



# PET Center of Excellence *newsletter*

## President's Report

*Katherine Zukotynski, MD, FRCPC*  
*PET CoE President*



Katherine Zukotynski,  
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Dear Friends and Colleagues, I recently attended an SNMMI meeting in Reston, VA, where I was reminded of the National Cherry Blossom Festival that takes place in Washington every April. This wonderful festival traces its origins back to the 1912 donation of several thousand cherry trees by Japan to the United States in the name of friendship.

Friendship is difficult to define accurately. It typically involves characteristics such as mutual understanding, empathy, honesty, and compassion, among others. Friendship also requires give and take, can sometimes have very difficult moments with twists and turns, and may even be intermittent. So saying, a successful long-term friendship can be very wonderful.

Indeed, the cherry blossom friendship got off to a rocky start when the original batch of cherry trees sent by Japan was found to be infested with bugs and worms and was consequently burned down to protect local crops. However, there was clearly a sense of trust and mutual admiration. The friendship held true, and a second batch of trees was immediately sent. Japan also donated several thousand more trees in 1965, which were accepted by Lady Bird Johnson, then First Lady.

There are several examples of friendships between people, organizations and countries throughout the world. To this day, the city of Halifax, Nova Scotia, sends an annual Christmas tree to Boston, Massachusetts, in recognition of that city's tremendous help during the great explosion of 1917. The Statue of Liberty, a symbol of American values, was a gift from the people of France. Doctors Without Borders, founded in 1971, is an independent international medical organization that tries to provide care and compassion to people who need help around the world.

In our own way, the PET Center of Excellence is trying to foster friendships

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## Beyond Malignancy: The Role of FDG PET/CT for Imaging Noninfectious Causes of Fever of Unknown Origin

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### Background

Fever of unknown origin (FUO) is a clinical entity that was initially defined in 1961<sup>1</sup> as an illness lasting for more than three weeks with fever higher than 38.3°C (101°F), documented on several occasions but with no definite diagnosis after one week of in-patient investigation.

There are hundreds of causes of FUO reported in the literature, and they can be divided into four major categories: infections, malignancies, noninfectious inflammatory diseases and miscellaneous disorders (such as drug fever for example). It is reported that even after extensive diagnostic workup, no definite cause will be found in up to 50% of patients<sup>2</sup>. Thus, it remains a major diagnostic challenge for clinicians.

However, a growing body of evidence suggests that <sup>18</sup>F-fluorodeoxyglucose (FDG) PET/CT is a powerful and reliable functional imaging tool that should be used early in the investigation of FUO<sup>3-5</sup>. Because FDG is generally avidly taken up by inflammatory cells, bacterial pathogens and neoplastic cells, and because of the ability to perform high-resolution whole-body imaging, FDG PET/CT is becoming the imaging modality of choice in the evaluation of FUO<sup>6</sup>.

A recent meta-analysis comparing nuclear medicine FUO test performance supported this hypothesis by showing that FDG PET/CT had a sensitivity of 86% and a specificity of 52% for localizing the source of fever. Its diagnostic yield (60%) was the highest among nuclear imaging tests<sup>7</sup>. FDG PET/CT imaging also has a very high negative predictive value for ruling out specific causes of FUO<sup>8-9</sup> and can provide valuable additional information, such as indicating a potential site for biopsy to confirm diagnosis. It is also potentially useful for assessing response to therapy<sup>10</sup>.

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within SNMMI and abroad. We have task forces looking at PET in conjunction with theranostics, pediatrics, clinical workflow and education, technical innovations, radiotracers and treatment response. We also host a PET/MR working group. Please do not hesitate to contact us if you would like to help! Our newsletter is now available to all. The last few issues provided an approach to fluciclovine and somatostatin receptor PET imaging, as well as FDG PET/CT for infection imaging. This issue reviews the role of FDG PET/CT for imaging non-infectious causes of fever of unknown origin, and next issues will discuss IV contrast and PET/CT as well as immunotherapy response assessment.

We have also organized several educational programs we hope you will enjoy. The first of these will be at the SNMMI Annual

Meeting (Saturday June 23 to Tuesday June 26) in Philadelphia. For details on the Center-sponsored categorical and CE sessions at the meeting, please see the PET CoE News article in this issue. In addition, we are excited to announce that our Peter Valk Memorial Lecture will be given Monday, June 25, at 10 AM by Peter Conti, MD, PhD, FSNMMI, and will be followed by the PETCoE Business Meeting. We hope to see you there!

Although this world might seem lonely at times, friendship brings lightness and warmth that are not to be forgotten. It is truly one of the great joys in life. To all those who have been my friend through the years, I will be forever grateful. You continue to make the journey worthwhile!

