2022 SNMMI Highlights Lecture: Oncology and Therapy, Part 1

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From the Newsline Editor: The Highlights Lecture, presented at the closing session of each SNMMI Annual Meeting, was originated and presented for more than 30 years by Henry N. Wagner, Jr., MD. Beginning in 2010, the duties of summarizing selected significant presentations at the meeting were divided annually among 4 distinguished nuclear and molecular medicine subject matter experts. Each year Newsline publishes these lectures and selected images. The 2022 Highlights Lectures were delivered on June 14 at the SNMMI Annual Meeting in Vancouver, Canada. In this issue we feature the first part of the lecture by Heiko Schöder, MD, MBA, Chief of the Molecular Imaging and Therapy Service in the Department of Radiology at Memorial Sloan Kettering Cancer Center and professor of radiology at Weill Cornell Medical College (both in New York, NY), who spoke on oncology and therapy topics at the meeting. Note that in the following presentation summary, numerals in brackets represent abstract numbers as published in The Journal of Nuclear Medicine *(2022;63[suppl 2]).*

It is a pleasure to present the highlights in oncology and therapy from the SNMMI Annual Meeting, and I thank the organizers for reinviting me. More than 400 abstracts were considered in preparing this lecture, and, needless to say, only a few could be included in the limited presentation time. I want to thank all the researchers who provided me with slides.

Trends

At the 2022 SNMMI Annual Meeting we saw a new trend in geographic origins of oncology abstracts, with almost half coming from Asia and Australia (48%) and smaller contributions from the United States (25%), Europe (18%), Canada (5%), Africa (2%), and South America (1.5%). Major representation from countries in this category came from China (105 abstracts), the United States (103), Italy (39), India (39), and Germany (29). Quantity is not always or necessarily quality; the majority of the highest rated abstracts came from North America (42%), followed by Asia/Australia (35%), and Europe (23%). In contrast to last year, when the subject-matter distribution was about 80% diagnostic and 20% therapeutic, this year we saw 76% diagnostic- and 24% therapeutic-related abstracts. This may indicate a general trend, part of the growing interest in nuclear medicine therapies that will be reflected in this lecture.

It is always interesting to look at general trends in subject matter. In terms of keywords in titles of oncologic and therapeutic presentations at this meeting, FDG was still dominant (105 abstracts). However, it was followed closely by prostate-specific membrane antigen (PSMA) (101), with fibroblast-activation protein inhibitor (FAPI) rapidly rising (29). (This trend is also reflected in the published literature). Top radiolabels represented in abstract titles included ^{18}F (121), ^{68}Ga (78), ^{177}Lu (37), and ^{225}Ac (11).

Heiko Schöder, MD, MBA

Clinical Diagnostics

FAPI Imaging

We will begin with the youngest and newest kid on the block, FAPI, and then review notable PSMA and FDG presentations. A large number of studies focused on FAPI, many of which were conducted in smaller patient samples. In general, these studies reported that FAPI has 1 or more advantages over FDG for disease detection and, in some instances, for staging. The studies provided evidence of FAPI benefit in differentiated thyroid cancer, gastrointestinal (GI) malignancies, breast cancer, hepatocellular carcinoma, and others. The theme is basically the same: FAPI provides very interesting data, but what we clearly need are more and larger prospective studies looking systematically at its utility in these diseases.

I have chosen only 1 of these FAPI abstracts to highlight here as an example. Chen et al. from the First Affiliated Hospital of Xiamen University (China) reported on "Comparison of ^{68}Ga-FAPI and ^{18}F-FDG uptake in patients with gastric signet-ring cell carcinoma: A multicenter retrospective study" [2370]. As you know, this disease is difficult to image with ^{18}F-FDG PET. Figure 1 highlights the higher uptake intensity and greater tumor-to-background ratios of the ^{68}Ga-FAPI agent. When compared with ^{18}F-FDG in 34 patients (16 men, 18 women; median age, 51 y [range, 25–85 y]), the FAPI agent had higher detection rates in primary tumors (73% vs 18%), local recurrence (100% vs 29%), nodal metastases (77% vs 23%), and distant metastases (93% vs 39%). (Both modalities missed 6 smaller [(0.3–1.1-cm] primary tumors.) More interesting, perhaps, is the fact that there were no lesion sites in which FDG provided an advantage over FAPI. In the majority of lesions FAPI provided more information. The authors concluded that their data suggest that "^{68}Ga-FAPI PET has the potential to replace ^{18}F-FDG PET in the diagnosis of patients with gastric signet-ring cell carcinoma."

Other notable studies on FAPI PET/CT were presented by: Fu et al. from the First Affiliated Hospital of Xiamen University (China), who reported on "^{68}Ga-FAPI PET/CT in metastatic differentiated thyroid cancer detection: Comparison with ^{18}F-FDG PET/CT" [2361]; Ballal et al. from the All India Institute of Medical Sciences (New Delhi) and the TRIGA Research Reactor/Johannes Gutenberg Universität Mainz (Germany), who reported on "Head-to-head comparison of ^{68}Ga-DOTA.SA.FAPi versus ^{18}F-FDG PET/CT in

