The Value Initiative has been doing great work in Advocacy, R&D, Quality Practice, Outreach, and Workforce Pipeline. They have been successful in raising awareness and advancing the field in measurable ways. You can learn more about it by visiting www.snmmi.org/VIResources. In the Advocacy domain, it is worth mentioning that Technegas has received FDA approval, and we have made significant progress through our work with CMS. The Centers for Medicare & Medicaid Services (CMS) have decided to remove the national coverage determination (NCD) at § 220.6.20. This means that the coverage with evidence development (CED) for positron emission tomography (PET) beta amyloid imaging will no longer be available. Medicare coverage determinations for PET beta amyloid imaging will now be made by the Medicare Administrative Contractors (MACs) under § 1862(a)(1)(A) of the Social Security Act (the Act).

It has been an exciting year for patients suffering from Alzheimer’s disease and SNMMI molecular brain imagers. In 2023, a new Alzheimer’s disease treatment was approved, and the national non-coverage decision for amyloid PET was lifted by CMS.

SNMMI has formed an ad hoc working group to develop and enhance the Society’s Brain Imaging Portal (www.snmmi.org/amyloid), offering a variety of resources for members, patients, and referring physicians. The group initially focused on amyloid PET imaging. In the coming year, it will add resources related to additional modalities, including tau PET imaging, FDG PET, and dopamine transporter SPECT.

The portal provides an authoritative source for brain imaging information and training. The working group is made up of physicians, technologists, and industry members who have worked together to ensure the resources are comprehensive across the disciplines.

Among the information and tools available on the portal are:

Amyloid Imaging Locator Map—The portal’s Amyloid Imaging Locator Map offers a simple way for patients and neurologists to find the imaging center nearest them. To date, 110 locations have opted to be listed on the map.

With the anticipated increased use of amyloid imaging to qualify patients for new therapies and the recent removal of the CMS non-coverage decision for the scans, the Society expects additional centers will wish to
be added. Members who would like to add their centers to the list can do so using the link above the map on the portal.

- **Patient Resource Page**—The portal’s Patient Resources section offers numerous SNMMI videos on amyloid imaging as well as the Society’s patient fact sheets regarding What is Nuclear Medicine and Molecular Imaging?. Molecular Imaging and the Brain, and Molecular Imaging and Alzheimer’s Disease, each available in both English and Spanish.

  In addition, it includes links to numerous helpful websites, including the Alzheimer’s Association, the New IDEAS Study, and the National Institute on Aging.

- **Amyloid Imaging Training**—The site includes two types of training. First is an Amyloid Imaging Library, developed by SNMMI to give physicians practice in interpreting the three FDA-approved amyloid tracers. The library contains full DICOM cases including PET, CT and/or MR images, and its workflow allows the learner to manipulate the images and to review the history, findings, and conclusions for the study.

  The second is links to vendor reader training sites for all three tracers, including Life Molecular Imaging, GE Healthcare, and Lilly Diagnostics.

- **Appropriate Use and Procedure Standards Tools**—The site includes a link to the SNMMI/Alzheimer’s Association’s Appropriate Use Criteria for Amyloid PET, which is currently under revision and will be updated with the new version once available. It also includes an infographic depicting the decision chain for appropriate use.

  In addition, it includes links to the SNMMI Procedure Standard-EANM Practice Guideline for Amyloid PET Imaging of the Brain and the SNMMI Procedure Standard for FDG-PET Brain Imaging 1.0.

- **Research and Educational Resources**—Finally, the portal includes dozens of links to articles related to brain imaging from the Journal of Nuclear Medicine and the Journal of Nuclear Medicine Technology as well as links to numerous continuing education activities and webinars presented by the Society and/or at the SNMMI Annual Meeting.

  Satoshi Minoshima, MD, PhD, FSNMMI
  Chair and Founder, SNMMI Value Initiative
  University of Utah, Salt Lake City

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**The Era of Nuclear Medicine: The Perspective of a Clinical Endocrinologist**

Philip E. Harris, BSc, MB BCh, PhD, FRCP FRSB – ITM Chief Medical Officer

An article by ITM, an SNMMI Value Initiative Industry Alliance Leadership Circle Partner

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**How does your background as a clinical endocrinologist relate to your vision at ITM?**

Prior to my clinical leadership role at ITM, I served as an endocrinologist/neoendocrinologist. There is a strong interplay between endocrinology and cancer. Many tumors are hormone sensitive, some secrete hormones, and others express endocrine receptors. Neuroendocrine tumors (NETs) demonstrate a consistently high and relatively homogeneous expression of the somatostatin receptor 2 (SSTR2). The high SSTR expression renders NETs particularly amenable to theranostic targeting with somatostatin analogues for both imaging and therapy.

ITM specializes in the production and development of radioisotopes and radiopharmaceuticals for cancer treatment. My role as Chief Medical Officer at ITM is focused on the development of novel imaging and radiotherapeutic agents for the management of cancers with a high unmet medical need. Our progress in drug development at ITM is based on the cumulative advancement of discoveries that have been made by those clinicians and scientists who have gone on before us. The father of theranostics is Saul Hertz, who developed radiiodine for the treatment of patients with thyrotoxicosis. Iodine-131 has subsequently become a standard treatment not only for thyrotoxicosis but also for thyroid cancer. As an endocrinologist, I have a particular
Where Dr Hertz did his seminal work.