(Beyond malignancy: The role of FDG PET/CT. Continued from page 1.)

It has been well documented that PET/CT is highly accurate for diagnosing the most frequent causes of FUO, namely infections<sup>6</sup> and malignancy<sup>11</sup>. However, it is also indicated for less common noninfectious inflammatory etiologies. This article will focus on a few of these pathologies.

### Large-Vessel Vasculitis

Systemic vasculitides are a group of inflammatory diseases characterized by infiltration of the blood vessel walls by FDG-avid leukocytes causing secondary damage that results in aneurysm formation (Figure 1), dissection, ischemia and stroke. They are classified according to the size of the vessels they commonly affect. For example, large-vessel vasculitis includes giant-cell arteritis and Takayasu arteritis. These diseases typically involve the aorta and its major branches, such as the cranial branches (temporal arteries) and extracranial branches (thoracic and abdominal aorta, aortic arch, subclavian and carotid arteries, and iliofemoral arteries).

These disorders commonly cause FUO and often present with vague and nonspecific symptoms, such as malaise and weight loss. Blood chemistry can show elevated C-reactive protein (CRP) and high erythrocyte sedimentation rate (ESR). Diagnosis usually relies on a positive biopsy, which is invasive and includes a significant risk of complication. Also, a significant number of biopsies can be falsely negative. Thus, there is interest for including imaging in the workup of large-vessel vasculitides.

However, the best imaging modality for assessing large-vessel vasculitis remains to be determined<sup>12</sup>. Anatomic imaging, such as computed tomography angiography and magnetic resonance angiography, depict vessel-wall edema and thickening, while functional imaging with FDG PET/CT images inflammation and should, therefore, better correlate with disease activity. Unfortunately, scientific evidence to support this hypothesis is still lacking.

Nevertheless, literature shows FDG PET/CT is useful and sensitive for diagnosing large-vessel vasculitis, mainly giant-cell arteritis and Takayasu arteritis<sup>13-14</sup>. Its role is limited in medium- and small-vessel vasculitis in part because of partial volume effect. One of the largest meta-analyses was published in 2016 and included 400 patients in a total of 8 studies<sup>13</sup>. The authors concluded that FDG PET had a pooled sensitivity of 75.9% and a specificity of 93.0% for giant-cell arteritis and Takayasu arteritis, suggesting it is more specific than sensitive for diagnosing large-vessel vasculitis. Other investigators found that PET may be more accurate in patients with giant-cell arteritis, with a reported sensitivity of 90% and an excellent specificity at 98% versus 87% and 73% respectively in patients with Takayasu arteritis<sup>14</sup>. These data confirmed the good overall diagnostic accuracy of FDG PET in the management of large-vessel vasculitis. Consequently, it has become widely accepted that functional imaging with FDG PET is essential in the evaluation of these inflammatory diseases.

Patients with untreated large-vessel vasculitis typically show moderate to intense linear and diffuse FDG uptake along the walls of the affected arteries. However, there are no definite and standardized criteria for diagnosis of vasculitis on PET images. Thus, the interpretation is based on semi-quantitative methods. One of the most commonly used methods compares vessel uptake with normal liver

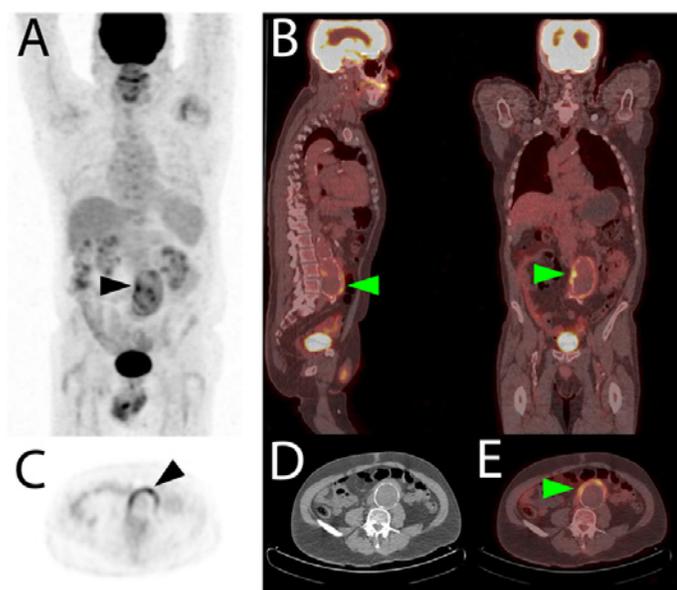


Figure 1: Inflammatory aneurysm of the abdominal aorta in a patient previously treated for large vessel vasculitis. A – Maximum Intensity Projection (MIP) of the FDG PET/CT study; B – Coronal and Sagittal Fused PET/CT images; C, D, and E – Axial PET, CT, and Fused PET/CT images.