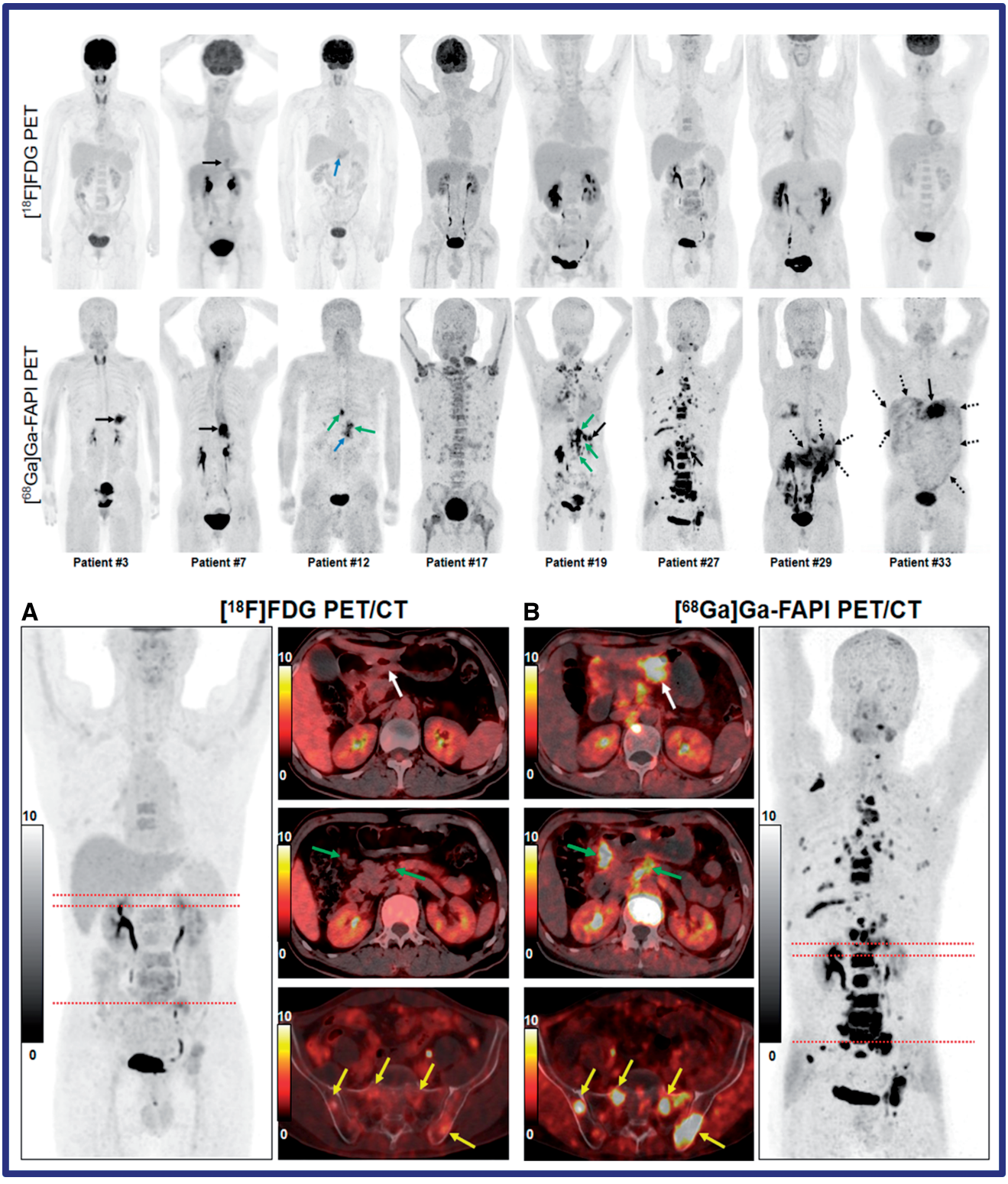

FIGURE 1. Comparison of ^{68}Ga-FAPI and ^{18}F-FDG PET/CT in gastric signet-ring cell carcinoma. Top: Example patients imaged with ^{18}F-FDG (top row) and ^{68}Ga-FAPI (bottom row) PET/CT. Bottom: Comparative imaging in a single patient with ^{18}F-FDG (left) and ^{68}Ga-FAPI (right) PET/CT. ^{68}Ga-FAPI imaging resulted in higher detection rates in primary tumors (73% vs 18%), local recurrence (100% vs 29%), nodal metastases (77% vs 23%), and distant metastases (93% vs 39%).

radioiodine refractory differentiated thyroid cancer patients" [2371]; Li et al. from Peking Union Medical College Hospital and the Chinese Academy of Medical Sciences (Beijing, China), who reported on "^{68}Ga-FAPI-04 and ^{18}F-FDG PET/CT for identifying primary and metastatic lesions in patients with gastrointestinal cancer: A comparative study"

[2369]; Novruzov et al. from the Azerbaijan National Centre of Oncology (Baku, Azerbaijan), who reported on "Head-to-head comparison of ^{68}Ga-FAPI-46 PET/CT and ^{18}F-FDG PET/CT in breast carcinoma staging: A clinical trial update from Azerbaijan" [2372]; Wu et al. from Peking Union Medical College Hospital and the Chinese Academy of Medical Sciences (both in Beijing, China), who reported on "^{68}Ga-FAPI and ^{18}F-FDG PET/CT in evaluation of primary and metastatic lesions in late-stage hepatocellular carcinoma" [2373]; and Pang et al. from the First Affiliated Hospital of Xiamen University/Xiamen University (China), who reported that "^{68}Ga-FAPI PET/CT improves tumor detection and staging in patients with pancreatic cancer and comparison with ^{18}F-FDG PET/CT" [2374].

Prostate Cancer

Prostate cancer remains a challenging problem worldwide. It is the dominant malignancy in the male population in 112 countries: all of North and South America, Australia, and much of Africa and Europe. *The Lancet* Commission on Prostate Cancer, introduced in 2021 (James et al., *The Lancet*. 2021;397[10288]:1865–1866), cites "genomic tools and imaging, particularly PSMA PET/CT" as "likely to be increasingly important in treatment decisions in the future." The commission will assess these and other diagnostic and treatment developments to determine "what is likely to constitute the best approach in different health care settings [including in lower middle–income countries] and make policy and clinical practice recommendations."

At this meeting, as in the peer-reviewed literature, some studies on PSMA agents in prostate cancer are exciting and others, although possibly less exciting, are essential for regulatory approval and for conduct of clinical trials. Kuo et al. from the University of Arizona (Tucson), Invicro (Needham, MA), Medstar Georgetown University Hospital (Washington, DC), Warren Alpert Medical School of Brown University (Providence, RI), and McMaster University (Hamilton, Canada), on behalf of the SPOTLIGHT Study Group, reported on "Inter- and intrareader reproducibility of ^{18}F-rhPSMA-7.3 PET image interpretation in patients with suspected prostate cancer recurrence: Results from a phase 3, prospective, multicenter study (SPOTLIGHT)" [2539]. Their data indicated a high degree of inter- and intrareader agreement across 3 blinded readers given the same set of scans after completing the same training. Interreader agreement was >75% overall and greatest for the pelvic lymph node region, with 87% concordance. Intrareader agreement was >85% overall. Although reproducibility was lower for the prostate/prostate bed than other regions, the substantial reproducibility in regions outside the prostate fossa is of clinical importance because of the potential to influence treatment selection. These types of studies are important for creation and validation of the large clinical trial data needed to obtain regulatory approval and reimbursement for PSMA agents and other novel radiopharmaceuticals and techniques.

Olivier et al. from the Centre Hospitalier Universitaire Nancy (France), the Centre Léon Bérard (Lyon, France), Centre Jean Perrin (Clermont-Ferrand, France), Hôpital Européen Georges-Pompidou (Paris, France), and ABX Advanced Biochemical Compounds (Radeberg, Germany) reported on a "Phase III study of ^{18}F-PSMA-1007 versus ^{18}F-fluorocholine PET to compare the detection rate of prostate cancer lesions in patients with biochemical recurrence after previous definitive treatment for localized prostate cancer" [2537]. This study contributed to the regulatory approval of PSMA-1007 in France. We all know instinctively that PSMA is a better imaging agent than others we have had available in prostate cancer, but it is important to have the hard data for regulatory approval. The design of this multicenter study is interesting. Patients (n = 190) in an intent-to-treat population with suspected prostate cancer recurrence underwent both choline and PSMA imaging in a random order. Blinded readers used a 3-point qualitative scale (no recurrence, undetermined, recurrence) to report findings. In 172 patients, PET imaging resulted in a more accurate diagnosis as determined by an independent panel of experts and additional data. Of these more accurate diagnoses, 72% were attributed to ^{18}F-PSMA-1007, 5% to ^{18}F-fluorocholine, and 23% to the 2 tracers equally. ^{18}F-PSMA-1007 PET/CT identified disease relapse in more patients than did ^{18}F-fluorocholine PET/CT, especially at low prostate-specific serum antigen levels.

