2011 SNM Highlights Lecture

From the Newsline Editor: The Highlights Lecture, presented at the closing session of each SNM Annual Meeting, was originated and presented for more than 33 y by Henry N. Wagner, Jr., MD. Beginning in 2010, the duties of summarizing selected significant presentations at the meeting were divided among 4 distinguished nuclear and molecular medicine subject-matter experts. These same experts presented the 2011 Highlights Lecture on June 8 at the SNM Annual Meeting in San Antonio, TX. The first 2 presentations appeared in the October issue of Newsline, and the remaining 2 are included here. Peter Herskovitch, MD, cochair of the SNM Scientific Program Committee, introduced Steven M. Larson, MD, and Harvey Ziessman, MD, who spoke on oncology and general nuclear medicine, respectively. Note that in the following presentation summaries, numerals in brackets represent abstract numbers from The Journal of Nuclear Medicine *(2011;52[suppl 1]).*

Oncology

More than 400 presentations on oncology were given at this year's SNM Annual Meeting (~300 on diagnosis, ~100 on therapy). By far the dominant theme was molecular imaging, that is, imaging the key biomolecules and molecular-based events that are fundamental to the malignant state. As I noted in last year's Highlights Lecture, we are increasingly familiar with the well-defined biology associated with molecular imaging and therapy in oncology. The concept of the "cancer phenotype," as presented by Lu et al. in *Cell* (2009;136:823; Fig. 1) illustrates the importance of metabolomics.

^{18}F-FDG PET and Tumor Biology

We understand the significance of glycolysis and the Warburg effect (the increase in glycolysis under aerobic conditions) at the same time that there is a growing recognition that glutamine and glutamate are also important. These concepts were reflected in presentations at this meeting. The Warburg effect has been the bedrock of tumor imaging for decades. We have seen diverse tumor types in which the maximum standardized uptake value (SUV_{max}), a relatively simple measure, correlates with biological aggressiveness and shortened survival in the pretreatment setting. We have also seen correlations with combinations of measures, such as total lesion glycolysis or the creative use of metabolizing tumor volume more than regional background. The literature is clear: the higher the SUV, the worse the tumor grade and prognosis. A number of presentations at this meeting added to our knowledge about the inverse correlation between SUV and prognosis, including studies that focused on head and neck tumors, multiple myeloma, metastatic lung cancer, gastric lymphoma, gall bladder cancer, and sarcoma.

New tracers and probes were introduced as well. Mittra et al. from Stanford University (CA) and Bayer Healthcare, Inc. (Mountville, NJ), reported on "Studies of the ^{18}F-L-glutamate derivative BAY 94-9392 in cancer patients: a novel radiopharmaceutical for PET imaging" [1900]. This tracer targets the complementary component of the metabolomics of cancer. Figure 2 shows beautiful uptake in brain tumor and in head and neck tumor. Uptake is in some cases better than that with FDG and in others similar to FDG. More studies will be performed in different tumor types.

Clinical Studies PET/CT FDG

Steven M. Larson, MD

More knowledge is emerging about the genetics of cancer, and we are seeing studies correlating FDG uptake with genetic markers. Garcia-Vellosa et al. from the Universidad de Navarra (Pamplona, Spain), reported on "Association of ^{18}F-FDG uptake in PET/CT and K-Ras mutation in advanced lung cancer" [428]. K-Ras mutation was found to be highly associated with high FDG uptake. The study included 44 patients with advanced non–small cell lung cancer (NSCLC). K-Ras mutations were identified in 18 patients (12 men, 6 women), all of whom were smokers and had high ^{18}F-FDG PET/CT SUV_{max} in primary tumor and nodal metastases.

Similar studies have been performed at Memorial Sloan–Kettering (New York, NY) in breast cancer, including ones with gene expression profiling, using gene set enrichment analysis to correlate FDG uptake in breast cancer with genetic signature. In these

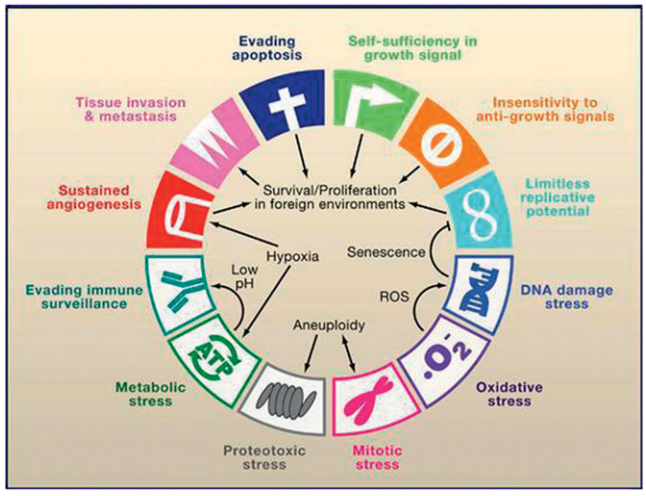

FIGURE 1. Lu's cancer phenotype schematic.