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uptake based on a 4-point scale<sup>15</sup>. No uptake is classified as grade 0, while FDG accumulation less than liver uptake is considered grade 1. Patients showing FDG uptake equal to (grade 2) or higher than liver uptake (grade 3) are interpreted as positive for vasculitis with high specificity<sup>16</sup>.

A similar method using an aorta-to-liver SUVmax cutoff ratio greater than 1.0 showed a high sensitivity and specificity of 89% and 95%, respectively, for large-vessel inflammation<sup>17</sup>. The main differential diagnosis for vascular uptake is atherosclerosis, which usually presents as mild, patchy and heterogenous FDG accumulation in the blood-vessel walls.

It has been reported that sensitivity of FDG PET/CT is hampered by active immunosuppressive treatment such as glucocorticoid therapy<sup>18</sup>. In this setting, a PET study could be falsely negative and therefore a PET/CT study should ideally be done before initiating active treatment. On the other hand, this may mean that functional imaging may be helpful for assessing response to therapy. Unfortunately, literature on this topic is scarce, and there is presently no clear scientific evidence to support this hypothesis<sup>19</sup>.

### Sarcoidosis

Sarcoidosis is a granulomatous inflammatory disease of unknown etiology that typically involves thoracic lymph nodes and lungs, although every organ can be affected. Symptoms vary and depend on the organs involved, but it is a common cause of fever of unknown origin. Patients with sarcoidosis also frequently present with dyspnea, cough and nonspecific systemic symptoms.

However, since sarcoidosis is often asymptomatic, it is commonly discovered incidentally on chest radiographs or CT. On anatomic imaging, it usually presents with mediastinal and bilateral hilar lymphadenopathies (up to 85% of patients) with or without signs of parenchymal lung disease such as peribronchovascular pulmonary nodules, alveolar cavitation and fibrosis. Some patients also show abdominal lymphadenopathies (30%) and splenomegaly<sup>20</sup>.

Although high-resolution CT is a good imaging modality for staging patients, it is unable to identify areas of active inflammation. On the other hand, functional imaging with PET is particularly useful for assessing active inflammation, especially in normal-sized lymph nodes, and for detecting occult extrathoracic disease sites such as bone, spleen or cardiac involvement. For example, a study published by Teirstein et al. revealed that FDG PET indicated active disease that was undetected by other imaging methods in 15% of patients<sup>21</sup>. Other investigators found that bone or bone marrow involvement was seen on PET in 34% of patients with sarcoidosis, but 94% of these lesions could not be detected on low-dose CT<sup>22</sup>. Overall, PET/CT compares advantageously with CT when it comes to mapping the extent of disease<sup>23</sup>.

It has been well documented that FDG PET/CT is more sensitive and accurate than gallium-67 scintigraphy for detecting active sarcoid lesions, with reported sensitivity higher than 95%<sup>24</sup>. PET also detects more extrapulmonary lesions. In general, the radiation

dose associated with FDG PET is significantly lower than with gallium-67, image resolution is better, and the procedure is also shorter. Consequently, FDG PET has largely replaced gallium-67 scintigraphy for patients with suspected sarcoidosis<sup>6</sup>.

Patients with active sarcoidosis investigated with metabolic imaging typically present with highly FDG-avid mediastinal and bilateral hilar lymphadenopathies (Figure 2). This characteristic pattern of uptake is a hallmark of the disease but is not pathognomonic. Since patients with sarcoidosis often have splenomegaly and sometimes even FDG-intense focal spleen or bone lesions, lymphoma and metastatic disease must be ruled out. Thus, definite diagnosis requires a biopsy showing noncaseating granulomas consisting of inflammatory cells. In this instance, FDG PET also has a role for identifying a suitable site to biopsy, as it can detect unsuspected sites of metabolically active disease<sup>25</sup>.

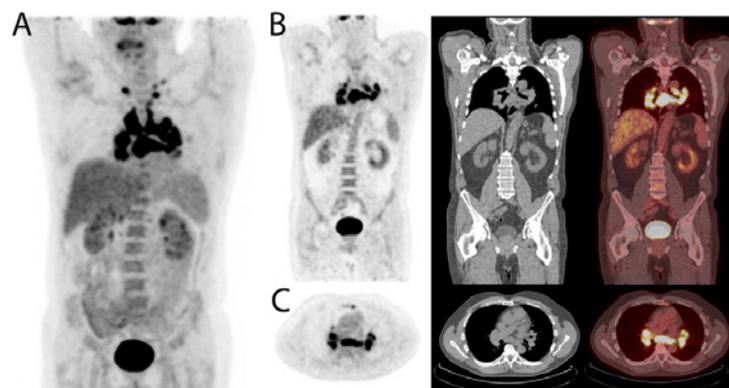


Figure 2: Sarcoidosis  
A – Maximum Intensity Projection (MIP) of FDG PET/CT study; B – Coronal PET, CT, Fused PET/CT images; C – Axial PET, CT, Fused PET/CT images.