In developing clinical trials to assess and validate PSMA imaging, it will be important to move beyond counting and measuring each individual lesion to the increasing application of artificial intelligence (AI) tools that facilitate lesion identification, tracking, activity measurement, and even assessment of volume change over time. Calais et al. from the University of California Los Angeles, Technical University of Munich (Germany), Stanford University (CA), EXINI Diagnostics AB (Lund, Sweden), Lund University (Sweden), Veterans Affairs Greater Los Angeles (CA), and Memorial Sloan Kettering Cancer Center (New York, NY) reported on a "Prospectively planned and independent validation of aPROMISE in a phase III CONDOR study for rapid lesion detection and standardized quantitative evaluation for ^{18}F-DCFPyL (PSMA) imaging in prostate cancer" [2496]. The aPROMISE tool performs both AI-based CT segmentation of bone and soft tissue and hotspot detection/segmentation to yield total PSMA SUV_{mean}, total PSMA tumor volume, and a total PSMA score (Fig. 2). The AI tool required relatively little observer interaction and was comparable or superior in accuracy to manual assessment. The time needed to score an ^{18}F-DCFPyL scan using aPROMISE in a patient with metastatic disease was dramatically shorter (median, 1.4 min) than manual reading time in the original CONDOR study (~15 min). The authors concluded that the AI-based total PSMA score "warrants future clinical investigation to define its clinical context of use as an imaging biomarker."

Many studies and guidelines have been published highlighting the importance of PET imaging for radiation treatment planning in lung, cervix, and other cancers. It comes as no surprise that PSMA can also contribute to radiation treatment planning in prostate cancer. In salvage radiotherapy, radiation

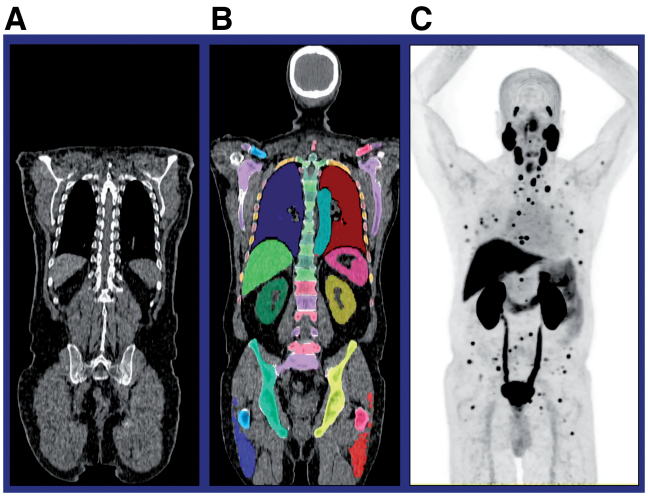

FIGURE 2. aPROMISE for rapid lesion detection and standardized quantitative evaluation for ^{18}F-DCFPyL (PSMA) imaging in prostate cancer. In this example ^{18}F-DCFPyL image (A), the aPROMISE tool performed both AI-based CT segmentation of bone and soft tissue (B) and hotspot detection/segmentation (C) to yield total PSMA SUV_{mean}, total PSMA tumor volume, and a total PSMA score. The time needed to score an ^{18}F-DCFPyL scan using aPROMISE in metastatic disease was dramatically shorter (median, 1.4 min) than average manual reading time (~15 min).

oncologists currently use contouring guidelines based on expert consensus (e.g., those from RTOG) to determine the volume to be irradiated, without reference to information from patterns of recurrence seen on advanced imaging such as PSMA PET. Can PSMA PET imaging contribute to refining planning treatment volumes? Sonni et al. from the University of California Los Angeles, the University of Miami Miller School of Medicine (FL), and the VA Greater Los Angeles Healthcare System (CA) looked at "PSMA PET mapping of postoperative local recurrence and impact on prostate fossa contouring guidelines for salvage radiation therapy" [2538]. This study analyzed the typical patterns of prostate fossa recurrence after radical prostatectomy using ^{68}Ga-PSMA-11 PET/CT and evaluated the location of recurrences as compared to RTOG clinical target volume (CTV) definitions. In 127 patients, the authors found that PSMA-positive prostate fossa recurrences were fully covered by the CTV in 68 (54%) patients, partially covered in 43 (34%), and fully outside the CTV in 16 (13%). Recurrences were in close proximity to the rectal wall in 9% and bladder wall in 3% of all patients. The heatmaps in the example in Figure 3 clearly show that the standard volume (green), would not have included disease as shown on the PSMA PET. The authors concluded that PSMA PET–based data should inform the update of commonly used prostate bed contouring guidelines and that new contouring guidelines should consider reducing coverage at the anterior and superior borders (near pubic bone) and extending coverage at the posterior, posterolateral, and inferior borders.

Duan et al. from Stanford University (CA) recently published data on a ^{68}Ga-labeled bombesin antagonist (^{68}Ga-RM2) targeting gastrin-releasing peptide receptors (GRPRs), which are overexpressed in prostate cancer (*J Nucl Med.* 2022; May 12 ahead of print). Their results showed high agreement between ^{68}Ga-PSMA-11 and ^{68}Ga-RM2 imaging in patients with newly diagnosed intermediate- or high-risk prostate cancer. Against this background we heard a presentation at this meeting that found somewhat different results (perhaps related to patient selection). Tang et al. from Xiangya Hospital/Central South University (Changsha City, China) reported on "Comparison of ^{68}Ga-GRPR PET/CT with ^{68}Ga-PSMA PET/CT in initial diagnosing of prostate cancer using histopathology: Results from 207 participants" [2540]. Overall, ^{68}Ga-PSMA PET/CT performed better than ^{68}Ga-GRPR PET/CT. Although ^{68}Ga-GRPR PET/CT showed higher sensitivity in imaging low-risk disease, uptake in benign prostatic hyperplasia and early clinically insignificant prostate cancer was greater. The authors concluded that ^{68}Ga-GRPR PET/CT "may not be a direct competitor or have a complementary role" to that of PSMA PET/CT in fully characterizing prostate cancer at different stages. They added that the fact that ^{68}Ga-GRPR uptake was not specific for prostate cancer may suggest that GRPR may not be an imaging target for initial diagnosis. This raises a number of questions about the role of GRPR in prostate cancer diagnosis and indicates that we need more data.