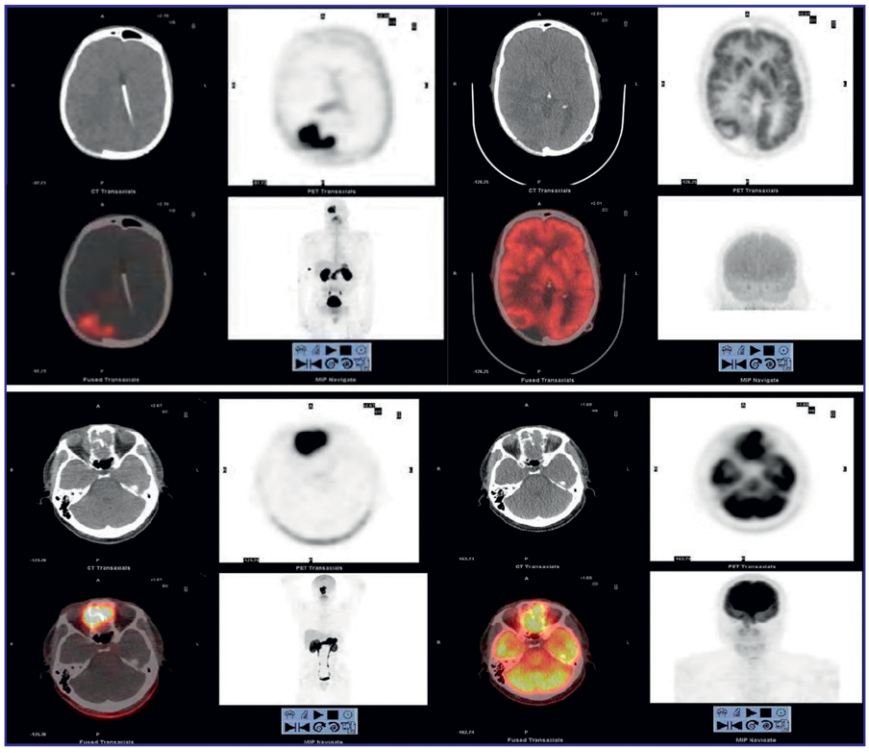

FIGURE 2. Comparative BAY9409392 (left) and FDG (right) axial PET/CT images of: (top) 63-y-old man with recurrent brain metastases to the right parieto-occipital region from lung cancer; (bottom) 45-y-old man with newly diagnosed nasopharyngeal cancer.

studies we found that tumors with the highest FDG signal have an excellent correlation with the basal type signature, which is associated with shortened survival. Although glycolysis is the most highly enriched metabolic pathway, others are also important. The c-myc signatures, for example, which many of the FDG-high samples harbor, will be useful as we explore both the applications of gene set enrichment analysis and the actual pathways and their correlates.

One international group is working to create an effective oncologic screen combining ^{18}F and Na^{18}F. Iagaru et al. from Stanford University Medical Center (CA), University of Pretoria (South Africa), Aalborg University Hospital (Denmark), and University Hospital of Coimbra (Portugal) reported on "Combined ^{18}F-NaF and ^{18}F-FDG PET/CT: initial results of a multicenter trial" [34]. The consortium put together a prospective study of 79 patients with proven malignancies who underwent separate ^{18}F PET/CT, ^{18}F-FDG PET/CT, and a combined ^{18}F/^{18}F-FDG PET/CT scan (total of 3 scans per patient) at distinct time points. The combined method was found to be effective (Fig. 3) (missing only 3 skull lesions), so the authors proposed combining ^{18}F-FDG and ^{18}F-NaF in a single evaluation, modulating the dose so that the amount of radiation would not be increased. The results would be cheaper and equally effective malignancy screening. Larger prospective trials are needed.

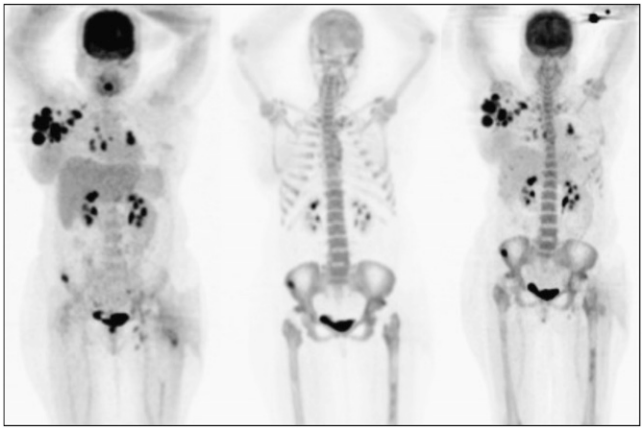

FIGURE 3. Comparative PET scans in patient with Ewing sarcoma acquired with: (left) ^{18}F-FDG, (middle) ^{18}F, and (right) combined ^{18}F/^{18}F-FDG "cocktail."

Cancer Biology and New Probes

^{18}F-choline is an interesting probe that appears to be incorporated in the membrane in proliferating cells. Talbot et al. from the Hopital Tenon (Paris, France) and the ICHOROPRO study team (France) reported on "Impact of fluorocholine (^{18}F) PET/CT in case of occult recurrence of prostate cancer" [1911]. They looked

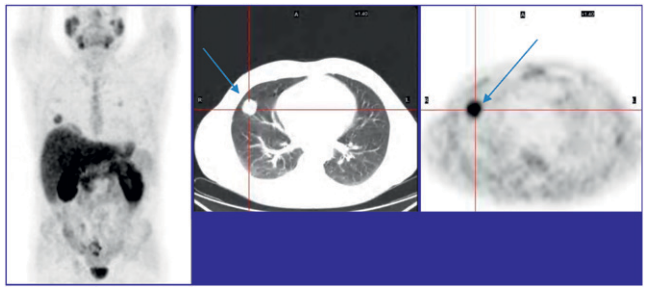

FIGURE 4. ^{18}F-fluorocholine uptake on PET/CT correlated well with high prostate-specific antigen levels in occult recurrence of prostate cancer. In this patient, bilateral lung foci corresponded to metastases of prostate cancer on postbiopsy histology.