Increasing evidence indicates FDG PET/CT has a significant impact on clinical management. A prospective study by Sobic-Saranovic et al.<sup>26</sup> demonstrated that positive PET findings modified treatment in 82% of patients, either by increasing doses of corticosteroids or by introducing a new drug. These results were consistent with another preliminary study that showed that PET influenced patient management in 63% of cases<sup>23</sup>. A few reports also highlighted the potential usefulness of FDG PET/CT for evaluating therapy response and for long-term follow-up of patients with sarcoidosis<sup>27</sup>, although more scientific evidence is needed to confirm its value in this clinical setting.

Finally, FDG PET/CT is becoming the imaging modality of choice for detecting cardiac sarcoidosis<sup>28</sup>. The Heart Rhythm Society even published new diagnostic criteria that include PET imaging in the assessment of cardiac sarcoidosis<sup>29</sup>. On metabolic imaging, cardiac involvement typically presents as multifocal and patchy areas of increased FDG uptake. This heterogeneity is the reason why cardiac biopsy has a low sensitivity, estimated to be between 20 and 30%. A meta-analysis published in 2012 confirmed that FDG PET/CT had a high accuracy for diagnosing cardiac sarcoidosis, with a reported pooled sensitivity of 89% and a specific-

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# PET in the News



The international literature on PET, PET/CT and PET/MR continues to grow at a pace that challenges both researchers and clinicians. The media has recognized the value of these modalities and regularly features advances in research and technology in the news. In each issue, the *PET CoE Newsletter* presents a tomographic slice of the breadth of PET media coverage that appears in publications around the world.

## **PET/MRI, PET/CT can add to initial breast cancer staging** **Aunt Minnie Europe**

**<sup>18</sup>F-PSMA-1007 PET/CT at 60 and 120 minutes in patients with prostate cancer: biodistribution, tumour detection and activity kinetics.**

**UroToday**

## **Key PET factors help assess Hodgkin's lymphoma outcome** **Aunt Minnie Europe**

**Subclinical Amyloid: Next Target for Alzheimer's Trials?**  
**MedPage Today**

**PET myocardial perfusion imaging more effective than SPECT scans in detecting coronary disease**  
**Science Daily**

## **Tau PET Imaging May Identify Alzheimer Risk** **Medscape**

## **New imaging approach offers unprecedented views of staph infection**

**MedicalXpress**

## **New Approaches to Understanding TB Can Help Inform Development of Better Vaccine**

**Contagion Live**

## **Imaging agent helps predict success of lung cancer therapy**

**MedicalXpress**

## **PET Beats CT in Study of Mesothelioma Staging Tools** **Surviving Mesothelioma**

## **Combining modalities: the advantages of PET-CT-UI** **Medical Physics Web**

**(Beyond malignancy: The role of FDG PET/CT. Continued from page 3.)**

ity of 78%<sup>30</sup>. PET also has significant advantages over magnetic resonance due to its ability to detect extra-cardiac sites of disease and the possibility of performing a PET study in patients with impaired kidney function or with metallic implants<sup>31</sup>. The main pitfall is the physiologic cardiac uptake that has to be suppressed for optimal image interpretation. Thus, patient preparation is critical and requires a low-carbohydrate, high-fat and high-protein diet for at least 24 hours prior to the test.

### **Conclusion**

Fever of unknown origin is a complex clinical situation that can be the presenting symptom of a wide range of diseases. In addition to its high accuracy for assessing malignancy and infection, it is now largely accepted that FDG PET/CT is an excellent, accurate and valuable diagnostic imaging method for characterizing noninfectious inflammatory causes of FUO, such as large-vessel vasculitis and sarcoidosis. Because of its high spatial resolution and its ability to perform whole-body scanning in a short amount of time, FDG PET/CT has several advantages over other nuclear imaging studies and anatomic imaging. Consequently, PET will probably become the imaging gold standard for various pathologies in the near future.

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## SNMMI's Clinical Trials Network: Launching New PET Phantom Program for Compliance with New Joint Commission Requirements

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In 2015, The Joint Commission published new "Diagnostic Imaging Requirements" that mandated phantom-based PET/CT scanner performance evaluations by diagnostic medical physicists. Image uniformity, high contrast resolution/system spatial resolution, low contrast resolution or detectability, and artifact evaluation are the newly required components. No guidance is given as to which phantoms or what criteria are to be used in these assessments.