Other Cancers

Carlsen et al. from the Righospitalet/Copenhagen University (Copenhagen, Denmark) reported on a "Prospective phase II trial of prognostication by ^{68}Ga-NODAGA-E [c(RGDyK)]2 PET/CT for integrin $\alpha_v\beta_3$ imaging in patients with neuroendocrine neoplasms (NENs)" [2209]. The authors used this novel tracer in PET/CT imaging in 97 patients with NENs of all grades (78% low-grade, 22% high-grade disease), and tumor SUV_{max} for each patient was evaluated as a predictor of progression-free and overall survival at follow-up of at least 1 y (median, 32 mo). During follow-up, 62 patients (64%) experienced progressive disease and 26

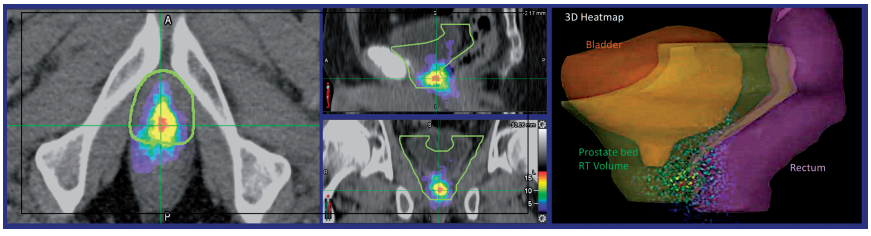

FIGURE 3. PSMA PET mapping of postoperative local recurrence compared with planning based on prostate fossa contouring guidelines for salvage radiation therapy. Patient example with: (left and middle) 2D heatmap of prostate bed recurrence on ^{68}Ga-PSMA-11 PET/CT and RTOG-based clinical treatment volume (CTV; green outline); (right) 3D heatmap of prostate bed recurrence on ^{68}Ga-PSMA-11 PET/CT and RTOG-based CTV, showing proximity to rectal and bladder walls. The authors concluded that PSMA PET–based data should inform the update of commonly used prostate bed contouring guidelines.

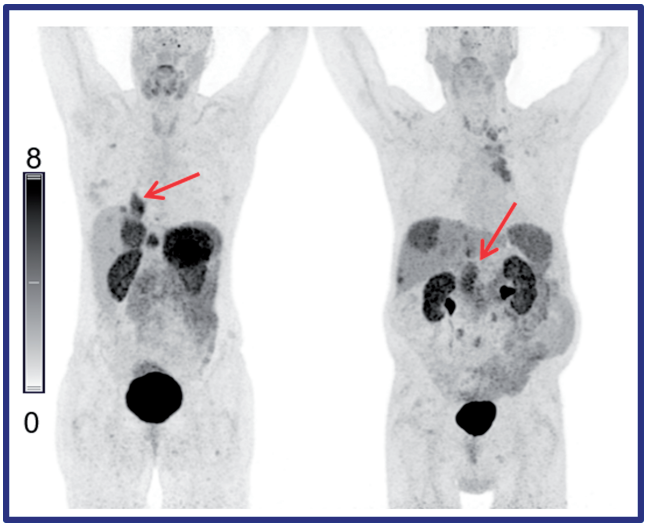

FIGURE 4. Prognostic utility of ^{68}Ga-NODAGA-E[c(RGDyK)]2 PET/CT integrin $\alpha_v\beta_3$ imaging in patients with neuroendocrine neoplasms (NENs). Example imaging in patients with a metastatic lung NEN (left) and a metastatic pancreatic NEN (right). Higher tracer uptake was significantly correlated with worse prognosis.

(27%) died. The intensity of ^{68}Ga-NODAGA-E[c(RGDyK)]2 uptake increased from grade 1 to grade 2 and was positive in almost all grade 3 patients (Fig. 4). Higher uptake correlated with worse prognosis. The suggestion is not that this tracer will replace DOTATATE but that it provides interesting additional prognostic information and so could serve as a companion diagnostic for treatments targeting $\alpha_v\beta_3$.

Ulaner et al. from the Hoag Family Cancer Institute (Irvine, CA) and the University of Southern California (Los Angeles) reported on "A prospective clinical trial of ^{18}F-fluorestradiol (^{18}F-FES) PET/CT compared to standard-of-care imaging in patients with newly diagnosed and suspected recurrent breast cancer" [2590]. ^{18}F-FES is an estrogen receptor–targeting PET tracer approved by the FDA as an adjunct to biopsy in patients with recurrent or metastatic breast cancer. Particular utility is expected in patients with lobular breast cancer and those with heterogeneous metastatic disease (to determine the extent of estrogen receptor–positive disease). The authors of this study plan to enroll a total of 120 patients in 2 cohorts: 1 with locally advanced stage 2B–3C cancer and 1 with treated breast cancer and suspected recurrence. Patients undergo both ^{18}F-FES PET/CT and standard-of-care imaging (either CT/bone scan or ^{18}F-FDG PET/CT). Preliminary results reported at the SNMMI meeting on the first 39 patients enrolled suggest that ^{18}F-FES PET/CT detects more unsuspected distant metastases at initial staging and also at the time of suspected recurrence and may outperform current imaging methods for detection of clinically significant and treatment-altering disease in patients in both study cohorts. These cohorts represent novel patient populations that could benefit from ^{18}F-FES PET/CT. Figure 5 shows comparative ^{18}F-FDG PET/CT and ^{18}F-FES PET/CT imaging in a 59-y-old woman with previously treated invasive lobular breast cancer and elevated tumor markers. Benign granulomatous inflammation produced false-positive findings for lung recurrence on ^{18}F-FDG PET/CT, but these lesions were not ^{18}F-FES avid. However, many ^{18}F-FES–avid nodal, GI, osseous, and peritoneal metastases were missed on ^{18}F-FDG imaging. Tissue sampling of a peritoneal lesion demonstrated recurrent lobular breast cancer.

One of the main applications for ^{18}F-FDG PET has been and remains lymphoma, in which the tracer is used for staging, restaging, response assessment, and (more than in any other disease) for the conduct of clinical trials. In these trials, we are increasingly interested in looking at more than just the number of lesions and visual criteria by applying radiomics principles to extract more information. Eertink et al. from Amsterdam University Medical Centers (The Netherlands), Erasmus Medical Centre (Rotterdam, The Netherlands), the Universitätsklinikum Essen (Germany), the University of Duisburg-Essen/University Hospital Essen (Germany), Universitätsklinikum Leipzig (Germany), Kings College (London, UK), Guy's and St. Thomas Hospital (London, UK), Istituto Imaging Della Svizzera Italiana/Ente Ospedaliero Cantonale, Semmelweis University (Budapest, Germany), and VU University Medical Center (Amsterdam, The Netherlands), on behalf of the PETRA Consortium, reported that "^{18}F-FDG PET radiomics features result in more accurate prediction of outcome for diffuse large B-cell lymphoma (DLBCL) patients than currently used International Prognostic Index (IPI) score" [2490]. This group has done remarkable work in collecting and analyzing these and

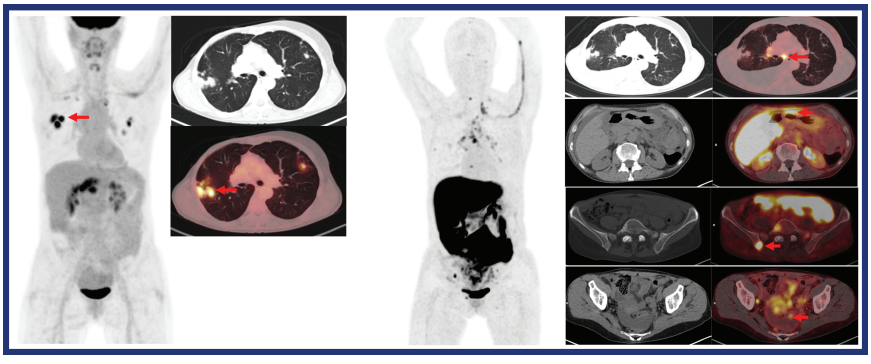

FIGURE 5. ^{18}F-fluorestradiol (^{18}F-FES) PET/CT vs standard-of-care imaging in newly diagnosed and suspected recurrent breast cancer. Comparative ^{18}F-FDG PET/CT (left) and ^{18}F-FES PET/CT (right) imaging in a 59-y-old woman with previously treated invasive lobular breast cancer and elevated tumor markers. Benign granulomatous inflammation produced false-positive findings for lung recurrence (arrows) on ^{18}F-FDG PET/CT; these lesions were not ^{18}F-FES avid. However, many ^{18}F FES-avid nodal, gastrointestinal, osseous, and peritoneal metastases (arrows) were missed on ^{18}F-FDG imaging. Tissue sampling of a peritoneal lesion demonstrated recurrent lobular breast cancer.

