Effective imaging and staging of prostate cancer (PCA) is critical for surgical and treatment planning. The rate of prostatectomy is increasing in high-risk prostate cancer patients, which means that there is an increasing, unmet need to detect regional and distant metastases prior to treatment. Additionally, patients who have undergone previous definitive therapy and then exhibit biochemical recurrence (BCR) present disease-management challenges for the clinician. Although monitoring of prostate specific antigen (PSA) is a reliable and cost-effective way to detect disease relapse, it cannot differentiate between local, locoregional or systemic recurrence. Current conventional imaging modalities, such as bone scintigraphy (BS) and computed tomography (CT), have considerable limitations, especially in the setting where patients have low PSA values.

Prostate-specific membrane antigen (PSMA) is a type II membrane protein originally characterized by the murine monoclonal antibody (mAb) 7E11-C5.3 and is expressed in all forms of prostate tissue, including carcinoma. \(^{1,68}\)Ga-PSMA-11 (Gallium-68 labeled HBED-CC PSMA) is a radioconjugate composed of a PSMA-targeting ligand (Glu-urea-Lys(Ahx) \(\text{Glu-NH-CO-NH-Lys(Ahx)}\)) conjugated via an acyclic radiometal chelator \(\text{N,N’-bis [2-hydroxy-5-(carboxyethyl)benzyl] ethylenediamine-N,N’-dicetic acid (HBED-CC)}\) to the radionuclide gallium-68. \(^\text{2}\) The introduction of \(^{68}\)Ga-PSMA-11 as a marker for PSMA expression with PET imaging demonstrated excellent results, especially for patients with BCR. It showed markedly improved detection rates in direct head-to-head comparisons or when compared to data from literature\(^3\) (see Figure 1).

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Figure 1. Multifocal local recurrence of prostate cancer in a 65-year-old patient (Gleason score 9, PSA nadir 0.01 ng/mL after external beam radiation therapy, staging PSA level 3.8 ng/mL). CT (A) was negative, whereas PET (B) and fused PET/CT (C) images revealed multiple \(^{68}\)Ga-PSMA-11 positive lesions in the prostate gland (SUV\(_{\text{max}}\) 11.3). This finding was confirmed by transrectal ultrasonography guided sextant biopsy.\(^3\)
268Ga-PSMA-11 PET/CT Clinical Trial.

A patient population that has a high potential for 68Ga-PSMA-11 uptake of both moderate- and high-risk prostate cancer subjects provides a way to detect the presence or absence of metastatic prostate cancer, especially in pre-prostatectomy patients and one in patients with biochemical recurrence. It is our goal with this clinical trial, in conjunction with other clinical studies, to show that the PET imaging agent 68Ga-PSMA-11 is safe and effective and should be approved for clinical use in patients with metastatic prostate cancer. Submission of a New Drug Application (NDA) to the FDA and generation of sufficient change of management data to support a positive coverage decision by the Center for Medicare and Medicaid Services (CMS) are planned. For more information on this study, contact CTN at ctnclinics@sunmmi.org.

References:

Message from the Co-Chairs: A New Chapter Begins for CTN

The Clinical Trials Network (CTN) is working with researchers and academic groups to assist with and collect data for the phase III multicenter study, which is designed to standardize PET/CT imaging. Study sites must validate their PET/CT camera using the newly designed CTN chest oncology phantom to ensure that imaging is standardized throughout the study sites (see article on page 4 of this issue).

Recruitment opened in 2016 at four sites in the United States. To address this unmet need, the Clinical Trials Network (CTN) is working with researchers and academic groups to assist with and collect data for a phase III multicenter study in subjects with pathologically proven prostate adenocarcinoma, who have received treatment with curative intent but now have a rising PSA, will be enrolled.

Objective: Determine sensitivity, specificity, positive, and negative predictive value of 68Ga-PSMA-11 PET/CT for detection of regional nodal metastases compared to pathology at radical prostatectomy (per patient, using nodal regional correlation).

The injected dose of 68Ga-PSMA-11 is 3–7 mCi, with a target dose of 5 mCi, and PET imaging begins at 75 minutes ± 25 minutes after injection. Eligible subjects undergo all conventional preoperative workup tests, including bone scintigraphy and either CT or magnetic resonance (MR) imaging. The injected dose of 68Ga-PSMA-11 is 3–7 mCi, with a target dose of 5 mCi, and PET imaging begins at 75 minutes ± 25 minutes after injection. Each on-site imaging investigator is unblinded to all imaging data (68Ga-PSMA-11 PET/CT and conventional imaging) and the medical record. Images are interpreted by a board-certified nuclear medicine physician or a board-certified radiologist experienced in imaging prostate cancer. Follow-up imaging is performed at 6 weeks, and a blinded fashion. Three different readers interpret PET data in a random order at separate reading sessions.

The CTN Education Committee developed an excellent webinar series for 2017. These six one-hour webinars present timely topics of interest for the entire community and offer CE credit at a nominal fee. Once presented and after the recording is finalized, all webinars are made available in the SNMMI Learning Center.