I also had the privilege of being a research fellow in endocrinology at Massachusetts General Hospital (MGH), thyrotoxicosis, goitres, and thyroid cancer with radioiodine.

Affinity with Dr Hertz, for two reasons. At Kings College Hospital London, my late nuclear medicine colleague, Dr Muriel Buxton-Thomas, and I treated countless patients with thyrotoxicosis, goitres, and thyroid cancer with radioiodine. I also had the privilege of being a research fellow in endocrinology at Massachusetts General Hospital (MGH), where Dr Hertz did his seminal work.

**What goals do you wish to accomplish with your team at ITM?**

I am a passionate advocate for the application of targeted radiopharmaceutical therapy for the treatment of patients with cancer. My vision is to develop a world-leading theranostics oncology group at ITM, built upon the foundation of the company’s robust radioisotope platform. ITM is a worldwide distributor of non-carrier-added (n.c.a.) ¹⁷⁷Lu, as well as a producer of ⁶⁸Ga generators and other novel radioisotopes. The combination of radioisotope production and distribution expertise, together with targeted radiopharmaceutical therapies, makes ITM unique in the field of theranostics. Our aim is to provide personalized targeted radiopharmaceutical therapy to cancer patients who have limited treatment options with the goal of improving their quality of life and life expectancy.

**What radiopharmaceuticals and clinical trials are supported by ITM?**

In general, ITM is dedicated to the development, production, and global supply of radioisotopes and targeted radiopharmaceutical agents for use in cancer treatment. Focusing on our late-stage clinical development program, we designed two Phase III trials, COMPETE and COMPOSE, evaluating the efficacy and safety of n.c.a. ¹⁷⁷Lu-edotreotide (a somatostatin analog-conjugated ligand to ¹⁷⁷Lu) in patients with advanced gastroenteropancreatic neuroendocrine tumors (GEP-NETs). The patient population in the COMPETE trial was well-differentiated, G1 and G2 GEP-NETs (Ki-67 index of 1-20%). The COMPOSE trial addresses patients with more aggressive GEP-NET disease: well-differentiated G2 and G3 (Ki-67 index of 15-55%). In both trials, patient randomization to n.c.a. ¹⁷⁷Lu-edotreotide or best standard of care (SoC) is based on localization of SSTR-positive GEP-NETs using a PET imaging modality. A third Phase III investigator-initiated trial in patients with pulmonary NETs has just started. We are also developing second-generation SSTR2 theranostics for NETs and other oncology conditions, as well as a novel renal protectant.

The NET development program is supported by a rich early development pipeline with novel targeting agents for advanced primary brain, prostate, bone, lung and ovarian cancers. Additionally, we are closely working with scientific colleagues to identify and translate novel targets such as fibroblast activating protein (FAP) into clinical development.

Both COMPETE and COMPOSE trials are designed to investigate the efficacy of n.c.a. ¹⁷⁷Lu-edotreotide in comparison with the best SoC for these patient populations. Concomitant somatostatin analogs are not required (unless utilized for symptom control), which means that some patients have received ¹⁷⁷Lu-edotreotide as a monotherapy.

COMPETE is unique as it will be the first Phase III trial to include prospective data in patients with pancreatic NETs with a Ki67 <10%. It is also the first Phase III trial to use n.c.a. ¹⁷⁷Lu, which is a radionuclide of high specific activity with negligible traces of long-lived metastable isotope. It includes 4 treatment cycles of n.c.a. ¹⁷⁷Lu-edotreotide at 12 weekly intervals in comparison to everolimus. Patients were included as first- or second-line therapy. Uniquely, there are 3 substudies which focus on dosimetry. Substantial dosimetric evaluation with 2D and hybrid 2D/3D imaging post-each infusion have been performed. Cumulative absorbed doses to kidneys, bone marrow, and target lesions are calculated from imaging and blood sample dosimetry. These substudies are of great importance in the development of a personalized, precision therapy approach to the management of patients with targeted radiopharmaceutical therapy. Enrollment for the COMPETE trial was completed in April 2022.

The COMPOSE trial uses a more intensive treatment regimen with 6 cycles of n.c.a. ¹⁷⁷Lu-edotreotide, at 6-8 weekly intervals. This is aligned with the intrinsic nature of a more aggressive disease with a higher proliferating Ki-67 index. COMPOSE will compare first- or second-line n.c.a. ¹⁷⁷Lu-edotreotide with best SoC. We also added exploratory arms to identify biomarkers and genomic aberrations, using both whole transcriptome and exosome sequencing, that may drive efficacy and optimize treatment based on individual organ dosimetry, toxicity, and genomic profile.

**What is your vision of the future use of radiopharmaceuticals in cancer treatment?**

I remember the first time I was first exposed to the...
The Era of Nuclear Medicine. Continued from page 3.