similar data and have already published a number of articles in this area. In their presentation at the SNMMI meeting, the authors reported on a study designed to externally validate the radiomics model developed in the HOVON-84 trial, using datasets from other DLBCL studies within the PETRA database, and to identify an optimal model to predict outcomes in that database by combining radiomics features and clinical parameters. They identified several criteria validated as providing prognostic information and applied these as model in other clinical trials including a total of 1,090 patients. The new PETRA model, combining quantitative radiomics features extracted from baseline ^{18}F-FDG PET/CT scans with components of the IPI score, significantly improved identification of patients at risk of relapse when treated with standard first-line treatment regimens compared with the IPI score alone. It is clear that these and other radiomics models will contribute to the use of multiple datapoints beyond SUV that will be crucial in the conduct of future clinical trials, particularly those drawing on multiple studies and very large patient populations.

We are often told that we are either not doing enough or are doing too much ^{18}F-FDG PET imaging. It is important that we address such criticisms with data on usage, utility, and compliance with validated guidelines. Sterbis et al. from the University of Colorado Medical Center (Aurora, CO) and the Edward Hines Jr. VA Hospital (Hines, IL) reported on "Lack of adherence to guideline-based imaging prior to adjuvant radiation in patients with non–small cell lung cancer (NSCLC)" [2596]. The authors used National Cancer Institute Surveillance, Epidemiology, and End Results program data (which should be taken with a grain of salt) in patients with NSCLC who had received adjuvant radiation therapy and undergone imaging with CT angiography or CT and/or PET with or without CT. They looked at adherence to National Comprehensive Cancer Network guidelines for imaging in this setting prior to adjuvant radiation therapy, which recommend that "PET/CT should be obtained preferably within 4 wk before treatment," ideally in the treatment position. In this study, only 56.3% of patients had preradiation imaging with PET. Predictors of decreased PET/CT usage included stage III or IV disease, initial treatment with chemotherapy or chemoradiation, black or other/unknown ethnicity, initial diagnosis with CT or CT angiography alone, and/or neuroendocrine or squamous cell biology. Both inferior overall survival and inferior cancer-specific survival were associated with decreased preradiation PET/CT usage. It is a challenge and an area of great concern that this modern and timely imaging technology is not widely enough available or routinely and equitably offered across all populations.

Dr. Schöder's lecture will be continued in the next issue of The Journal of Nuclear Medicine *and will cover clinical radionuclide therapy and experimental studies.*

SNMMI Adopts New Strategic Plan

Munir Ghesani, MD, SNMMI President

For more than 50 years, SNMMI has successfully educated professionals, policymakers, and the general public about nuclear medicine and molecular imaging. Advances in the field have signaled an expansion of the profession and its ability to contribute to improved health outcomes, necessitating that SNMMI leaders examine the society's long-range future. This past spring the SNMMI leadership did just that, participating in a 1½-day strategic planning session.

To inform the strategic planning session, an environmental assessment was conducted to engage as many voices as possible. The assessment included one-on-one interviews, an external environmental scan, and a survey of 383 members from a wide cross-section of the organization. Board members reviewed and prioritized SNMMI's strategic opportunities and discussed membership expectations. They also addressed, discussed, and refined SNMMI's mission and vision statements and identified strategic objectives and initiatives.

With the completion of the strategic planning process, I am pleased to share SNMMI's new vision and mission statements:

- **Vision:** SNMMI is the leading global organization transforming the science and practice of diagnostic and therapeutic nuclear medicine.
- **Mission:** Empowering our members to transform the science and practice of precision nuclear medicine for diagnosis and therapy to advance patient care.

To support the society's vision and mission statement, 9 new strategic goals—with corresponding objectives and tactics—have been identified.

Goal 1: Expand integration of best practices in all aspects of nuclear medicine to optimize patient care and access. To achieve this goal, SNMMI will work toward greater inclusion of nuclear medicine in the guidelines of the National Comprehensive Cancer Network, increase the number of designated Therapy Centers of Excellence, and incorporate best practices in all aspects of nuclear imaging and therapy.

Goal 2: Attract and engage a diverse, multidisciplinary, and global membership by offering opportunities, services, and resources that anticipate and fulfill members' needs. Objectives include reimagining the SNMMI membership structure, improving member benefits and services, improving membership communication, and increasing the society's brand awareness. The society will also build a forward-thinking leadership and career development program and improve the diversity and inclusiveness of SNMMI volunteer opportunities.

Munir Ghesani, MD

Goal 3: Ensure high-quality, focused, needs-based education for all segments of the profession that is easily accessible and documentable to increase utilization. This goal will be achieved by increasing utilization of educational resources for both members and nonmembers.

Goal 4: Accelerate discovery, research, and translation in nuclear medicine and molecular imaging through funding, education, and support for professionals. SNMMI will work to increase research funding and its infrastructure for research, as well as education, training, and mentorship for research personnel. The society will lead multicenter clinical trials through the SNMMI Clinical Trials Network and Therapy Clinical Trials Network and enhance research on artificial intelligence, machine learning, and deep learning, among other objectives.

Goal 5: Ensure that patients and the medical community recognize the value of nuclear medicine, molecular imaging, and radionuclide therapy. This goal will be achieved by educating patients, referring physicians, and other medical societies about radiopharmaceutical therapies. SNMMI will also expand outreach at the regional, local, and institutional levels; increase awareness among health care administrators; and promote media coverage of nuclear medicine and molecular imaging.

Goal 6: Sustain and grow a diverse and qualified workforce that is prepared for current and future diagnostic and therapeutic nuclear medicine needs to provide equitable care. SNMMI will analyze and assess workforce needs, showcase the field as a thriving career path, and foster the growth, value, and diversity of early career nuclear medicine and molecular imaging professionals. SNMMI will also ensure that nuclear medicine and molecular imaging programs have the necessary informational resources to be successful.

Goal 7: Position SNMMI to address the rapidly changing needs of the profession and members. SNMMI will review its organizational structure and core membership offerings, as well as those of outside organizations. The society will develop a sustainable organizational model considering SNMMI membership priorities, staffing, and fiscal health.