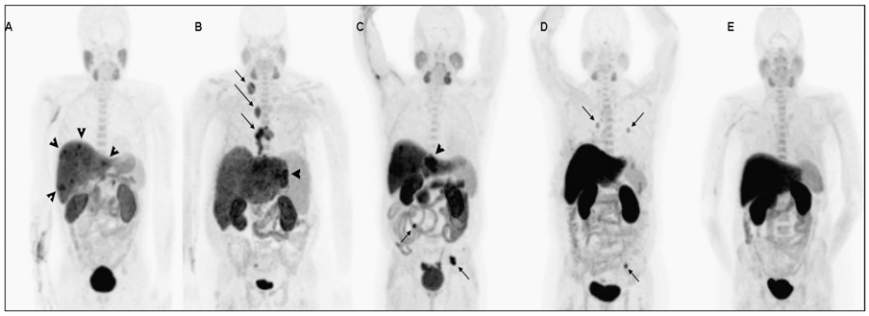

FIGURE 5. ^{18}F-fluorocholine PET/CT assessment of hepatocellular carcinoma (HCC) and remnant liver function. Despite high background activity, HCC could still be discriminated on the basis of tumor uptake.

at 181 patients who were progressing with prostate-specific antigen (PSA) increases and found that focal hot spots could be detected in 106 (59%) (Fig. 4). The median PSA for PET-positive patients was 4.9 ng/mL, and all 16 with PSA > 14 had positive ^{18}F-choline PET/CT results. The median PSA levels of those with negative images was 2.8 ng/mL, suggesting that it is in part the size of the recurrence that is the differentiating factor. The results in these studies changed management in >50% of patients referred for occult recurrence of prostate cancer without conclusive results on MR imaging and bone scintigraphy. In particular, ^{18}F-choline PET/CT provided targets for localized therapy in 43 (24%) patients, beneficially delaying the onset of hormone therapy, which ultimately results in hormone resistance.

^{18}F-fluorocholine is also an interesting tracer for hepatocellular carcinoma (HCC), a setting in which FDG is problematic. Kwee et al. from the Queen's Medical Center (Honolulu, HI), the University of Hawaii (Honolulu), and Philips Research (Briarcliff Manor, NY) reported on "^{18}F-fluorocholine PET/CT assessment of HCC and remnant liver function" [1825]. In images from a pilot study with 21 patients with HCC, the authors observed a trend toward lower hepatic ^{18}F-fluorocholine uptake in cirrhotic than in noncirrhotic patients. Figure 5 shows relatively high uptake in hepatic carcinomas. Despite high background activity, HCC could still be discriminated on the basis of tumor uptake, and it is clear that, despite variations in uptake, it is possible to image the activity of HCC in that setting.

Another facet of molecular imaging is the assessment of angiogenesis, with the development of new probes underway. Iagaru et al. from Stanford University Medical Center (CA) and the National Institute of Biomedical Imaging and Bioengineering (Bethesda, MD) reported on "^{18}F FPPRGD$_2$ PET/CT in breast cancer: a novel PET radiopharmaceutical for imaging $a_v\beta_3$ integrin levels" [74]. The researchers saw quite good uptake in both primary and metastatic lesions in patients with breast cancer (Fig. 6). In some cases that showed low FDG uptake they noted good uptake with the novel tracer, which appears to be a safe way to look at angiogenesis and may have some advantages over the monomer in terms of uptake.

Molecular Imaging Probes

More than 130 new molecular entities were presented as radiolabeled forms at this meeting. These included small molecules, antibodies, modified nanoparticles, aptomers, antisense particles, viruses, and cells. These were used in biologic characterization of molecules, radiolabeled drugs, and imaging of processes related to metabolism: angiogenesis, hypoxia, glycolysis, amino acid transport, glutaminolysis, proliferation, hormone receptors, apoptosis, and enzymes (metalloproteases, aromatases). In addition, these were modified in a number of instances by multimodality probes, often combining optical approaches with radioprobes.

This year we saw a new emphasis on optical imaging, which, with its tremendous potential in the laboratory, is now beginning to push into clinical applications. Areas of interest are diverse, including bioluminescence, fluorescence, Raman, photoacoustic, and Cerenkov imaging. Gambhir's group at Stanford is working on Raman molecular imaging, which uses a laser to excite an uncommon but exquisitely specific type of optical scatter and was the basis for C.V. Raman's 1930 Nobel prize. Raman molecular imaging can be highly specific and highly sensitive if directed at the right sites. The Stanford group has developed a beautiful nanoparticle with internal gold and silica. The silica can amplify a laser signal in association with the gold, and a fraction of the resulting scatter is the Raman signal. The group has proposed modifying these nanoparticles in various ways to make them more stable in vivo and more specific in tumor binding. They are doing preliminary work in spraying the particles onto the site of suspicious colon cancer and then looking at that site with a laser, with resulting signal that is exquisitely specific for probes that can be sent in along with the nanoparticle.

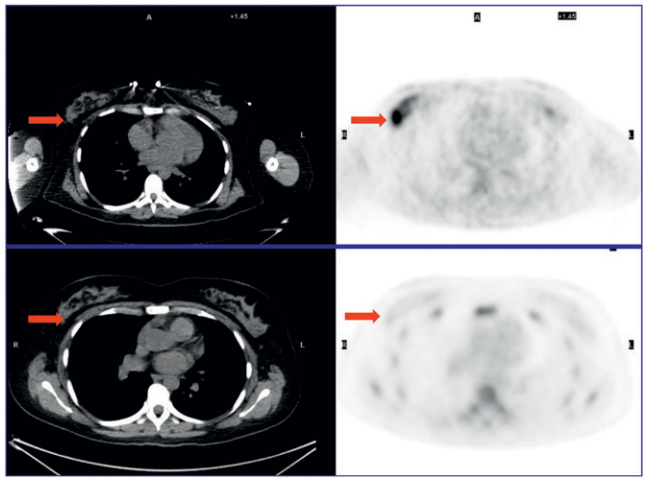

FIGURE 6. "^{18}F-FPPRGD$_2$ PET/CT $a_v\beta_3$ integrin expression imaging in breast cancer. Images acquired with (top) ^{18}F-FPPRGD$_2$ and (bottom) ^{18}F-FDG.