**ITM-11 COMPOSE Trial Design**

**Comparator Arm**
- n.c.a. $^{177}$Lu-Edotreotide by intravenous infusion
- Either CAPTEM or everolimus or FOLFOX therapy as prescribed by the study doctor

**Cycle 1**
- Week 0
- Week 6

**Cycle 2**
- Week 14

**Cycle 3**
- Week 22
- Week 30

**Cycle 4**
- Week 38

**Follow-up**
- Observation up to approx. 2 additional years

**COMPOSE Phase III** — A prospective, randomized, controlled, open-label, multicenter trial of n.c.a. $^{177}$Lu-edotreotide (7.5 GBq/cycle; 6 cycles) vs. standard of care with CAPTEM, everolimus or FOLFOX therapy in GEP-NETs (NCT04919226).

The Ether Dome at MGH. A personal reflection of a remarkable landmark where I attended weekly endocrinology rounds.

The potential of theranostics in a meaningful way was when I visited Wolfgang Weber, M.D, Ph.D during his time in Freiburg, Germany. Dr Weber showed me his early clinical results with the somatostatin antagonist, JR-11. It was a light bulb moment for me and from that time on, I was hooked. Since then, my whole focus has been on developing targeted radiopharmaceuticals for cancer patients. In the last few years, there has been a metaphorical explosion in the application of targeted radiopharmaceuticals for positron emission tomography (PET) imaging and therapy, with therapies approved in NET and prostate cancer. I have no doubt that progress will continue an upward trajectory, although the application of theranostics for new cancer conditions is likely to be challenging. Novel targets and radioisotopes such as $^{225}$Ac, $^{212}$Pb, $^{67}$Cu, $^{161}$Tb, as well as combination therapies will undoubtedly have important roles to play.

I feel enormously privileged to have had the opportunity to play a small role in the development of this exciting field. My only regret is that I will not be actively involved for the next 20 years because *tempus fugit!* During this time, we can expect to see a paradigm shift in the way that theranostics is applied to the management of cancer. I think we can justly say that Saul Hertz’s revolutionary legacy is safe with his many talented successors, who continue to drive theranostics to new and, until recently, undreamt-of heights. It is particularly pleasing for me, that it was an endocrine condition that lit the fuse!

Philip E. Harris, BSc, MB BCh, PhD, FRCP FRSB
ITM Chief Medical Officer
From a practical point of view, I think we can certainly see some advantages regarding patient throughput and department flow as there are no drug distribution and delivery constraints with an on-site manufacturing point-of-care model. To say the least, it can be challenging to keep an imaging department on schedule when having to rely on just-in-time delivery of radiopharmaceuticals from a centralized manufacturer, but for a facility who has the ability to manufacture PET radiopharmaceuticals on-site, perhaps your schedule becomes a little more robust, a little more flexible. So, I think that’s the essence of point-of-care practicality. We have the opportunity to re-think the radiopharmaceutical distribution model and its limitations, including the need for longer half-life isotopes, while enjoying some of the advantages point-of-care manufacturing affords, such as flexibility in novel imaging protocols and departmental flows.

What kind of timeline are we looking at in terms of having PET point-of-care manufacturing available in clinical practice?

I won’t speculate on the timing, but I can say that we at MedTrace are tirelessly working to make point-of-care manufacturing for ultra-short half-life radioisotopes practically available and a real possibility! We are certainly hoping to see favorable results from our ongoing Phase 3 trial and welcome the additional work it would create as we seek regulatory approval for $^{15}$O-water along with the P3 point-of-care manufacturing system.

MedTrace has an automated manufacturing system, P3 MT-100, which is in use at several hospitals around the world as part of the company’s Phase 3 Clinical Trial, which seeks to evaluate the diagnostic accuracy and safety of $^{15}$O-water as a myocardial perfusion PET imaging agent.

You’ve worked in the nuclear medicine and imaging arena for more than 25 years. What do you see as the biggest challenges for making PET point-of-care manufacturing available in clinical practice?

Today, most PET radiopharmaceuticals are produced at centralized locations and distributed. However, there are logistical limitations to this model and that is why it becomes increasingly interesting, and perhaps important, to consider point-of-care manufacturing. The industry stakeholders in this space, including MedTrace, are now investigating how we might shrink the entire PET radiopharmaceutical manufacturing footprint and put it in a “box” placed right at the point of patient care. The challenge here is that the drug manufacturer will, of course, be held accountable for everything that goes on within this box, and to the same caliber of standards as those expected from a more traditional PET manufacturing facility. It is a regulatory challenge, but it will be fun to figure all of that out! Based on ongoing conversations with both regulatory authorities and other manufacturers of ultra-short half-life PET radiopharmaceuticals, the interest in pursuing solutions to these challenges appears to be gaining momentum. Some of these concepts, as outlined in a recently posted FDA discussion paper (Distributed Manufacturing and Point-of-Care Manufacturing of Drugs), were also entertained at the November 2023 FDA PET Drugs Workshop (co-organized by the FDA, SNMMI, MITA, and the Coalition of PET Drug Manufacturers).

Tell us more about that. How do you see PET point-of-care manufacturing influencing the future of imaging?