Since most PET/CT scanners in the U.S. are hospital-based, and 82 percent of hospitals are currently Joint Commission-accredited, these new required evaluations impact the majority of PET/CT scanners in the U.S. In order to aid the PET/CT imaging community come into compliance with these new requirements while also providing meaningful and actionable scanner performance information, SNMMI's Clinical Trials Network (CTN) has developed and is currently launching a phantom-based PET/CT scanner evaluation program designed specifically to address this new compliance need.

The proposed phantom program requires sites to perform two phantom scans. The first scan images a standard uniform 20-cm-diameter cylinder phantom filled with aqueous [<sup>18</sup>F] FDG. Data from this scan are used to meet mandated image

uniformity and spatial resolution measurements. The second phantom scan uses a new version of the SNMMI CTN anthropomorphic oncology phantom with 12 spheres ranging in size from 7 to 37 mm, imaged at a 4:1 sphere-to-background ratio.

The phantom data are acquired using the site's standard oncology protocol, including time-per-bed position and reconstruction parameters (advanced reconstructions allowed). Image data yields a contrast recovery coefficient curve, clinically relevant noise assessment, and assessment of low-contrast lesion detectability. The site simply needs to upload the DICOM datasets to the CTN server, and a cloud-based software program will automatically identify the phantom type, analyze the images, and generate a comprehensive Joint Commission-compliant scanner performance report. A qualified medical physicist reviews the images and the report results and generates a final evaluation, including recommendations for correcting any problems identified.

Most hospital sites operating PET/CT equipment do not have in-house expertise to meaningfully collect and analyze this newly mandated data, nor do they necessarily have easy access to contract physicists with requisite expertise to develop

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# Encouraging Medical Student Interest in Nuclear Medicine

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As the snow melts and the days get longer, we start looking forward to a new season, and for hundreds of medical students across North America, that means licensing exams and graduation. A whole new crop of future doctors is getting ready to take their places in residency programs across the country and internationally. These students are the future faces of their respective fields, among them the next generation of family physicians and general surgeons, ophthalmologists and psychiatrists and, hopefully, the next nuclear medicine specialists.

Yet over the past decade, the number of ACGME nuclear medicine programs has declined from 56 in 2009-2010, to a current 41, based on the ACGME website (1,2). In Canada, there are only five programs, two of which had unfilled spots after the first match this year. The field of nuclear medicine is full of exciting new advances, but how do we ensure that we will have the physicians to put them into practice?

When medical students are considering choice of specialty, we're looking at everything from scholarly areas of interest, to preferred patient population, to lifestyle and location. The job market is certainly a factor. Difficulty with employment for nuclear medicine graduates is a known problem that would discourage medical students from considering the specialty. Proposed solutions include residencies with dual certification pathways between nuclear medicine and diagnostic radiology, which would produce highly qualified applicants with good job prospects (1). To avoid having lots of carriages and no horses though, there need to be medical students who want to apply to these programs in the first place, and that means students interested in nuclear medicine.

Many of my classmates are unaware that nuclear medicine exists, or unaware of what it entails, aside from maybe the names of a few studies that are ordered by their specialty of interest. Often, students don't know about the

specialty until late in clerkship, by which time it may be too late to make a competitive application to a nuclear medicine/radiology program. By including nuclear medicine more prominently in the mainstream pre-clerkship curriculum, the specialty can be introduced to students while they still have time to engage in the shadowing and research projects that help us make career decisions. Including it more prominently in oncology teaching would be a logical fit, where students can see the exciting ways nuclear medicine contributes to diagnosis and management. PET/CT is a visually appealing modality with a huge breadth and depth of clinical applications, and it could be a great way to introduce students to the field.

As medical students, we also do much of our learning from each other outside the classroom. Word of mouth and social media are omnipresent. Supporting students in telling one another about nuclear medicine will be a key component in encouraging future applicants. Many schools already have radiology interest groups; given the relationship between nuclear medicine and radiology and the future of combined residency programs, this is a logical platform to reach the medical student body. And, by reaching medical students, we increase nuclear medicine residency matches and develop the next new cohort of nuclear medicine physicians.

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a meaningful program. The SNMMI CTN has developed this program to fill the void and is poised to work directly with hospital sites or contract physics groups to aid with compliance, and to enhance existing quality control programs. These annual phantom assessments are not covered in the scanner manufacturer's preventative maintenance requirements.