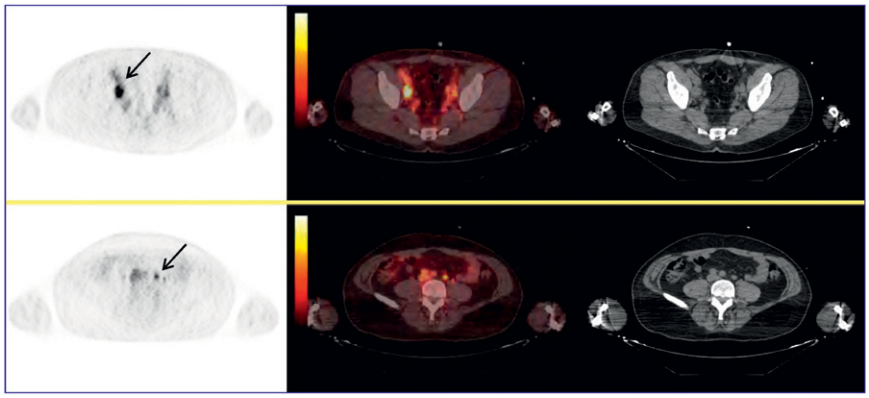

FIGURE 7. ^{18}F-DCFBC PET in metastatic prostate cancer. Uptake of this novel tracer is seen in lymph nodes in pelvic sidewall.

What are the clear winners among the 130 probes presented at this meeting? Cho et al. from Johns Hopkins University and Johns Hopkins University School of Medicine (Baltimore, MD) reported on "Initial clinical assessment of DCFBC-PET for metastatic prostate cancer" [41]. Figure 7 shows uptake of this ^{18}F-labeled tracer in the lymph nodes in the pelvic sidewall. This tracer is quite promising, because prostate-specific membrane antigen (PSMA) is an excellent target in prostate cancer.

Another new probe, a ^{68}Ga-bombesin analog, has been introduced for prostate cancer by Bayer. In 1 of several clinical trials sponsored by Bayer Schering Pharma AG and reported on at this meeting, researchers successfully identified 6 of 6 gastrin-releasing peptide receptor–positive primary prostatic cancers (Fig. 8). This probe will best be used in well differentiated tumors and may be most helpful in guiding biopsies to sites. I should note that ^{68}Ga is making a comeback, and we may see it become more important as a radiolabel in the years ahead.

Mechanism of Action

A number of antibodies were described at this meeting, as well as many positron-labeled forms under development, include those using ^{124}I (with a half-life of 4.2 d), ^{89}Zr (78 h), ^{77}Br (57 h), ^{86}Y (14.7 h), ^{64}Cu (12.7 h), ^{18}F (110 min), and ^{68}Ga (60 m). Next year we should see the results of initial clinical studies with some of the long-lived forms being explored. The advantages to positron imaging are obvious. Wilex AG (Munich, Germany) has now submitted to the U.S. Food and Drug Administration (FDA) their full phase 3 study for ^{124}I-cG250, which targets carbonic anhydrase IX in clear cell cancer and is being used to noninvasively immunotype cancers. I believe this is a harbinger of many approaches we will use in taking advantage of antibody specificity.

At this meeting we saw once again the promise and versatility of making not only IgG molecules that are radiotracers but also antibody forms, including intact antibodies, Fab'2, Fab, sFv, diabodies, and minibodies. Olafsen et al. from the University of California at Los Angeles (UCLA) David Geffen School of Medicine, ImaginAb, Inc. (Inglewood, CA), and Weill Cornell Medical College (New York, NY) reported on "Assessment of in vivo internalization by microPET imaging of PSMA-expressing xenografts using ^{64}Cu vs ^{124}I-radiolabeled minibodies" [141]. Figure 9 is an example in a mouse model using these anti-PSMA minibodies. The ^{124}I shows high background, but even at 44 h retention in the tumor with much less background was seen with the ^{64}Cu label. Figure 10 shows imaging with a prostate stem cell antigen, which again offers the possibility for imaging at 44 h with this affinity matured A11 minibody.

Multistep Radioimmunotherapy

I believe the future will include significant efforts in multistep targeting. Schoffelen et al. from Radboud University Nijmegen Medical Centre (The Netherlands), Garden State Cancer Center (Belleville, NJ), Immunomedics, Inc. (Morris Plains, NJ), and IBC Pharmaceuticals, Inc. (Morris Plains, NJ) reported on a "Phase I clinical study of the feasibility of pretargeted radioimmunotherapy [RIT] in patients with colorectal cancer" [358]. This is the work that has been championed by Sharkey and Goldenberg and their

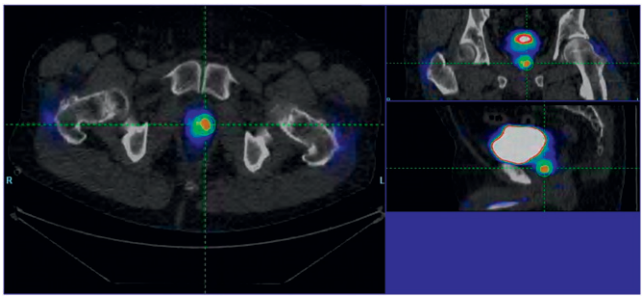

FIGURE 8. BAY 86-7548, a ^{68}Ga-bombesin analog, is proving effective at identifying gastrin-releasing peptide receptor–positive primary prostatic cancers.

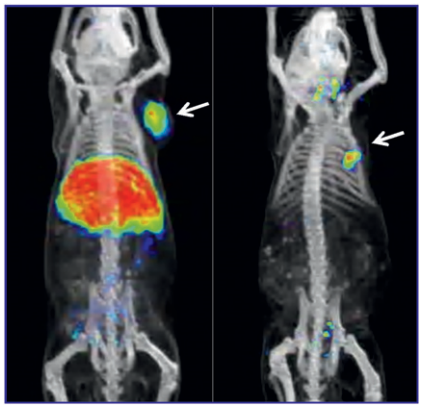

FIGURE 9. The huJ591 anti–prostate-specific membrane antigen minibody, labeled with either ^{64}Cu (left) or ^{124}I (right), can be employed for rapid imaging of prostate cancer xenografts.