Things are becoming really interesting as more institutions are beginning to offer whole-body PET/CT imaging. I think by combining the ability to produce ultra-short half-life PET radiopharmaceuticals at the point-of-care with the capacity to perform whole-body PET/CT imaging, we will begin to see correlatives that have never been seen before. What if we had the ability to perfuse multiple organs, look at blood flow throughout the body, and quantify it all in one imaging session? And by using ultra-short half-life PET isotopes, perhaps we may even be able to get multiple serial infusions and images under different conditions back-to-back while the patient remains in the scanner.
Growing Theranostics Program Is Now Everyday Clinical Practice in Finland

Claudette Lew | Photography – Matti Immonen
An article by Siemens Healthineers, an SNMMI Value Initiative Industry Alliance Leadership Circle Partner

Cancer treatment has made tremendous progress in recent years, and the latest advancement in precision therapy is theranostics. “There’s a lot of excitement around theranostics right now,” said Veera Ahtiainen, MD, oncologist in the Molecular Radiotherapy Unit at The Comprehensive Cancer Center in Helsinki, Finland. Part of HUS Helsinki University Hospital, The Comprehensive Cancer Center is a world-renowned center for the treatment of cancer patients, using theranostics to treat many of them. “There’s a clear advantage in its possibilities to be used in prediction, for personalization in treatment, and to provide precision medicine for cancer patients. We can diagnose and treat cancer, evaluate and measure the effectiveness of a given treatment, and carry out a treatment in a more targeted manner. We can better influence the care path of cancer patients and improve the patient’s quality of life.”

An Established Theranostics Program
The unit is an integral part of The Comprehensive Cancer Center and uses a combination of molecular imaging and targeted radiotherapy to diagnose and treat cancer patients. As the country’s largest and most versatile cancer center, it continues to be a critical resource for patients throughout Finland, reaching those living as far north as Lapland.

The team has seen the number of theranostics patients double in the last seven years. At present, roughly 60 percent of their theranostics treatments are for prostate cancer, and 40 percent are for treating neuroendocrine tumors, thyroid cancers, and other malignancies.

PET/CT for Patient Selection
The Molecular Radiotherapy Unit uses a combination of imaging techniques, including PET/CT, to determine the location and extent of the cancer in the patient’s body. “We use image guided patient selection,” explained Dr. Ahtiainen. Utilizing the available diagnostic information, the team can design a personalized treatment plan that is tailored to the patient’s individual needs.

SPECT/CT for Imaging Enabled Treatment Evaluation
Another benefit of the theranostics approach is the potential to measure treatment effectiveness. The team uses quantitative SPECT/CT to monitor the patient’s response throughout the treatment and adjusts the treatment plan as necessary. The Molecular Radiotherapy Unit also performs SPECT/CT-based dosimetry to ensure the patient receives the most effective treatment possible while minimizing any potential side effects.

“Once patients begin treatment, we perform post-therapy imaging with our SPECT/CT. To individualize the treatment, molecular imaging is extremely valuable from a clinical perspective,” explained Vappu Reijonen, medical physicist, “because molecular imaging not only allows us to determine patients who benefit from the treatment, but it also allows us to see exactly what we treat.”

At the center, patients are evaluated with Siemens Healthineers Symbia Pro.specta SPECT/CT after each cycle of theranostics treatment. “From the posttreatment scans, we assess, together with laboratory results and the patient’s clinical condition, the safety and tolerability of the treatment, and that we are seeing uptake in the tumor tissue, in comparison to normal tissue uptake. Cycle by cycle, we can observe the changes in the uptake in the tumor tissue and how the organs at risk are getting the accumulated dose. It’s important for us to approach theranostics treatments from the perspective of using quantification and dosimetry for safety, as well as tracking effectiveness” noted Dr. Ahtiainen.

Facilitating the Theranostics Workflow
Considering the high volume of patients the center sees for post-treatment scanning, the team routinely uses the Symbia Pro.specta SPECT/CT system to facilitate their theranostics workflow. “We’ve designed our workflow to accommodate our patient volume so that it’s feasible for us, but also for our patients. During scans, patients need to breathe freely and sometimes move. It’s really important that the patient is comfortable during imaging, and with respiratory motion correction, we can minimize those artifacts,” explained Reijonen.

The team relies on the system’s intuitive interface and features that automate steps across the workflow to support them from patient setup through final imaging, resulting in consistent, reproducible studies. “Using the features on our Symbia Pro.specta, we can now implement treatment

Continued on page 8. See Growing Theranostics Program.
Advanced Dosimetry: Are you more ready than you thought for a higher standard of care?

Laurie Conrad, BSRT, Director, Vox Assure, Voximetry
An article by Voximetry, an SNMMI Value Initiative Industry Alliance Principal Member Partner

Do you consider yourself an “informed early adopter” or a “wait-and-see-er” when it comes to dosimetry guidance? Your answer could be impacting your radiopharmaceutical therapy (RPT) patient outcomes.

In nuclear medicine today, wait-and-see-ers are pointing to staffing shortages, lack of training, scanner schedule limitations, additional costs, and unclear guidelines on how to use dosimetry metrics in patient management. The result is a one-size-fits-all dosing strategy for RPT patients.

In contrast, the NM informed early adopters point to clinical evidence showing DG-RPT (dosimetry guided radiopharmaceutical therapy) improves patient outcomes. For many patients, the use of dosimetry as a biomarker enables a reduction in normal tissue toxicity and an increase in tumor dose. Garske-Romain et al. have shown that when doses of $^{177}$Lu-DOTA were escalated until the kidneys reached an absorbed dose of 23Gy, patients with neuroendocrine tumors had a 54-month overall survival versus 25 months for those whose doses were not escalated.