The program is not designed to address MIPPA accreditations. Further, the new Joint Commission Diagnostic Imaging Requirements also mandate documentation of a number of other elements of practice including radiation safety, radiation exposure records, quality control and maintenance recording, and patient handling procedures that are outside the scope of the scanner performance evaluation targeted by this program. For full details of the Joint Commission Diagnostic Imaging Requirements issued August 10, 2015, see: [https://www.jointcommission.org/assets/1/18/AHC\\_DiagImagingRpt\\_MK\\_20150806.pdf](https://www.jointcommission.org/assets/1/18/AHC_DiagImagingRpt_MK_20150806.pdf)

For more information on this program, or to schedule your PET scanner evaluation, email [ctnadmin@snmmi.org](mailto:ctnadmin@snmmi.org).

# Interpretative Criteria for Prostate-Specific Membrane Antigen (PSMA)-Targeted PET Imaging: Structured Reporting as a New Paradigm for Nuclear Medicine

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While few may have predicted that the publication of the first-in-human experiences with  $^{18}\text{F}$ - and  $^{68}\text{Ga}$ -labeled [1,2] radiotracers for positron emission tomography (PET) imaging of prostate-specific membrane antigen (PSMA) would precipitate radical changes in imaging and clinical management paradigms for patients with prostate cancer (PCa), this has nonetheless come to pass. In a little more than five years, hundreds of publications on PSMA-targeted PET imaging have been written, with no indication that this new sub-field within nuclear medicine will stop growing anytime soon. The superiority of PSMA-targeted PET over conventional imaging and over other PCa-targeted agents is increasingly apparent with the ever-growing body of literature.

A number of trends have become apparent as PSMA-targeted PET has emerged as the incipient standard-of-care for PCa imaging around the world. First, with such a sensitive way to image PCa, focal therapies for recurrent and oligometastatic disease have gained traction [3]. Second, as with any new imaging modality, a number of potential false-positive and false-negative findings that can confuse scan interpretation have been discovered [4]. Third, the potential inclusion of PSMA-targeted agents in future therapy-based clinical trials has suggested that uniform ways of reporting findings will be of value in collecting and analyzing the large volumes of imaging data that will necessarily arise from such trials.

Recently, two interpretive frameworks for PSMA-targeted PET were proposed and published in the same issue of *The Journal of Nuclear Medicine*:

- 1) PSMA Reporting and Data System (PSMA-RADS) Version 1.0 [5], and
- 2) Prostate Cancer Molecular Imaging Standardization Evaluation (PROMISE) [6].

PSMA-RADS is structured around a five-point scale with higher numbers indicating increasing likelihood of the presence of PCa. Thus, a PSMA-RADS-1 lesion is definitively benign, whereas a PSMA-RADS-5 lesion is absolutely indicative of PCa. PSMA-RADS-3 lesions are subdivided into those with low level uptake that are indeterminate for PCa involvement and those with or without uptake that are suspicious for other malignancies and necessitate further work-up. Both an overall PSMA-RADS scan score and scores for individual lesions are recommended to be provided.

PROMISE, on the other hand, defines a molecular imaging tumor-node-metastasis (miTNM) system in which lesions are scored based on their uptake relative to various reference tissues (blood pool, liver or spleen, and parotid gland), and then T, N, and M designations are provided based on patterns of uptake from detailed and standardized anatomic templates. PROMISE also includes primary intraprostatic PCa information that is not a part of the PSMA-RADS framework. A complete and detailed description of the systems is beyond the scope of the current discussion; however, interested readers are directed to references [5] and [6], as well as an accompanying commentary [7].

Having multiple different frameworks available for classifying the findings on PSMA-targeted PET imaging studies may be valuable as each framework may find utility in different clinical contexts. For example, PSMA-RADS is very suited for defining reader confidence in the presence of PCa within individual lesions in patients with relatively limited disease that might be eligible for focal therapy with curative intent. It is also the simpler and more easily clinically adopted of the proposed interpretive criteria, although this comes with an attendant decrease in the anatomic detail that is included.

In contradistinction, PROMISE is a very thoroughly inclusive system that may be most advantageous for large clinical trials where numerous imaging parameters are to be included from each patient. Clinical adoption of PROMISE will necessarily involve a steeper learning curve given its more detailed structure. Overtures in the community have already been made regarding a summit of the investigators from PSMA-RADS, PROMISE, and an earlier proposed system [8] along with other leaders in the PSMA field in order to reach a consensus set of interpretive guidelines, although this may be unnecessary if the different proposed frameworks are found to each have utility for different purposes.