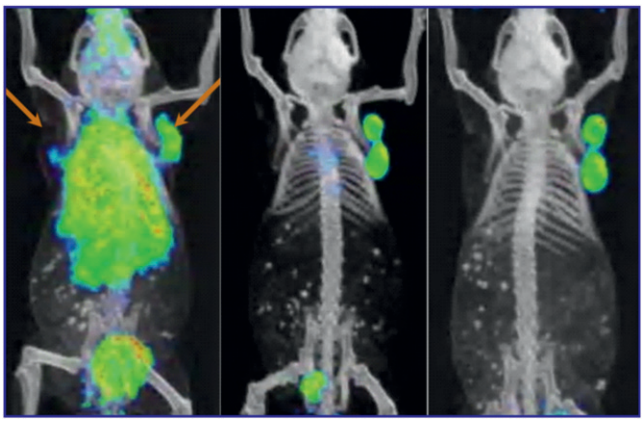

FIGURE 10. This affinity matured A11 minibody can produce high-contrast images of prostate stem cell antigen expression at (left to right) 4, 20, and 44 h post-injection.

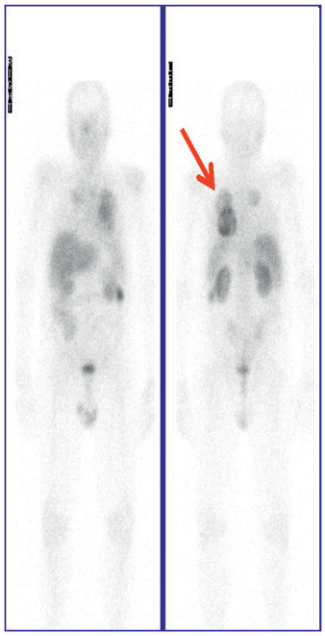

FIGURE 11. Pretargeted radioimmunotherapy in a colorectal cancer patient imaged with ^{111}In and in whom ^{177}Lu therapy has been initiated. ^{111}In/^{177}Lu-labeled diHSG peptide rapidly targets tumor, producing imaging with high tumor-to-background ratios.

colleagues over a number of years, and it is now coming to fruition with beautiful reagents that take advantage of avidity, which means multiple binding, as well as a highly versatile probe that can actually be used to measure radiotracers like lutetium, indium, and ^{68}Ga. Figure 11 shows initial images in a patient imaged with ^{111}In and in whom ^{177}Lu therapy has been initiated. Results showed that the ^{111}In/^{177}Lu-labeled diHSG peptide rapidly targets tumor in patients with colorectal cancer, producing imaging with high tumor-to-background ratios. High doses of the ^{177}Lu-IMP288 agent can be administered safely, although bone marrow toxicity is dose limiting. We look forward to more information from these studies.

Molecular-Targeted Radiotherapy

Peptide-receptor radiotherapy continues to develop, with growing numbers of applications. Kulkarni et al. from the Zentralklinik Bad Berka (Germany) reported on "Peptide receptor radionuclide therapy of neuroendocrine tumors: relationship between tumor dose and molecular response as measured by somatostatin receptor PET/CT" [301]. This group showed for the first time a strong relationship between deposition of radiation in the tumor (dose) and response of patients' tumors to radiation. For example, doses delivered to lesions showing a therapy response (143 Gy mean/79 Gy median) were significantly higher than doses to lesions showing minor progression or progressive disease (23/20 Gy) (Fig. 12). These doses are large—it is likely that internal emitters may have lower relative biological effectiveness values than external radiation, so that high doses must be delivered into these tumors. From the same group, Prasad et al. from the Zentralklinik Bad Berka (Germany) and University Hos-

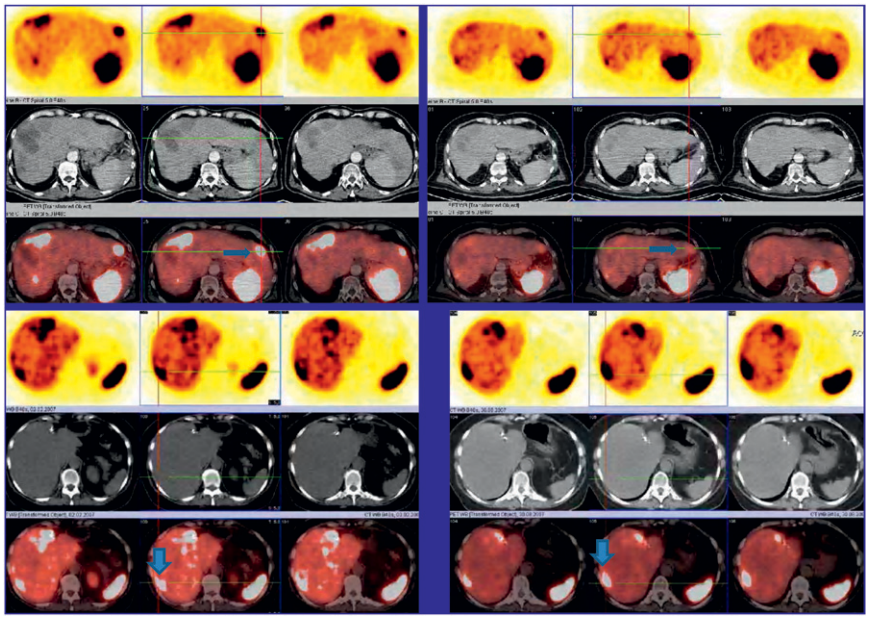

FIGURE 12. ^{68}Ga-DOTATOC PET/CT imaging before (left) and after (right) peptide-receptor radiotherapy in a responder (top; 42% reduction in SUV_{max}; 371 Gy dose to tumor) and nonresponder (bottom; 125% increase in SUV_{max}, 25 Gy dose to tumor).