In Y90-microsphere treatments of locally advanced hepatocellular carcinoma, Garin, Tselikas et al. showed that patients in the personalized dosimetry group had an overall survival rate of 26.6 months versus 10.7 months. Radiopharmaceutical therapies are now being used earlier in the treatment of cancer patients. This is of great relevance as there are early papers suggesting declines in renal function can occur in patients treated with $^{177}$Lu PSMA agents potentially related to radiation dose to the kidneys, among other factors.

These same early adopters are accelerating their action on training staff, investing in software to reduce scan times, and performing dosimetry on patients with known risk factors. The result is better management of individual patient risk factors that includes documentation of delivered dose that can be considered in follow-up patient management decisions, similar to the process in External Beam Radiotherapy.

To be fair, the wait-and-see-ers, taking the position of the naysayer, have a point. Post-pandemic workforce shortages have permeated all areas of healthcare. Administrators are pressured to justify the person-hours required to support new programs prior to moving forward, and educating teams on a new procedure is challenging when resources are tight. For most clinics, SPECT/CT availability poses a challenge.

But early adopters are finding ways to meet these challenges and help patients while maintaining a healthy financial model. Innovative technologies are part of these solutions to make theranostics treatments simple.

Healthtech companies like Voximetry are using innovation to tackle the hurdles of multiple, long, SPECT scan times and complex dosimetry methods. With Torch® Dose Assessment software in the clinic, enhanced staff efficiency is possible with a simple five-step workflow users are calling the “Apple” of the industry. This includes extremely accurate calculations, and soon will enable shorter SPECT scan times – all powered by lightning-fast GPU-accelerated Monte Carlo proprietary algorithms and AI. The entire process, inclusive of contouring regions of interest, calculating dose, performing an assessment, and printing a plan, can be quickly performed by either a nuclear medicine technologist and/or physicist, with final review completed by the physician.

Training for staff will be available in early 2024 via the SNMMI Dosimetry Training and Certificate Program designed for technologists, physicists, and physicians. This is a self-paced online course that covers the basics of performing dosimetry. The physicist’s component of the course includes a practicum. SNMMI, as well as AAPM, also provide best practice guidelines and offer theranostics-focused educational tracks at their member meetings. Industry initiatives, working collaboratively with professional societies, have also stepped in to support educational needs. Voximetry can provide inexperienced users with best practice guidelines and customizable workflows to expedite time to go-live with Torch®. Templates to assist the administrative team with billing and reimbursement are available through the Vox Assure program.

Also, informed early adopters are implementing alternate workflows that demonstrate strong potential for reduced imaging with minimal compromise to accuracy. Torch® software from Voximetry can generate dose estimates from single time point imaging which provides an option for centers with limited scanner accessibility or in settings where return patient visits are not feasible.

Providers actively billing for reimbursement are reporting smooth revenue collection from payers. Revenue Cycle

Continued on page 8. See Advanced Dosimetry.
Coding Strategies® suggests using current radiation oncology and imaging CPT codes with appropriate documentation and medical necessity for SPECT/CT imaging, complex dosimetry, special or continuing physics consults and physician payments. The reimbursement varies based on the number of SPECT/CT scans acquired and the number of dose assessments performed per course of treatment. Revenue per patient can range from $7,000 for administrations with single time point imaging with a single complex dose calculation to over $30,000 for multi-timepoint assessments with secondary dose checks. In bundled or value-based care payment models, using dosimetry as a biomarker for therapy can reduce costs by avoiding toxicities and associated adverse events resulting from overdosage to non-target tissues. For other patients, increased doses may result in improved tumor control, reducing the need for additional care.

While additional clinical data demonstrating deeper insight into the value of dosimetry as a biomarker will further clarify when and how to best select patients and optimize care, there is data today that offers a clear, documented path to improved patient outcomes and quality of life. The question is whether your site is ready to join the early adopter movement to begin making a difference now.

REFERENCES


Our nuclear medicine technologists have given a lot of positive feedback about the everyday user-experience when imaging with Pro.specta,” noted Reijonen.

Evolutiong Theranostics into Routine Clinical Practice

The Molecular Radiotherapy Unit is constantly evaluating the effectiveness of its treatments through ongoing research and clinical trials. This ensures that the unit’s treatment protocols are based on the latest scientific evidence and are optimized for the best possible outcomes for patients. “New treatments can quickly become part of the clinical routine,” explained Dr. Ahtiainen.

DISCLAIMERS
Symbia Pro.specta™ SPECT/CT is not commercially available in all countries. Due to regulatory reasons, its future availability cannot be guaranteed.