While many of the details of how to make use of these newly suggested reporting guidelines for PSMA-targeted PET imaging have yet to be worked out, the overall trend in medical imaging towards structured reporting (e.g. BI-RADS, PI-RADS, LI-RADS, LUNG-RADS, TI-RADS, etc.) indicates that similar frameworks are likely to become important across nuclear medicine. Although the interpretive pitfalls differ from one class of radiotracers to the next, it may be possible to adapt the key aspects of the frameworks for PSMA-

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targeted PET to other agents, thus facilitating clinical adoption of an overall reporting system (or systems) with variations to account for different radiotracer characteristics. An example of this would be the very recently proposed somatostatin receptor (SSTR)-RADS version 1.0 [9], which builds off of the PSMA-RADS framework but includes SSTR PET-specific details.

It is relatively assured that none of the current proposed systems for PSMA-targeted PET represents a finalized version, as such systems must necessarily evolve to accommodate new data and undergo revision as aspects are validated or invalidated. However, beyond PSMA-targeted PET, these frameworks indicate an important paradigm that nuclear medicine should embrace: structured reporting that assures adequate communication between image interpreters and treating clinicians, promotes the selection of appropriate therapies, and facilitates the collection of data from large clinical trials.

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## PET CoE News

### Looking Forward to the 2018 SNMMI Annual Meeting

The PET Center of Excellence is sponsoring great sessions at the 2018 Annual Meeting in Philadelphia (June 23-26), including one categorical session on June 23 and 4 CE sessions:

**CAT7: PET/CT and PET/MR for Adults and Children: Fundamental and Evolving Practices** (June 23, 8 AM – 4 PM): Sponsored with the Pediatric Imaging Council and Computer and Instrumentation Council, this categorical seminar will provide practitioners—physicians, physicists/ scientists, technologists and residents/students—with a practical nuts and bolts review of clinical PET/CT and PET/MR. It will cover new technological developments in PET/CT and PET/MR instrumentation and the emerging role of machine learning, choosing and optimizing PET/CT and PET/MR protocols, and practical approaches to radiation dose reduction. Advanced concepts will also be addressed, including an approach to PET/CT and PET/MR with new FDG-approved radiotracers, as well as updates on PET for brain, myocardial, prostate and neuroendocrine conditions. (Additional registration fees may apply.)

**CE01: PET/CT Before, During and After Tumor Ablation** (June 23, 1:30 – 3 PM): This session will provide a state-of-the-art review of diagnostic PET/CT interpretation as related to tumor ablation procedures, highlighting unique PET/CT advantages with the potential to improve interventional oncologic procedure outcomes.

**CE29: PET/CT: Therapy Response Assessment** (June 24, 4:45 – 6:15 PM): Practical clinical aspects of therapy response assessment using PET/CT in human solid tumor will be covered, including quantitative criteria, structured qualitative criteria, and immunotherapy assessment.

**CE36: Peter E. Valk, MD, Memorial Award and Lecture; PET CoE Business Meeting** (June 25, 10 – 11:30 AM): At this session, Peter S. Conti, MD, PhD, FSNMMI, will be honored with the 2018 Peter E. Valk, MD, Memorial Award and give a lecture titled "PET – The Final Frontier or a Stepping Stone?". The PET Center of Excellence will hold its annual business meeting after the lecture.

**CE55: Targeted PET in Oncology** (June 25, 3 – 4:30 PM): The role of targeted PET in selecting patients for systemic therapies will be addressed, with a focus on targeted therapies in breast cancer, imaging of PARP inhibitor targets, and immune checkpoints.

Register today at [www.snmmi.org/AM2018](http://www.snmmi.org/AM2018) Build your schedule online or download the [meeting app](#) for easy access!

## Novel PET Imaging Agent Could Help Guide Therapy for Brain Diseases

Researchers have developed a new imaging agent that could help guide and assess treatments for people with various neurological diseases, including Alzheimer's, Parkinson's, and multiple sclerosis. The agent, which is used in positron emission tomography (PET) scans, targets receptors in nerve cells in the brain that are involved in learning and memory. The study is featured in the April issue of *The Journal of Nuclear Medicine*.

Swiss and German scientists developed the new PET radioligand, <sup>11</sup>C-Me-NB1, for imaging GluN1/GluN2B-containing N-methyl-D-aspartate (NMDA) receptors (a class of glutamate receptor) in nerve cells. When NMDA receptors are activated, there is an increase of calcium (Ca<sup>2+</sup>) in the cells, but Ca<sup>2+</sup> levels that are too high can cause cell death. Medications that block NMDA receptors are therefore used for the treatment of a wide range of neurological conditions from depression, neuropathic pain and schizophrenia to ischemic stroke and diseases causing dementia.