Goal 8: Engage stakeholders to develop, promote, implement, and sustain policies to ensure equitable patient access to appropriate nuclear medicine procedures. Objectives for this goal include working closely with the Centers for Medicare & Medicaid Services, legislators, and

private payers to advocate on reimbursement and patient access issues and educating stakeholders about changes to relevant public policy requirements. SNMMI will leverage coalitions to advocate for issues of mutual interest and focus on state level advocacy, in addition to other objectives.

Goal 9: Ensure that the Annual Meeting remains relevant by continuously reimagining the meeting in ways that meet the changing needs of the nuclear medicine and molecular imaging community. This goal will be achieved by creating a 3-year plan to reimagine the meeting, creating meaningful networking opportunities, and introducing innovative programming.

We look forward to working with members from all areas of the field on this new strategic plan. Together we can transform the science and practice of diagnostic and therapeutic nuclear medicine.

SNMMI and Lobular Breast Cancer Alliance Research Grant

The SNMMI Mars Shot Fund and the Lobular Breast Cancer Alliance announced on October 3 that applications are being accepted for the new and jointly sponsored $100,000 Invasive Lobular Carcinoma (ILC) Research Grant. This initiative, a first-time collaboration between the 2 organizations, aims to fund a research project focused on advancing ILC breast cancer imaging and treatments to improve patient outcomes.

To be selected, research projects must focus on ILC and molecular imaging or therapy for lobular breast cancer. Priority projects may have molecular imaging as the primary focus of the proposed research, or, alternatively, researchers may investigate methods that integrate other imaging and/or molecular science with radionuclide methods, including hybrid imaging techniques such as PET/CT, SPECT/CT, and PET/MR imaging. Patient advocates will be included as voting members in the application review process.

Applications are due by December 15. Additional information on application and proposal submission is available at: https://www.snmmi.org/AboutSNMMI/Content.aspx?ItemNumber=41839&utm_source=Email&utm_medium=Informz&utm_campaign=Email%20Outreach&_zs=iOqn91&_zl=qKHr6.

SNMMI

DOE Breaks Ground for Stable Isotope Production and Research Center

The U.S. Department of Energy (DOE), in coordination with Oak Ridge National Laboratory (ORNL; TN), on October 24 held a groundbreaking event on the ORNL campus for the Stable Isotope Production and Research Center (SIPRC), which will expand the nation's capability to enrich stable isotopes for medical, industrial, and research applications. DOE also announced $75 million to support the SIPRC with funding provided through the Inflation Reduction Act, which in FY 2022 delivered $1.55 billion to the Office of Science to accelerate national laboratory infrastructure projects.

SIPRC will provide DOE with multiple production systems that can enrich a wide range of stable isotopes. The facility includes space to add additional systems and expand the building footprint in the future as demand increases. SIPRC will be part of the DOE Isotope Program, which produces and sells isotopes that are in short supply or otherwise unavailable. The research conducted at SIPRC supports the Program's innovative work to develop advanced manufacturing techniques and novel isotope separations to build out a safe and reliable domestic supply chain.

The facility is scheduled for completion in 2025 and will be housed in the same space as the Enriched Stable Isotope Prototype Plant. SIPRC will establish a domestic full-production cascade for enriched stable isotopes. It will also reduce the nation's reliance on foreign sources of enriched stable isotopes by facilitating new capabilities to produce useful quantities of priority stable isotopes. This will address the void left when operation of the Oak Ridge calutrons ceased in 1998.

U.S. Department of Energy

NIH to Investigate Function of Every Human Gene

The National Institutes of Health on September 27 announced the launch of a program intended to better understand the function of every human gene and to generate a catalog of the molecular and cellular consequences of inactivating each gene. The Molecular Phenotypes of Null Alleles in Cells (MorPhiC) program, managed by the National Human Genome Research Institute (NHGRI), aims to systematically investigate the function of each gene through multiple phases that will each build on the work of the previous.

The program will be funded initially for 5 y for a total of $42.5 million. Phase 1 of the program will focus on 1,000 protein-coding genes and serve as a pilot phase, with 3 goals: exploring multiple methods of inactivating (knocking out) gene function, developing molecular and cellular systems that model multiple human tissues and developmental stages, and developing molecular and cellular approaches to cataloging gene function that other researchers can reproduce.

"The function of thousands of genes is still a mystery, and they likely serve vital biological roles," said Colin Fletcher, PhD, NHGRI program director in the Division of Genome Sciences. "Understanding fundamental biology can help us figure out why certain diseases occur and how we can develop drugs to target and treat those diseases."

More than 6,000 of the estimated 19,000 protein-coding genes have not been well studied. Among those that have been studied, only small subsets of their functions are well characterized. All data over the course of the project will be made available to the broader research community. If Phase 1 is successful, NIH will activate a second phase to characterize a larger set of human genes.

"MorPhiC is meant to add another layer of functional information between the gene knockout at the DNA level and the organism-level effects. We want to catalog the effects of knocking out each gene within cells and—together with information from other studies—use that to understand how genes function to produce an organism," said Adam Felsenfeld, PhD, NHGRI program director in the Division of Genome Sciences. Recipients of funding for phase 1 of the MorPhiC program include researchers at Northwestern University Feinberg School of Medicine (Chicago, IL), the University of California San Francisco, Sloan Kettering Institute for Cancer Research (New York, NY), Jackson Laboratory (Farmington, CT), and the University of Miami (FL).

National Institutes of Health

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 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 include a small section on noteworthy reviews of the literature.

^{68}Ga-DOTATATE PET/CT in Sarcoidosis

Lee et al. from the Hospital of the University of Pennsylvania (Philadelphia) and the Brigham and Women's Hospital/Harvard Medical School (Boston, MA) reported on October 20 ahead of print in the *Journal of Nuclear Cardiology* on the potential clinical utility of ^{68}Ga-DOTATATE PET/CT compared with that of ^{18}F-FDG PET/CT for diagnosis and response assessment in cardiac sarcoidosis. The study included 11 patients who underwent imaging with both tracers, and the 2 studies were interpreted independently before comparison. The researchers found that patient-level concordance between studies with the 2 tracers was 91%, with 10 patients having multifocal DOTATATE uptake indicating active cardiac sarcoidosis and 1 with diffuse DOTATATE uptake. Segment-level agreement between the 2 types of studies was 77.1%. The SUV_{max}-to-blood pool ratio was lower with ^{68}Ga-DOTATATE PET/CT (3.2 ± 0.6) than with ^{18}F-FDG (4.9 ± 1.5). Eight patients also underwent follow-up ^{68}Ga-DOTATATE PET/CT, which showed 1 case of complete response and 1 of partial response, compared with 3 complete and 1 partial response on follow-up ^{18}F-FDG PET/CT. The authors summarized their findings that "compared to ^{18}F-FDG PET/CT, ^{68}Ga-DOTATATE PET/CT can identify active cardiac sarcoidosis with high patient-level concordance but with moderate segment-level concordance, low signal-to-background ratio, and underestimation of treatment response."