The statements by Siemens Healthineers customers described herein are based on results that were achieved in the customer’s unique setting. Since there is no “typical” hospital and many variables exist (e.g., hospital size, case mix, level of IT adoption), there can be no guarantee that other customers will achieve the same results.
Structured Reporting for Prostate Specific Membrane Antigen (PSMA) PET

Hong Song, MD, PhD and Andrei Iagaru, MD – Division of Nuclear Medicine and Molecular Imaging Department of Radiology, Stanford University

An article by Lantheus, an SNMMI Value Initiative Industry Alliance Leadership Circle Partner

A well-structured PSMA PET ($^{18}$F-DCFPyL, $^{68}$Ga-PSMA11) report should fulfill the basic criteria of a good radiologic report. Structured reporting for PSMA PET scans should generally adhere to the following guidelines: The report must begin by clearly identifying the patient, including relevant clinical history, and stating the indication for the study (e.g. staging, biochemical recurrence, etc.). The technique used in the scan should be documented, specifying the radiotracer dose administered and the timing of imaging post-injection. Additionally, if any contrast agents were utilized, that should be noted. In the findings section, a comprehensive description of abnormal PSMA uptake is essential. This should include details on the anatomic location, size, and intensity of the uptake. Reference uptake in the mediastinal blood pool, liver and parotid glands should be provided and compared to. If any associated CT or MRI findings are present, they should be described as well. The impression section should be concise and will be most valuable in addressing the clinical question posed by the referring physicians and providing actionable recommendations, such as follow-up imaging or biopsy, etc.

Since PSMA PET can be ordered for various clinical scenarios, reporting radiologists should be familiar with these different clinical settings and interpret the imaging finding accordingly. The clinical indications for PSMA PET/CT in prostate cancer are based on The Joint SNMMI and EANM procedure guideline1, SNMMI Appropriate Use Criteria for PSMA PET Imaging2 and NCCN Guideline for prostate cancer3. These indications include initial staging for unfavorable intermediate, high risk and very high risk prostate cancer; tumor localization in prostate cancer patients with biochemical recurrence (BCR) or persistent prostate specific antigen (PSA) after primary definite treatment (BCP); tumor localization in castration resistant prostate cancer who is non-metastatic on conventional imaging (nmCRPC); restaging and assessing eligibility for PSMA-targeted radioligand therapy (RLT); and potentially indicated for treatment response after systemic therapy and radiogand therapy.

Several PSMA PET standardized reporting guidelines are available to characterize the lesions found on PSMA PET. For example, PROMISE criteria propose assigning each lesion as positive, negative, or equivocal based on types of lesions (prostate bed, lymph nodes, bone and visceral organ lesions), locations, findings on anatomic images and PSMA uptake level4. PSMA-RADS uses a 5-point scale to grade likelihood of prostate cancer for each lesion based on similar lesion characteristics5. E-PSMA reporting guideline updated from the early Delphi consensus6, uses a 5-point scale to interpret lesions on PSMA PET7. An independent evaluation revealed that these three criteria exhibit substantial to almost perfect interreader, intrareader, and intercriteria agreement across most situations8. Based on the classification criteria of these guidelines, lesions found on PSMA PET can be categorized into specific diagnoses such as “benign,” “probably benign,” “equivocal,” “probable,” or “definite” prostate cancer and/or metastasis.” Furthermore, it is vital to categorize the uptake locations as “local” (prostate/bed), “regional nodes,” or “distant metastases”. For structured reporting of these lesions, PROMISE criteria proposed miTNM (molecular imaging TNM) classification which summarizes the findings in the prostate bed, lymph node and distant metastases. The miTNM findings are then applied in different clinical scenarios for the final impression that addresses the specific clinical question. For initial staging, the structured miTNM classification system from PROMISE can be used for reporting. Wherever possible, T staging relevant findings such as extent of tumor involvement in the prostate gland, involvement of seminal vesicle and possible invasion of adjacent structures such as rectum, bladder, muscles, and pelvic wall should be included. MR prostate is typically performed to better characterize the prostate tumor locally and can be used to compare and confirm these findings on PSMA PET. The N stage is primarily based on regional lymph node involvement. Regional nodal stations such as

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internal iliac, presacral nodes and lower retroperitoneal nodal stations such as common iliac and paraaortic nodes should be mentioned if present since they may be treated with extended pelvic lymph node dissection and/or extended field radiation. Note that the recently updated PROMISE version 2 now reports common iliac lymph nodes in the mT1a category. PSMA PET is highly sensitive for detection of distant metastases at staging (M stage) which is crucial since patients with metastatic disease are treated differently. If oligometastatic disease (< 5 lesions) is present, they should be reported for potential metastasis-targeted therapy.

For BCR or BCP patients, the miTNM classification system can also be used for reporting. Similar to staging, if oligometastatic disease is present, it should be mentioned for possible metastasis-targeted therapy. Additionally, para-aortic lymph node metastasis should be mentioned since they may be included in the extended field radiation given pelvic radiation is commonly employed to treat BCR patients.

For nmCRPC patient, the miTNM classification system can also be used for reporting. Since these patients are non-metastatic on conventional imaging, the M staging on PSMA PET is of utmost importance as it could lead to change in patient management.

For assessing eligibility for PSMA-targeted RLT, the PSMA PET report, besides reporting disease status such as disease extent and status (stable, progression etc.), should include assessment of PSMA positive and PSMA negative lesions, as established by the VISION trial. PSMA positive lesions are defined as having PSMA uptake greater than that of the liver parenchyma, while PSMA negative lesions are defined as having PSMA uptake equal to or lower than liver in lymph nodes < 2.5 cm in short axis, solid organ lesions and bone lesions with soft tissue components < 1.0 cm in short axis.