Future webinars—3 pm ET
June 29—Career Pathways Through Medical Imaging: speaker—Ruth Tesar and Lance Burrell
August 17—RECIST Overview and Other Response Measurement Criteria: speakers—Trinity Urban and Cheryl Sadow
October 19—FDOPA: Its Use in CHF and Renal Status: speaker—Lisa Stotes
December 14—Lutetium—Incorporating It in Your Hospital: speaker—Jonathan Strosberg

Check the CTN website for a list of all CTN educational offerings.
Resized CTN Phantom Used in 68Ga PSMA Trial

Phillip Alvarado, CNMT; Paulo Castaneda, CNMT; and Andrei Iagaru, MD
Sanford Healthcare, CA

The Clinical Trials Network (CTN) team provides an established workflow for preparing 68Ga DOTATATE and 68Ga-DOTATOC with PET/CT. These two radiotracers have been used extensively outside the United States, and 68Ga-DOTATOC was introduced clinically in the U.S. by researchers at the University of Iowa and Vanderbilt University, respectively, before more widespread use and eventual FDA approval in June 2016. Moving forward, CTN helps a group of investigators interested in jointly pursuing clinical trials in the U.S. to evaluate the performance of 68Ga-DOTATATE in prostate cancer at both initial diagnosis and biochemical recurrence. Therefore, a need for an updated phantom to perform 68Ga PET site validation became apparent.

CTN redesigned its chest oncology phantom in 2016, and it was recently used at UCLA and Stanford to validate scanners for a 68Ga-DOTATATE trial. Here we report our experience at Stanford University. Preparing and scanning the new CTN phantom will appear familiar to those who have used the older CTN phantom for 18F-FDG. The provided instructions are clear and easy to follow, making it a user-friendly process. We highly recommend checking for any phantom leaks prior to the actual phantom scanning as suggested in the instructions. Weating a lab coat is also advised, as minor splashes did occur. The two most important aspects of a smooth and successful filling process is cleaning a workspace and carving out uninterrupted time in the schedule, it takes approximately 30 minutes from start to finish. Since precise timing for filling and scanning the phantom is required, it is crucial that one has all supplies prepared and ready prior to starting the scanning process. Exact timing for each procedure and accurate documentation of the data are also critical. When done correctly, the process results in high-quality images as seen in Figure 1 from our two scanners: GE Discovery M640 (DWI) and 68Ga DOTATATE (GE Healthcare, Waukesha, WI).

In conclusion, a newly designed CTN chest oncology phantom used to validate scanners for the 68Ga-DOTATATE trial was shown to be successful and paves the way for standardized data acquisition among the sites participating in this study. As additional data are collected on phantom performance and image quality, we anticipate that its use in future clinical trials will be expanded.

References:

WHAT'S HAPPENING

Learning the Pathway to Radiotracer Development and Approval: My Experience as a CTN Intern

Robert R. Flavell, MD, PhD, Assistant Professor in Residence, Section of Nuclear Medicine, Department of Radiology and Biomedical Imaging, University of California–San Francisco

Learning the pathways to approval of new radiopharmaceuticals and practical aspects of running clinical trials is a daunting task. Overall, my experience at the 2017-2018 Clinical Trials Network (CTN) internship has been a rapid education in this regard. In my opinion, this is an underrecognized group that works diligently behind the scenes to translate research into the clinic by helping to promote the approval of new radiopharmaceuticals and educating users on the use of these new tracers. They have recently played a pivotal role in the development of new radiotracers—most notably, 68Ga-DOTATATE and 18F-fluciclovine—with many others in the pipeline.

My main project as the CTN intern was to develop a reader training course, in collaboration with investigators from multiple institutions, for physicians and technologists performing and interpreting 68Ga-DOTATATE PET/CT scans. This was a timely and valuable project, as the radiotracer was recently approved by the FDA after having been shown by researchers to be highly promising for the treatment and management of neuroendocrine tumors. Although using this radiotracer with PET is a powerful technology, there are several pitfalls in successfully performing and interpreting these exams. In addition to addressing these concerns, detailed guidelines for imaging personnel with all levels of experience is provided in this new reader training course found in the SNMMI Learning Center (https://www.snmmilearningcenter.org). This project also had a direct educational impact on me, as I was exposed to a large pool of interesting and challenging cases, had the opportunity to meet and learn from my new colleagues and participated in some groundbreaking work.

I would like to thank members of the Clinical Trials Network for their mentorship and guidance throughout my two-year internship. I would strongly recommend this program to anyone with an interest in radiopharmaceutical development, clinical translation of approved radiotracers and image standardization. This group has strong leadership and diverse experience thanks to the wide variety of its members—physicians, technologists, physicists, and radiologists. I wish the interns for the coming two-year period, Courtney Lawhn Heath and Colin Young, the best of luck in their endeavors and encourage them to take full advantage of this remarkable opportunity!
CTN is offering a number of continuing education sessions, including a full-day categorical, that offer attendees essential information on a variety of timely topics. Include these sessions in your schedule to ensure you have the latest information on new radiopharmaceuticals, novel therapy approaches and implementing methods to improve the standardization of images.