Journal of Nuclear Cardiology

Predictive and Prognostic Imaging Biomarkers in the TheraP Trial

The TheraP Trial Investigators and the Australian and New Zealand Urogenital and Prostate Cancer Trials Group published on October 14 ahead of print in *Lancet Oncology* an analysis from their landmark trial, focusing on ^{68}Ga–prostate-specific membrane antigen (PSMA)–11 PET and ^{18}F-FDG PET parameters as predictive and prognostic biomarkers in patients receiving ^{177}Lu-PSMA-617 or cabazitaxel for metastatic castration-resistant prostate cancer. After reviewing the overall protocol and criteria for the TheraP study, a multicenter, open-label, randomized phase 2 trial with 200 participants (99 treated with the PSMA agent and 101 with cabazitaxel), the authors evaluated an SUV_{mean} of ≥10 on ^{68}Ga-PSMA-11 PET as a predictive biomarker of response. A metabolic tumor volume of ≥200 mL on ^{18}F-FDG PET was tested as a prognostic biomarker. Over a median follow-up of 18.4 mo, 35 of the men assigned to ^{177}Lu-PSMA-617 and 30 assigned to cabazitaxel therapy had high PSMA uptake (SUV_{mean} ≥ 10). The odds of prostate-specific antigen (PSA) response to the PSMA agent were significantly higher for those with SUV_{mean} ≥ 10 than those with SUV_{mean} < 10. The PSA response rate in patients with SUV_{mean} ≥ 10 was 91% for ^{177}Lu-PSMA-617 and 47% for cabazitaxel treatment. Corresponding response rates in patients with SUV_{mean} < 10 were 52% and 32%. High metabolic tumor volumes (≥200 mL) on ^{18}F-FDG PET were seen in 30% of patients assigned to ^{177}Lu-PSMA-617 treatment and 30% of those assigned to cabazitaxel. The authors concluded that "in men with metastatic castration-resistant prostate cancer, PSMA PET SUV_{mean} was predictive of higher likelihood of favorable response to ^{177}Lu-PSMA-617 than cabazitaxel, which provided guidance for optimal ^{177}Lu-PSMA-617 use." High ^{18}F-FDG PET metabolic tumor volumes were associated with lower responses, regardless of randomly assigned treatment, an indication that additional research may define the need for treatment intensification.

Lancet Oncology

PET/CT and Prognosis in RT of Rhabdomyosarcoma

Cheriyalinkal Parambil et al. from Tata Memorial Hospital/Homi Bhabha National Institute (Mumbai, India) reported on October 14 ahead of print in the *Journal of Pediatric Hematology/Oncology* on a study of the prognostic significance of persistent ^{18}F-FDG avidity on PET in residual masses after definitive radiation treatment in pediatric rhabdomyosarcoma. The retrospective study included 63 children with group III (n = 55) and group IV (n = 8) rhabdomyosarcoma who underwent PET/CT imaging at 3 mo after radiation for local control. Residual masses were visualized in 10 patients (15.9%), and anatomic residual disease was visualized in 24 (38.1%), with no ^{18}F-FDG–avid areas in 29 (46.0%). Over a median follow-up of 38 mo, 3-y event-free survival for children with ^{18}F-FDG–avid residual masses was 40.0% compared with 71.9% for those who had no such masses. Three-year overall survival of patients with ^{18}F-FDG–avid residual masses was 50.8% compared with 77.0% for the remaining patients. These results were sustained on multivariate analysis. The authors concluded that "persistent metabolic activity in residual disease postchemoradiotherapy in rhabdomyosarcoma may portend a poorer prognosis with an increased risk of relapse." They added that "this subset of high-risk patients needs to be identified, and further trials are warranted

to develop strategies to improve their outcomes."

Journal of Pediatric Hematology/Oncology

^{11}C-Choline PET/CT in Primary Hyperparathyroidism

In a study published on October 10 ahead of print in *Surgery*, Saha et al. from the Mayo Clinic (Rochester, MN) reported on ^{11}C-choline PET/CT in evaluation of primary hyperparathyroidism, with a focus on utility when conventional imaging techniques fail to provide accurate preoperative localization. The study included 43 patients in whom multiple standard imaging modalities had failed to localize disease and who underwent limited-coverage neck-and-chest ^{11}C-choline PET/CT. Thirty-three patients had positive findings on ^{11}C-choline PET/CT. Of the 25 patients who proceeded to surgery, 18 were reoperations. Twenty of the 25 patients achieved an operative cure. ^{11}C-choline PET/CT was found to have a sensitivity of 64% and positive predictive value of 72%, with 5 false-positive findings (lymph nodes, normal parathyroid, and a recurrent laryngeal nerve neuroma). These results were compared with those from standard imaging modalities, including ultrasound, ^{123}I-sestamibi, and 4D CT. The authors concluded that ^{11}C-choline PET/CT "is a useful adjunct for parathyroid localization in a complex population of patients who have failed standard localization techniques, including ultrasound, ^{123}I-sestamibi, 4D CT, and/or prior operations." They added that although ^{11}C-choline PET/CT may not be needed routinely, "it may aid in preoperative localization in the reoperative setting."

Surgery

Clinical Experience with Implementation of 2015 ATA Guidelines

Wu et al. from the University of Calgary/University of Calgary Cumming School of Medicine (Canada) reported on October 13 ahead of print in *Thyroid* on the clinical outcomes of the implementation of the 2015 American Thyroid Association (ATA) guidelines for management of thyroid nodules and differentiated thyroid cancer (DTC) using the modified ATA recurrence risk (RR) stratification system. A total of 479 patients with DTC were assigned a modified ATA RR (253 [53%] low-, 129 [27%] intermediate-, and 97 [20%] high-RR) and American Joint Committee on Cancer 8th-edition stage. These and the ATA recommendations guided surgical management, radioiodine treatment, and adjuvant therapies. Responses to treatment were evaluated at 2 y after surgery, which included 227 (47%) total thyroidectomies plus radioiodine, 178 (37%) total thyroidectomies only, and 74 (16%) lobectomies. The 2-y responses to treatment were excellent for 66 (89%) patients undergoing lobectomy, 149 (84%) with total thyroidectomy only, and 121 (53%) with total thyroidectomy plus radioiodine treatment. Of patients stratified at low-RR, 216 (85%) had excellent responses to treatment, 32 (13%) had indeterminate treatment responses, 4 (2%) had biochemical incomplete responses, and 1 had a structural incomplete response to treatment. Of patients stratified at intermediate-RR, 83 (64%) saw excellent, 30 (23%) saw indeterminate, 7 (6%) saw biochemical incomplete, and 9 (7%) saw structural incomplete treatment responses. With the worst study outcomes, patients in the high-RR saw 37 (38%) excellent responses, 18 (19%) indeterminate, 10 (10%) biochemical incomplete, and 32 (33%) structural incomplete responses to treatments. The authors concluded that the "2015 ATA RR stratification system is useful for predicting disease status at 2-y posttreatment in patients with DTC" and "may reduce thyroid cancer overtreatment by including lobectomy as a definitive treatment option for low-risk thyroid cancers and selective use of radioiodine for intermediate- and high-risk patients."