For treatment response after systemic therapy or RLT, it is crucial to provide an overall impression of response including complete or partial response, mixed response, stable disease, or disease progression. While the Prostate Cancer Working Group (PCWG) criteria include only PSA and conventional imaging for treatment assessment, PSMA PET-based treatment assessment criteria, such as the PPP criteria and more recently the RECIP 1.0 criteria have been proposed, but not yet evaluated in large prospective trials. Currently, some of the quantitative tools, such as PSMA avid total tumor volumes are not readily available. Before automated quantitative tools such as FDA approved aPROMISE are widely adopted, treatment assessment still mainly relies on visual assessment of changes in PSMA uptake and extent. Heterogeneity is a characteristic of advanced prostate cancer, and mixed response is quite common to systemic therapy especially after PSMA RLT. This can become challenging in the absence of quantitative tools to determine disease status. Additionally, PSMA-negative disease could develop after several cycles of PSMA RLT, especially in the liver, and can only be detected on anatomic images. This needs to be described in the impression since it will change management and outcome.

For other potential indications, such as prostate lesion biopsy guidance and initial diagnosis of prostate cancer, PSMA PET is combined with multiparametric MRI to improve the sensitivity of biopsy and accuracy of diagnosis. However, these indications for PSMA PET are not performed routinely and remain to be validated.

In summary, structured reporting improves clarity, reduces ambiguity, and standardizes communication of PSMA PET findings. The PROMISE, PSMA-RADS and E-PSMA systems all help categorize the likelihood of prostate cancer lesions. A concise impression with clear diagnostic certainty and actionable recommendations benefit patient care.

**REFERENCES**


Curium Women in Theranostics

Jenny Yessaian RN, MBA – Senior Director of Marketing
An article by Curium, an SNMMI Value Initiative Industry Alliance Leadership Circle Partner

Over five years ago, I took on the responsibility of coordinating a commercial advisory board. My approach to planning the advisory board was highly systematic, emphasizing the inclusion of experts from diverse regions of the country. During discussions about potential attendees with the board chair, Dr. Pamela Kunz, brought to my attention the importance of considering gender equity in the panel composition. These opportunities literally and figuratively give experts a seat at the table for key decisions, and often yield other leadership opportunities, such as clinical trial steering committees.

I was surprised that as a woman, I hadn’t previously considered this aspect. While I had always prioritized expertise and geographical representation, I had overlooked the crucial element of gender balance. It was at that moment I resolved to become part of the solution. I consider myself lucky to work for Curium, an employer that aligns with and supports this mission. My co-chair Jennifer Janowitz and I are empowered to bring this vision to reality through Curium’s Women in Theranostics initiative.

At Curium, the vision for this initiative is to transform the theranostics field by championing gender equity and creating opportunities for women to thrive. We see a future where women are not only equally represented but also actively engaged in shaping the advancement of theranostics.

Through the Women in Theranostics initiative, we aspire to become a beacon of change, setting the standard for gender equity within the industry. By fostering collaboration and diversity, and empowering women at every level, we aim to drive innovation, improve patient outcomes, and inspire a new generation of female leaders in theranostics with equal access to opportunities across the various fields from Oncologists to the Nuclear Medicine technicians and Nuclear Medicine physicians. We strive to lead the industry by emphasizing gender equality with our external partners within areas such as advisory boards, symposiums, clinical trials, authorship and as advisors.

The field of theranostics is expanding, yet there is a crucial need to boost participation in these programs, particularly encouraging more women to join the sector. At present, we need to drive higher awareness and exert focused effort towards enhancing gender equality in theranostics. To achieve this, it is essential to enhance training and garner greater support from our male advocates across the industry. #He4She

Our goal is for Curium’s Women in Theranostics initiative to drive positive transformation and serve as a model for the entire industry.

REFERENCE
United Imaging is no stranger to long axial field of view (FOV) systems, with the 194 cm uEXPLORER system that has been available in the U.S. since 2019. With its ability to perform high resolution total-body PET scans, the system is particularly beneficial in oncology for comprehensive cancer staging, treatment planning for theranostics and restaging. Drawing on insights gained from the development of total-body systems, United Imaging has unveiled an innovative and scalable next-generation detector, uExcel UDP.

The uExcel UDP utilizes high-performance LYSO crystals with superior light yield and fast decay time for optimal intrinsic energy and time performance in PET detectors. The smaller the crystal size, the better the system’s spatial resolution. The detectors are equipped with crystal elements measuring 2.76 mm × 2.76 mm in size, which provide a NEMA resolution of 2.9 mm. The crystal array unit incorporates a patented “built-in light guide” technology, eliminating the need for a separate light guide layer in traditional designs and significantly improving light collection efficiency by minimizing light loss.

uExcel UDP utilizes the dedicated PET ASIC, known as the uExcel ASIC, which is designed at United Imaging’s microchip factory. The uExcel ASIC showcases an impressive readout bandwidth surpassing 1.2 Gbps. This capability effectively addresses detector dropout concerns, particularly during high count rates associated with bolus injections, ensuring precise atrial input function measurements. The high bandwidth ASIC enables the ability to collect all the lines of responses for whole-body PET/CT systems, greatly improving the sensitivity of the system. uExcel ASIC reduces SiPM Background noise, allowing an improved timing resolution to under 199 ps. uExcel ASIC also includes features like SiPM background noise monitoring, temperature monitoring, and voltage compensation, thereby elevating the detector’s reliability.

