cases showing increases in the number of the lesions after the Lasix study. Additional analyses indicated significantly improved contrast-to-noise ratios in the post-Lasix imaging (by 49.6% ± 24.5%), where substantial agreement was also noted between physicians when comparing lesion clarity and delineation. The authors concluded that postdiuretic ^{68}Ga-PSMA imaging at ±15 min "clears the unwanted activity in the urinary tract which in turn improves the contrast-to-noise ratios, thus leading to decline in false-positive findings, improved diagnostic certainty of physician, and better detection of indeterminate lesions."

Asian Pacific Journal of Cancer Prevention

GLP-1 R–Targeted Imaging in Insulinoma

Shah et al. from Seth GS Medical College/KEM Hospital (Mumbai, India), New York Medical College/Metropolitan Hospital Center (NY), and Tata Memorial Centre (Mumbai, India) reported on January 1 ahead of print in *Clinical Endocrinology (Oxford)* on a systematic review of the published English literature on the utility of glucagon-like peptide-1 receptor (GLP-1 R)–targeted imaging in insulinoma, with an accompanying individual patient data metaanalysis and calculation of performance parameters for histopathologic diagnosis of insulinoma. For the metaanalysis, a total of 179 cases (316 lesions) reported in 16 publications were included. For insulinoma localization, GLP-1 R–targeted PET/CT (both sensitivity and positive predictive value, 94%) performed better than GLP-1 R–targeted SPECT/CT (sensitivity, 63%; positive predictive value, 94%). Sensitivity was lower in malignant insulinomas, and specificity was higher in cases with multiple endocrine neoplasia type-1 syndrome. A few patients showed false-positive uptake in Brunner's gland, normal pancreas, and other β-cell pathologies and false-negative results in pancreatic tail lesions/malignancy with GLP-1 R–targeted imaging. True-negative results indicated the correct diagnosis of other endogenous hyperinsulinemic hypoglycemia subtypes. The authors concluded that for insulinoma localization, GLP-1 R–targeted PET/CT should be preferred over GLP-1 R–targeted SPECT/CT because of higher sensitivity and specificity, with certain false-positive and -negative limitations.

Clinical Endocrinology (Oxford)

PET/CT and CECT in Recurrent Gastric Cancer

In an article in the February issue of *Experimental and Therapeutic Medicine* (2021;21[2]:164) Zhang et al. from the Ninth People's Hospital of Chongqing (China) reported on a metaanalysis designed to evaluate the accuracy of ^{18}F-FDG PET/CT and contrast-enhanced CT for primary TNM staging and diagnosis of recurrent gastric cancers. The systematic search resulted in inclusion of a total of 58 studies with 9,997 patients. The sensitivity and specificity for nodal staging of gastric cancer were 49% and 92%, respectively, for ^{18}F-FDG PET/CT and 67% and 86%, respectively, for contrast-enhanced CT. The sensitivity and specificity for metastasis staging were 56% and 97%, respectively, for ^{18}F-FDG PET/CT and 59% and 96%, respectively, for contrast-enhanced CT.

The pooled sensitivity and specificity for diagnosing disease recurrence were 81% and 83%, respectively, for ^{18}F-FDG PET/CT and 59% and 96%, respectively, for contrast-enhanced CT. The authors concluded that although both ^{18}F-FDG PET/CT and contrast-enhanced CT were highly useful for diagnosing recurrent gastric cancer, "these techniques cannot be used to exclude or confirm the presence of lymph node metastases or recurrent gastric cancer tumors but can be used for the confirmation of distal metastasis."

Experimental and Therapeutic Medicine

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 December, January, and February. Murray and Du, from the Royal Marsden NHS Foundation Trust and Institute of Cancer Research (Sutton, UK), provided an overview of "Systemic radiotherapy of bone metastases with radionuclides" in the February issue of *Clinical Oncology (Royal College of Radiology)* (2021;33:98–105). In an article in the December issue of *Translational Andrology and Urology* (2020;9:2908–2919), Kim, from the National Cancer Center (Goyang-si, Korea), reviewed the "Role of PET/CT in muscle-invasive bladder cancer." The "Role of nuclear imaging to understand the neural substrates of brain disorders in laboratory animals: Current status and future prospect" was outlined by D'Elia et al. from the National Research Council of Italy and University "Roma Tre" (both in Rome, Italy) in the December 11 issue of *Frontiers in Behavioral Neuroscience* (2020;14:594509). Dev et al. from the Massachusetts General Hospital/Harvard Medical School (Boston, MA) published "Neuroimaging in frontotemporal lobar degeneration: Research and clinical utility" in *Advances in Experimental Medicine and Biology* (2021;1281:93–112). In the January 1 issue of *Nanotheranostics* (2021;5:90-112), Abousaway et al. from the Dana-Farber Cancer Institute/Harvard Medical School and Brigham and Women's Hospital/Harvard Medical School (Boston, MA) reported on "Noninvasive imaging of cancer immunotherapy." Sier et al. from the Leiden University Medical Center, the University of Twente (Enschede), Uni-Qure (Amsterdam), and Percuros BV Leiden (all in The Netherlands), University Medicine Center Göttingen/Max-Planck-Institute for Experimental Medicine (Germany), and the University of Sheffield (UK) offered perspective on "Cell-based tracers as Trojan horses for image-guided surgery" in the January 13 issue of the *International Journal of Molecular Sciences* (2021;22:E755). In an article published on January 13 in *Diagnostics (Basel)* (2021;11:E117), Luining et al. from the Amsterdam University Medical Center (The Netherlands) reviewed "Nuclear imaging for bone metastases in prostate cancer: The emergence of modern techniques using novel radiotracers." Ha et al. from Korea University (Sejong, South Korea) reported on "Inhibitors of prostate-specific membrane antigen in the diagnosis and therapy of metastatic prostate cancer: A review of patent literature" on January 17 ahead of print in *Expert Opinion on Therapeutic Patents.*

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technologists who have questions about what they can and cannot do in their states.

All of SNMMI's advocacy work this year took place against the backdrop of COVID-19, and SNMMI led multiple discussions on the impact on nuclear medicine and molecular imaging. The Society participated in letter-writing campaigns with coalition partners to address hero's pay, personal protective equipment shortages, and regulatory relief requests. Finally, SNMMI acted to ensure that nuclear medicine technologists were included in initial vaccine phases.

SNMMI has taken many positive steps in achieving its advocacy goals in the past year, and we look forward to carrying on this important work in the coming year.