Thyroid

Cardiovascular Complications and Long COVID

In an article published on September 23 in *Frontiers in Cardiovascular Medicine* (2022;9:968584), Murata et al. from Nihon University School of Medicine (Tokyo, Japan) reported on a study using multimodality imaging to investigate the prevalence of cardiovascular disorders, particularly in patients with cardiovascular "long COVID." The study drew patients from a total of 584 individuals admitted to the hospital with COVID-19 between January 2020 and September 2021. At clinical assessment over a median follow-up of 163 d, 52 (9%) patients with complaints of chest pain, dyspnea, or palpitations were suspected to have cardiovascular long COVID and were enrolled in the study. Patients underwent electrocardiography, chest X-ray imaging, and echocardiography, as well as cardiac MR and SPECT/CT imaging depending on initial findings. Cardiovascular disorders were present in 27%; of these, 15% had myocardial injury, 8% had pulmonary embolisms, and 4% both. Patients with cardiovascular disorders had significantly higher incidences of severe COVID conditions (36% vs 8%) and in-hospital cardiac events (71% vs. 24%) than those who did not. A severe COVID condition and in-hospital severe condition proved to be independent risk factors for cardiovascular disorders in cardiovascular long COVID patients. No patients died during the study period, and no adverse events were reported. The authors cited other investigators' observations that long COVID itself is unlikely to result in organic cardiovascular disease, and, when it does, is likely to be quite mild. Despite the fact that patients with long COVID and cardiovascular complications tended to have longer-lasting symptoms of long COVID, the prognosis did not seem to be worse. They concluded that "early detection of cardiovascular problems in cardiology for symptomatic long COVID patients may inform patients of the duration of symptoms and allow symptoms to be shortened through appropriate therapeutic intervention."

Frontiers in Cardiovascular Medicine

PSMA PET/CT and Dose-Escalated Salvage RT in PCa

Tamihardja et al. from the University of Würzburg (Germany) reported on

October 10 in *Cancers (Basel)* (2022; 14[19]:4956) on a study of oncologic outcomes with prostate-specific membrane antigen (PSMA) PET/CT–guided salvage radiotherapy for localized macroscopic prostate cancer recurrence. The study included 367 men who received such radiation treatment after radical prostatectomy. Of these, 111 patients were staged by either ^{68}GA-PSMA-I&T or ^{18}F-PSMA-1007 before radiation. A total of 59 (53.2%) of these patients were treated for PSMA PET–positive macroscopic prostatic fossa recurrence. Over a median follow-up of 38.2 mo, the 3-y biochemical progression-free survival rate was 89.1% and the 3-y metastasis-free survival rate reached 96.2%. The cumulative 3-y late grade 3 genitourinary toxicity rate was 3.4%, with no late grade 3 toxicities reported. The authors concluded that "PSMA PET/CT-guided dose-escalated salvage radiotherapy with a simultaneous integrated boost to the local recurrence achieved encouragingly high rates of 3-y biochemical progression-free survival, metastasis-free survival, and overall survival," with effective disease control and low toxicity rates.

Cancers (Basel)

Choroid Plexus Imaging in Presymptomatic MS

In an article published on October 13 in *Neurology, Neuroimmunology, and Neuroinflammation* (2022;9[6]:e200026), Ricigliano et al. from the Sorbonne Université; Paris Brain Institute, ICM, CNRS, Inserm; St Antoine Hospital; Pitié-Salpêtrière Hospital; Hôpital Fondation Adolphe de Rothschild; Université Paris-Saclay, CEA, CNRS, Inserm; and Service Hospitalier Frédéric Joliot, Orsay (all in Paris, France) reported on a study assessing whether imaging characteristics of the choroid plexus are detectable at the earliest stages of multiple sclerosis (MS), before clinical symptom onset. The retrospective study included 27 individuals with presymptomatic MS, 97 with clinically definite MS (CDMS), and 53 healthy controls, all of whom underwent cross-sectional 3T-MR imaging. A subset of 22 CDMS individuals, 19 healthy controls, and 1 individual with presymptomatic MS (imaged 8 mo before conversion to CDMS) also underwent translocator protein (TSPO) ^{18}F-DPA-714 PET imaging. Choroid plexus ^{18}F-DPA-714 uptake was calculated as the average SUV. Compared with healthy controls, individuals with presymptomatic MS had 32% larger choroid plexuses, similar to those with MS. Baseline PET imaging in the presymptomatic case who later developed MS showed 33% greater choroid plexus inflammation than in healthy controls. Postmortem studies in the choroid plexus of this individual identified a population of CD163$^+$ mononuclear phagocytes expressing TSPO in MS, possibly contributing to the increased ^{18}F-DPA-714 uptake. The authors concluded that "by identifying an imaging signature in choroid plexuses already in presymptomatic MS, our work supports their role from the early phases of disease development and encourages further investigations on the involvement of choroid plexus immune infiltration and blood–cerebrospinal fluid barrier dysfunction in disease onset."

Neurology, Neuroimmunology, and Neuroinflammation

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 September and October. Linguanti et al. from the University of Florence and the IRCCS-Humanitas Research Hospital (Rozzano; both in Italy) reported in the September 27 issue of *Cancers (Basel)* (2022;14[19]:4700) on "Metabolic imaging in B-cell lymphoma during CAR-T cell therapy." In the October 17 issue of the *Medical Journal of Australia* (2022;217[8]:424–433), Williams et al. from the Royal Melbourne Hospital, Peter MacCallum Center Centre, Monash University, Cabrini Institute/Cabrini Health (all in Melbourne, Australia), Singapore General Hospital, and University College London (UK) presented "Modern paradigms for prostate cancer detection and management." An overview of "Positron emission tomography in autoimmune encephalitis: Clinical implications and future directions" was provided by Li et al. from Beijing Tiantan Hospital/Capital Medical University and the China National Clinical Research Center for Neurological Diseases (both in Beijing, China) on October 19 ahead of print in *Acta Neurologica Scandinavica.* Hawkey et al. from Duke University School of Medicine (Durham, NC) and Tulane Cancer Center (New Orleans, LA) published an assessment of "The value of phenotypic precision medicine in prostate cancer" on October 6 ahead of print in the *Oncologist*. "Novel tracers for molecular imaging of interstitial lung disease: A state of the art review" was offered online ahead of print in the September 21 issue of *Autoimmunity Reviews* by Broens et al. from the Vrije Universiteit Amsterdam (The Netherlands). The October issue of *Surgical Oncology Clinics of North America* published several reviews of state-of-the-art imaging techniques, including Szidonya et al. from the Oregon Health and Science University (Portland), Semmelweis University (Budapest, Hungary), University of Iowa Hospitals and Clinics (Iowa City), and University of Colorado School of Medicine (Aurora) with "Molecular and anatomic imaging of neuroendocrine tumors (2022;31[4]:649–671); Graves et al. from the University of California Davis (Sacramento), the University of California, San Francisco, and New York University Langone Health (NY) with "Innovations in parathyroid localization imaging (2022;31[4]:631–647); and Goodman et al. from the University of California, San Francisco, with "Molecular imaging for estrogen receptor-positive breast cancer: Clinical applications of whole body and dedicated breast positron emission tomography" (2022;31[4]: 569–579).