CAT8: Riding the Moonshot: Establishing the Role of Molecular Imaging in Immunotherapy  
Co-sponsored with the Committee on Young Professionals  
Saturday, June 10: 8:00 AM–4:00 PM

CE30: Integrating Newly Approved Radiopharmaceuticals into Your Clinic  
Co-sponsored with the PET Center of Excellence  
Monday, June 12: 10:00–11:30 AM

TS36: New Tracers in the Clinic: What Technologists Need to Know  
Co-sponsored with the SNMMI-TS  
Tuesday, June 13: 3:00–4:30 PM

CE84: Clinical Trials Regulations and Billing  
Sponsored by CTN  
Tuesday, June 13: 3:00–4:30 PM

Additionally, CTN is providing an opportunity for all imaging and industry personnel to present and discuss the latest information on Gallium-68 in an open, non-CE session.

Gallium Information Session  
Monday, June 12: 12:30–1:30 PM

Please join us for the latest information on new PET imaging agents and how they impact patient care. To view the entire educational program and develop your personalized schedule, visit snmmi.org/AM.

In 2009, I was hired on at an academic teaching institution as a staff nuclear medicine technologist. It didn’t take long before students started shadowing me and, surprisingly, I found myself enjoying the hands-on clinical instruction. However, transitioning to a formal role as a clinical instructor definitely presented me with some unique challenges. I quickly realized we had no formal process in place for student orientation, nor any standards to assist students while they-acclimated to the facility and their positions. This means that some students were receiving it as their best effort while others did the minimum to get by—and there was nothing I could do about it. This lack of formal guidelines led me to create a comprehensive student manual that outlined what was expected of all students, how and where they could obtain help when needed and what options existed for additional learning opportunities if they so wished.

Five years later, this student manual has become an important part of our student orientation. I can attest to the fact that it has helped both the students and instructors immensely. From day one, students are aware of what is expected of them and what they can expect from me and any staff member at our institution. Not only are they taught methods to help attain clinical competence, but they also observe our physicians, in real-time, as they interpret exams. As part of our program, students observe in various radiology areas and may participate in research projects throughout their academic program. Exposure to clinical research could open up additional opportunities for them down the road. Students recognize that our goal is to provide the most well-rounded clinical education program possible—but they have to be completely engaged to receive the benefits.

I personally encourage anyone who is interested in instructing students to take the challenge, keeping one key goal in mind: develop a program whose ultimate objective is to create an environment that promotes hands-on learning and encourages professional development beyond the classroom. But do not take this role lightly—you are shaping the future of bright, young minds.

How to Image Patients Receiving Lutetium 177—Dotatate Therapy

Bill Scheve, CNMT, ARRT (NJ); Richard Laforest, PhD; and Dmitry Beyder, MPA, CNMT

PET Imaging Team, Barnes-Jewish Hospital/Washington University, St. Louis

177Lutetium-labeled (177Lu)DOTATATE therapy is a novel method for treating patients with neuroendocrine tumors. The radiation dose delivered to the tumors results from the high-energy beta rays and contributes to shrinking the size of the tumor by targeting somatostatin receptors at the surface of cancer cells. Knowing how to image the tumor correctly is crucial for effective treatment planning.

177Lu is a medium energy beta emitter and has two gamma emissions: 208 keV @ 10% and 113 keV @ 6%. Unlike Yttrium-90, which is a pure beta emitter, these peaks allow for high-quality therapy SPECT imaging, using a medium-energy parallel-hole collimator. Several imaging options are available. For example, energy windows can be set to capture both gamma rays for maximum sensitivity.

In our institution, we opted to configure the 177Lu isotope with a 20% window on the 208 keV gamma ray, with adjacent scatter correction windows above and below to provide both optimal qualitative and quantitative images.

Consideration for contrast and noise was a major part of setting up post-reconstruction parameters. The images looked awesome!
CTN Offers Services for Academic Clinical Research

The Clinical Trials Network offers a variety of services to assist academic investigators with their clinical research.

- Trial design using PET imaging
- Protocol and study document development
- Reader training for new radiopharmaceuticals
- Expert analysis of PET images
- Scanner validation and QC troubleshooting
- IND/ANDA preparation for FDA review
- Access to information on investigational PET agents for use in clinical trials

Contact CTN for more information at ctnadmin@snmmi.org.

Save the Dates

SNMMI 2017 Annual Meeting
June 10–14, 2017 • Denver, CO

53rd DIA Annual Meeting
June 18–22, 2017 • Chicago, IL

World Molecular Imaging Congress 2017
September 13–16, 2017 • Philadelphia, PA

2017 NANETS Symposium
October 19–21, 2017 • Philadelphia, PA

30th Annual Congress of the European Association of Nuclear Medicine
October 21–25, 2017 • Vienna, Austria

2017 IEEE Nuclear Science Symposium and Medical Imaging Conference
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RSNA 103rd Scientific Assembly and Annual Meeting
November 26–December 1, 2017 • Chicago, IL

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