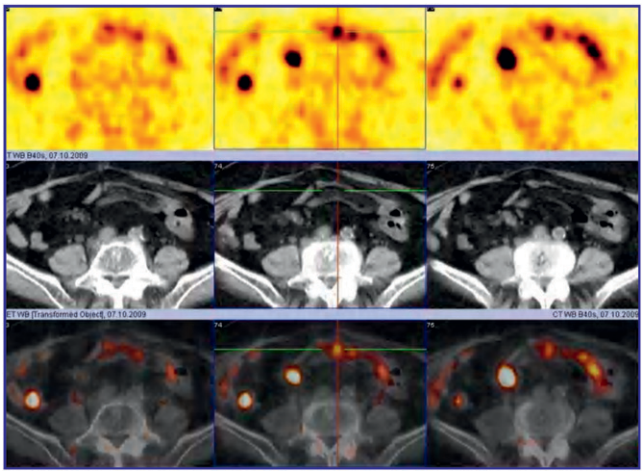

FIGURE 13. ^{68}Ga-DOTATOC PET/CT somatostatin receptor imaging in a multifocal neuroendocrine tumor of the ileum. At least 13 subcentimeter foci were observed on PET/CT.

pital Jena (Germany) reported on "Detection of unknown primary in patients with neuroendocrine tumors using Ga-68 somatostatin receptor PET/CT: results in 129 patients" [1347]. They were able to detect 58% of occult neuroendocrine tumors (Fig. 13), a rate superior to that with ^{111}In-octreoscan.

Biomarkers

Biomarkers are a critical part of our future. The FDA defines a biomarker as a "biochemical feature or facet that can be used to measure the progress of disease or the effects of treatment." Biomarkers look at treatment response, where one is hitting a target (e.g., androgen receptor imaging with ^{18}F-fluorodihydrotestosterone [^{18}F-FDHT]), metabolic response (e.g., glycolysis with ^{18}F-FDG), or anatomic response (e.g., with 3D volumetric CT)—but overall the goal is to develop a surrogate marker that will be such an effective indicator of response that it can be used in early studies to accurately predict clinical outcome. Among the candidates is ^{18}F-fluorothymidine (^{18}F-FLT). Garcia-Velloso et al. from the Clinica Universidad de Navarra (Pamplona, Spain), Marqués de Valdecilla (Santander, Spain), Hospital Basurto (Bilbao, Spain) and Onkologikoa (Donostia, Spain) reported on "Imaging early changes in proliferation during Bevacizumab therapy in locally advanced breast cancer with ^{18}F-FLT PET/CT" [367]. Mean SUV in primary tumors decreased by >30% in 20 patients with initiation of Bevacizumab therapy.

^{18}F-FDHT and ^{18}F-FDG are excellent tracers for evaluating castrate-resistant prostate cancer. Jadvar et al. from the University of Southern California (Los Angeles) reported on "Treatment response assessment of metastatic prostate cancer with FDG PET/CT" [1908]. The study included 37 men with metastatic castrate-resistant prostate cancer who underwent imaging before and 1 y after new treatment. They found that treatment-related decline in bone metastasis metabolism on PET is associated with an increase in lesion density on CT (Fig. 14)—in other words, they identified an inverse relationship between FDG uptake and CT findings. Functional imaging is proving in many cases to be more sensitive than anatomic imaging for monitoring treatment response, especially in bone. Last year I was among the authors of a study published by Scher et al. (*Lancet.* 2010;375:1437–1446) that showed the efficacy of ^{18}F-FDHT PET/CT as a predictive and targeted response biomarker in patients with castrate-resistant metastatic cancer considered for therapy with an androgen receptor antagonist. Almost all of these patients saw their tracer uptake drop significantly after treatment.

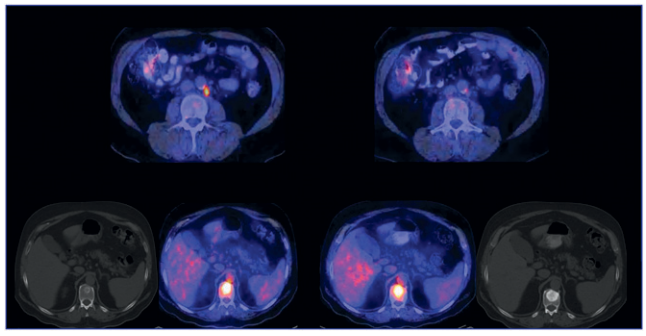

FIGURE 14. Treatment response assessment of metastatic prostate cancer with ^{18}F-FDG PET/CT. Treatment-related decline in bone metastasis metabolism on PET was associated with an increase in lesion density on CT.

Biomarker Imaging and Automation: New Vocabulary

Biomarker imaging will require a new degree of automation as well as a new vocabulary for the majority of tumors in patients. The PET Response Criteria in Solid Tumors, as introduced by Wahl et al., has made the acronym PERCIST a part of this new vocabulary. SUV peak, total lesion glycolysis, metabolizing tumor volume, and bone scan index are all terms that will become a part of our oncology vocabularies. Leal et al. from Johns Hopkins University (Baltimore, MD) reported on "A PERCIST 1.0 based computer aided detection (CAD) system: performance compared to an expert reader in the evaluation of breast cancer" [363]. They have also been able to extend this not only to their usual PERCIST and SUV peak but also to incorporate concepts such as total lesion glycolysis, which incorporates all of the voxels that are greater than the background (which they define as $SUV_{mean} \pm 2$ liver standard deviations). Using the PERCIST 1.0 preferred metric of SUV lean (SUL) peak, they were able to detect disease in 27 of 29 (>93%) cases. The PERCIST 1.0–based computer-assisted detection tool showed a high level of concordance with expert readers.