A substantial portion of the 511 keV gamma photons undergo Compton reactions, resulting in energy deposition in multiple crystals, particularly noticeable in long axial FOV systems. This next-generation PET ASIC is equipped to perform energy and time recovery of these Compton scattering events, leading to a significant 30% improvement in system sensitivity.

Continued on page 13. See United Imaging Leads.
NorthStar Medical Radioisotopes: Enabling Radiopharmaceutical Company Success

The exceptional promise of Radiopharmaceutical Therapy needs a robust and reliable infrastructure for radioisotope manufacture and related services.

Stephen Merrick, Executive Chairman – NorthStar Medical Radioisotopes LLC
An article by NorthStar Medical Radioisotopes LLC, an SNMMI Value Initiative Industry Alliance Principal Member Partner

We see many articles and hear many presentations which describe the potential benefits of Radiopharmaceutical Therapy (RPT). However these benefits are dependent on four supporting pillars:

1. Robust and reliable commercial scale manufacture of Medical Radioisotopes
2. Adequate development capacity for Patient Doses
3. Sufficient manufacturing capacity for Patient Doses
4. Efficient management of logistics for Patient Doses

NorthStar recognizes the importance of all of these foundational capabilities. With well over $500m invested to date, over 250 employees and a strategically located 55 acre campus, NorthStar is demonstrating that it plans to become an indispensable strategic partner for all radiopharmaceutical companies – truly walking the talk.

Commercial Scale Manufacture of Medical Radioisotopes

The industry has seen positive steps forward with the manufacture of nca Lu-177, although there do remain concerns over supply of the target isotope material (very pure Yb-176). However, there are other promising Continued on page 14. See NorthStar Medical Radioisotopes.

NorthStar Medical Radioisotopes: Enabling Radiopharmaceutical Company Success

The exceptional promise of Radiopharmaceutical Therapy needs a robust and reliable infrastructure for radioisotope manufacture and related services.

Stephen Merrick, Executive Chairman – NorthStar Medical Radioisotopes LLC
An article by NorthStar Medical Radioisotopes LLC, an SNMMI Value Initiative Industry Alliance Principal Member Partner

With the increases in sensitivity and signal-to-noise ratio (SNR), uExcel UDP enables the reduction of partial volume effects of small lesions by increasing the matrix size and decreasing the size of each individual pixel. A higher matrix size offered by our systems results in improved spatial resolution, and with a 1024 x 1024 matrix, there are more pixels available to represent the same physical area compared to a typical PET’s 256 x 256 matrix. This finer pixelation allows for better visualization of smaller structures.

The uExcel UDP is currently available on the uMI Panorama family of systems with long axial FOV ranging from 35 cm to 148 cm. This next-generation PET detector improves image resolution, reduces partial volume effects, and provides high sensitivity. This enables low dose, long delay or fast scan times for whole-body imaging. Leveraging cutting-edge technologies and a commitment to excellence, United Imaging is actively shaping the future landscape of molecular imaging with its forward-thinking approaches and state-of-the-art solutions.

United Imaging Leads. Continued from page 12.

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Image Courtesy of the First People’s Hospital of Kunshan, JS, CHN
radioisotopes that are in such short supply that clinical trials are on-hold or progressing too slowly. NorthStar is addressing this challenge for both Cu-67 and nca Ac-225. NorthStar is already shipping Cu-67 for use in clinical trials and plans to start shipping Ac-225 in the second half of 2024. NorthStar’s approaches are designed to allow scale-up as demand grows from small early stage clinical trial volumes to (hopefully) very large commercial volumes.

Flexible Patient Dose Development Capacity

Maximizing the utility of radiopharmaceuticals needs careful selection of the targeting molecule, radioisotope and chelators/linkers to ensure that maximum binding is achieved over as long a period as practical. Using existing licensed laboratories, NorthStar is currently able to provide these services and with the completion of a patient dose development and manufacturing (or CDMO) facility at the end of 2024, will be able to offer even more extensive development facilities for multiple projects.

Sufficient Patient Dose Manufacturing Capacity

NorthStar’s 53,000ft² CDMO facility will have the capacity to manufacture patient doses for clinical trials and commercial launches. This facility will have eight suites with scope to fit out an additional 11,000ft² depending on market needs. The radioisotopes the facility is designed to manage are Cu-64, Cu-67, Ga-68, Zr-89, In-111, Lu-177, Ac-225 and others. NorthStar also has space on its 55 acre campus to build additional facilities, including a high volume manufacturing operation.

Efficient and Reliable Logistics

NorthStar has extensive experience with managing logistics for radioisotopes and is rapidly gaining experience with RPT patient doses, having already shipped to multiple US locations and Australia. Getting patient doses to the right place at the right time is critical for physicians and patients.

Conclusion

NorthStar is positioned to be a leading end-to-end strategic partner for Radiopharmaceutical companies and looks forward to making very significant contributions to the success of Radiopharmaceutical Therapy and facilitating positive patient outcomes.

REFERENCE

1. There are many different terms in use but RPT is used for consistency.
Value Initiative Board

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