"The significance of the work lies in the fact that we have for the first time developed a useful PET radioligand that can be applied to image the GluN2B receptor subunit of the NMDA receptor complex in humans," explains Simon M. Ametamey, PhD, of the Institute of Pharmaceutical Sciences, ETH Zurich, in Switzerland. "The availability of such a PET radioligand would not only help to better understand the role of NMDA receptors in the pathophysiology of the many brain diseases in which the NMDA receptor is implicated, but it would also help to select appropriate doses of clinically relevant GluN2B receptor candidate drugs. Administering the right dose of the drugs to patients will help minimize side-effects and lead to improvement in the efficacy of the drugs."

For the study, <sup>11</sup>C-Me-NB1 was used in live rats to investigate the dose and effectiveness of eliprodil, a drug that blocks the NMDA GluN2B receptor. PET scans with the new radioligand successfully showed that the receptors are fully occupied at neuroprotective doses of eliprodil. The new radioligand also provided imaging of receptor crosstalk between Sigma-1 receptors, which modulate calcium signaling, and GluN2B-containing NMDA receptors.

Ametamey points out, "These results mean that a new radiopharmaceutical tool is now available for studying brain disorders such as Alzheimer's disease, Parkinson's disease and multiple sclerosis, among others. It joins the list of existing PET radiopharmaceuticals used in imaging studies to investigate and understand underlying causes of these brain disorders." He adds, "Furthermore, future imaging studies using this new radioligand would throw more light on the involvement of NMDA receptors, specifically the GluN2B

receptors, in normal physiological processes such as learning and memory, as well as accelerate the development of GluN2B candidate drugs currently under development."

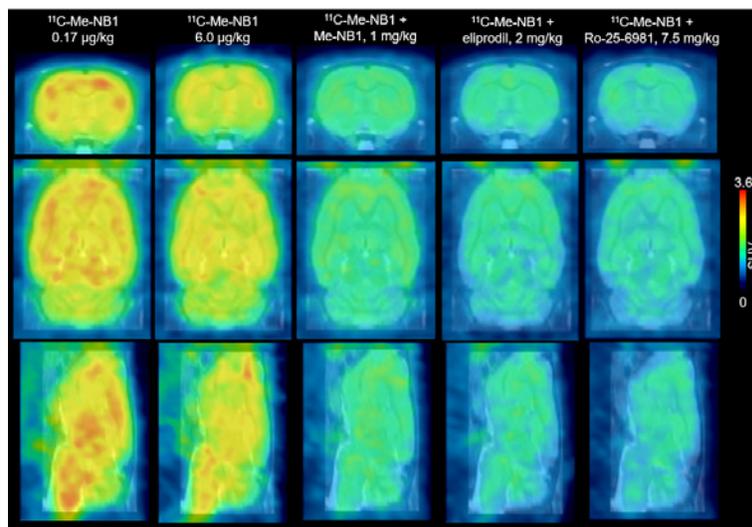


FIGURE: Rat brain <sup>11</sup>C-Me-NB1 PET images (0-60 min) superimposed on an MRI template. Credit: SD Krämer et al., ETH Zurich, Zurich, Switzerland

*Authors of "Evaluation of <sup>11</sup>C-Me-NB1 as a potential PET radioligand for measuring GluN2B-containing NMDA receptors, drug occupancy and receptor crosstalk" include Stefanie D. Krämer, Thomas Betzel, Ahmed Haider, Adrienne Herde Müller, Anna K. Boninsegni, Claudia Keller, Roger Schibli and Simon M. Ametamey, Institute of Pharmaceutical Sciences, ETH Zurich, Zurich, Switzerland; Linjing Mu, University Hospital Zurich, Zurich, Switzerland; and Marina Szermerski and Bernhard Wünsch, University of Munster, Munster, Germany.*

## Calendar of Events

### CARS 2018 Computer Assisted Radiology and Surgery: 32nd International Congress and Exhibition

June 20 – 23, 2018 • Berlin, Germany  
[www.cars-int.org](http://www.cars-int.org)

### SNMMI 2018 Annual Meeting

June 23 – 26, 2018 • Philadelphia, Pennsylvania  
[www.snmmi.org/AM2018](http://www.snmmi.org/AM2018)

### Total Body PET - From Mice to Men

June 30 – July 2, 2018 • Gent, Oostvlaanderen, Belgium  
[medisip.elis.ugent.be](http://medisip.elis.ugent.be)

### 2nd World Congress on Radiology and Oncology

July 16 – 17, 2018 • Dubai, United Arab Emirates  
<https://radiology-oncology.annualcongress.com>

### 11th Global Infections Congress

July 26 – 27, 2018 • Melbourne, Australia  
<https://infectiousdiseases.conferenceseries.com/>

### 4th World Congress on Medical Imaging and Clinical Research

September 3 – 4, 2018 • London, UK  
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