A similar approach was taken by Tixier et al. from INSERM (Brest, France) and Centre Hospitalier Universitaire Morvan (Brest, France), who reported on "Intratumor heterogeneity on baseline ^{18}F-FDG PET images characterized by textural features predicts responses to concomitant radiochemotherapy in esophageal cancer" [1785]. They found that the baseline prediction of total lesion glycolysis (which is simply $SUV_{mean} \times$ metabolizing tumor volume) is highly predictive in most patients who will respond to treatment (Fig. 15).

Hypothesis 2011

One of the hypotheses that emerges clearly from work presented at this meeting is that advances in technology and cancer biology will make quantitative molecular imaging the first step in targeted therapy. This will most likely be true for drug

FIGURE 15. Total lesion glycolysis (TLG) measured on ^{18}F-FDG PET baseline imaging was found to predict radiochemotherapy response in patients with locally advanced esophageal cancer. Higher accuracy was found for TLG incorporating metabolically active tumor volume (MATV) and SUV_{mean} than MATV alone.

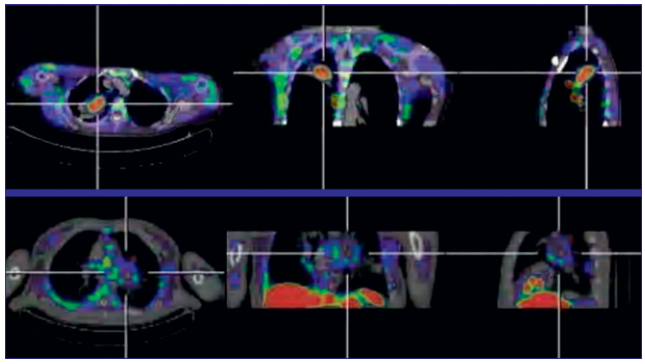

FIGURE 16. PET imaging of activating epidermal growth factor receptor mutations in non–small cell lung carcinoma. Patient with exon 19 mutation (top) showed high uptake, predicting beneficial results with ^{11}C-methyl-erlotinib. Patient without the mutation (bottom) had no uptake.

effect as well. A number of investigators have utilized this concept and looked at the concentration of drug in tumor and have begun to do the quantitative imaging that will be needed to define relationships between effect and concentration. For example, Bahce et al. from VU University Medical Center (Amsterdam, The Netherlands) reported on "A potential clinical PET tool for quantitative imaging of activating epidermal growth factor receptor [EGFR] mutations in non–small cell lung carcinoma" [600]. They looked at ^{11}C-methyl-erlotinib. We know that lung mutations in EGFR occur in 10%–20% of patients who are responsive to treatment with erlotinib. These "dramatic responders" are usually women, have adenocarcinoma, are of Asian ethnicity, and are not smokers. Mutation analysis, however, is problematic, because the tumors must be biopsied. The researchers explored imaging with ^{11}C-methyl-erlotinib. Their results showed dramatic differences between uptake in patients who had characteristic mutations at exon 19 and those who did not (Fig. 16). If proven in larger series, this will be truly an interesting approach to look at stratification of patients.

Lee et al. from the David Geffen School of Medicine at UCLA reported on "Tumor metabolic phenotyping and treatment stratification by PET" [23]. This group is taking advantage of biology to "sort" tumors by their uptake. Cytidine deaminase inactivates some nucleoside analog prodrugs, of which there are many types, and the nucleoside analogs radiotracers can be used to demonstrate differential uptakes (Fig. 17). In the not-too-distant future we may be able to image our patients and determine the likelihood of success before initiation of therapy with toxic and expensive prodrugs.

Glimpses into the Future

A brief look at the future of molecular targeted radiotherapy yields mixed results. ^{131}I-Bexxar, despite being an extraordinarily effective drug, has not been accepted as widely as it should be. Buchegger et al. from University Hospitals of Lausanne and Geneva (Switzerland) and the Fred Hutchinson Cancer Research Center at the University of Washington (Seattle) reported at this meeting that "Six of 12 relapsed/refractory indolent lymphoma patients treated 10 years ago with tositumomab and ^{131}I-tositumomab remain in complete remission" [356]. In their experience, ^{131}I-Bexxar outperformed radiotherapy in treatment of advanced-stage follicular lymphoma, which is often slowly progressive and cannot be cured by conventional treatments. After repeated conventional treatments, relapse becomes more rapid and the disease may transform to higher grades or become resistant to chemotherapy. The reported results suggest that the ^{131}I-tositumomab carries tremendous advantages.

Another glimpse of our future in molecular targeted radiotherapy, even in radioresistant solid tumors, was presented by Stillebroer et al. from Radboud University Nijmegen Medical Center (The Netherlands), who reported on "RIT with Lu-177 labeled anti-CAIX monoclonal antibody in advanced renal cell carcinoma" [359]. They successfully imaged uptake of ^{177}Lu-cG250, targeting metastases in the lung, lymph nodes, and remaining kidney and indicating stabilization of previously progressive metastatic disease in their patient group. Goldsmith et al. from New York–Presbyterian Hospital/Weill Cornell Medical College

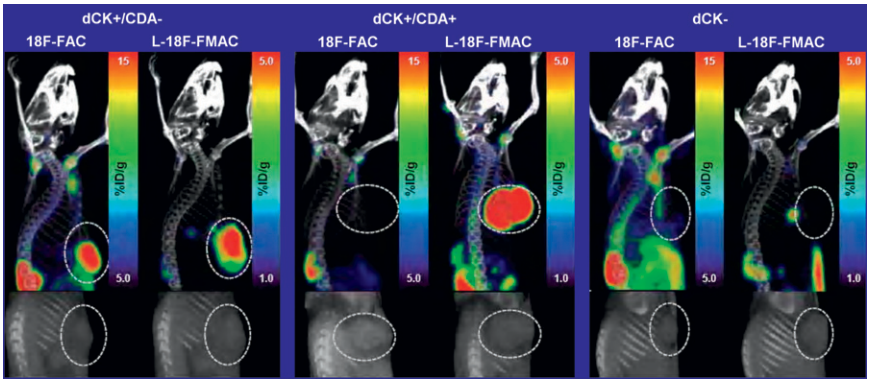

FIGURE 17. dCK/CDA metabolic phenotyping and nucleoside analog drug response.

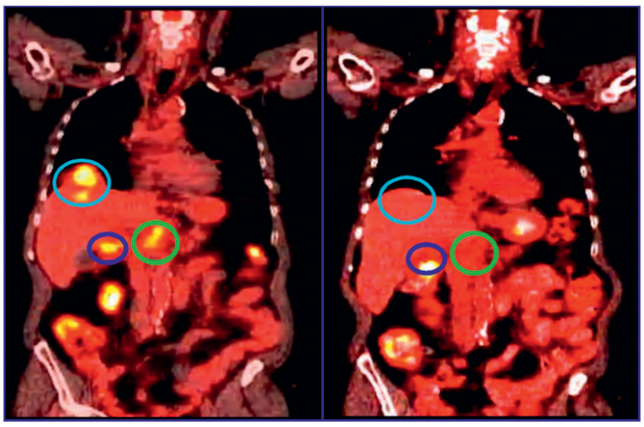

FIGURE 18. PET/CT imaging at baseline (left) and 4 wk after (right) fractionated radioimmunotherapy with ^{90}Y-clivatuzumab tetraxetan plus gemcitabine in advanced pancreatic cancer. Treatment response is highlighted in large liver lesion (light blue), portacaval lymph nodes (dark blue), and primary pancreatic tumor (green).

(New York, NY), a consortium of universities and medical centers, and Immunomedics, Inc. (Morris Plains, NY), reported on "Fractionated RIT with ^{90}Y-clivatuzumab tetraxetan (^{90}Y-PAM4) plus gemcitabine (Gem) in advanced pancreatic cancer" [357]. Figure 18 shows uptake with FDG before treatment and 4 wk after treatment in a patient. The study included 38 patients, 58% of whom survived ≥ 6 mo, 26% ≥ 12 mo, and 5 of whom were still alive 15–25 mo from start of treatment.

Conclusion

It is challenging to look ahead and pick the winners from the more than 130 new tracers presented at this meeting. The following have great promise: ^{68}Ga-bombesin–like peptides in prostate; ^{18}F-glutamine, which reflects novel metabolomics, and other novel glutamine tracers; ^{18}F-DCFBC, which targets PSMA; new small molecules for reliable targeting; and optical imaging alone and in combinations. The Warburg effect is a powerful window on the biology of human cancer for diagnosis and staging and for biomarkers in treatment response. I would urge the cancer imaging community to do a better job in organizing true studies that are adequately powered so that we can meet the high bar the FDA has set in terms of first validating tracers as to reproducibility and next qualifying them for specific uses. This is different from staging and detection—this is looking at treatment response. We can do this as a professional society if we work together with other organizations.

Other substrates, including ^{18}F-choline, ^{11}C-choline, and ^{18}F-amino acids, may add to our capabilities, as well as new radiotracers for cancer pharmacology. We are moving toward individualized treatment based on highly individualized imaging. Imaging biomarker studies are in their infancy, but we are beginning to see emerging efforts to define novel response parameters that go beyond the Response Evaluation Criteria in Solid Tumors. We need a data-based consensus on functional response parameters, including definition of these parameters and ways to design the studies.

Exploration of antibodies and variants, peptides, affibodies, and other platforms, especially with PET nuclides, is expanding. Multistep RIT is showing its advantages for therapeutic index, and I believe that targeted radiotherapy is a big part of our future. We must continue to push forward the good drugs like Bexxar and point out to our colleagues that these are excellent drugs for specific purposes. We must overcome the economic disadvantages of these compounds and promote their clinical advantages so that they are introduced and used widely. Encouraging results in radioresistant solid tumors also offer near-term possibilities that merit further exploration.

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General Nuclear Medicine

The Scientific Program Committee (SPC) accepted 215 abstracts in the category of general nuclear medicine for this Annual Meeting. The SPC defines general nuclear medicine into subcategories that one would expect (endocrinology, gastroenterology, hematology/infectious disease, musculoskeletal, pediatrics, pulmonary, renal/hypertension, operations/outcomes research); however, it also includes ones that might not be expected (oncology, ^{18}F-FDG, and therapy currently in clinical practice).

Bone SPECT/CT

Last year I highlighted a number of presentations on bone SPECT/CT. Hassan et al. from Guy's and St. Thomas Hospital National Health Trust (London, UK) this year had 2 presentations on bone SPECT/CT: "The potential role of radionuclide bone SPECT/CT in patients with complicated painful knees" [514] and the "Role of ^{99m}Tc-MDP bone SPECT/CT in localization, diagnosis, and treatment of patients with wrist pain." The knee study included 35 patients, and the wrist study included 53 patients. The authors found that bone SPECT/CT was superior to planar imaging at localizing, characterizing, and guiding disease management. Figure 19 is an example of a patient with bilateral amputations and suspected osteomyelitis. The whole-body bone scan could not differentiate between soft tissue and bone uptake. SPECT suggested that the uptake was superficial; the SPECT/CT fused image confirmed that this was soft tissue and corresponded to heterotopic ossification seen on CT. Another example (Fig. 20) illustrates a patient with bilateral renal transplants, on steroids, with bilateral knee pain. SPECT/CT clearly demonstrated that the nondescript focal knee uptake seen on planar and SPECT images was localized to the femoral condyles and not soft tissue, suggesting the diagnosis of bilateral avascular necrosis, which was later confirmed.

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