



# PET Center of Excellence newsletter

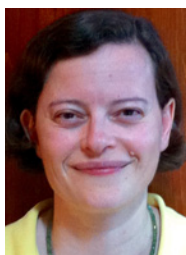
## President's Report

Katherine Zukotynski, MD, FRCPC  
PET CoE President

Dear Friends and Colleagues,

Have you ever wished upon a star?

SNMMI held its Mid-Winter Meeting in January 2018 in Orlando, Florida, on the doorstep of Disney World.



Katherine Zukotynski,  
MD, FRCPC

According to many, Walter Elias Disney was a dreamer. Born in December 1901 in Chicago, he started his career as an illustrator. His path to stardom was by no means smooth, and he spent several years trying to create an establishment that would be profitable. The famous Mickey Mouse was born in 1928, but even then it took a few more years before fortune smiled. Supposedly based, at least in part, on the Tivoli Gardens in Denmark, Walt Disney's first theme park, Disneyland, opened in Anaheim on July 17, 1955. By the end of its first year, it had attracted 3.6 million visitors. The exhibit "It's a Small World" was developed for the 1964 New York World's Fair as a tribute to UNICEF and was funded by PepsiCo. The plans for Disney World were made public in 1965.

It seems somehow appropriate that the FDA announced approval of Lutathera ( $^{177}\text{Lu}$ -DOTATATE) while the SNMMI Mid-Winter Meeting was underway, and many of us were on the doorstep of Disney World. Certainly, the concept of theranostics is not new. Indeed, radioiodine imaging and therapy recently celebrated its 75<sup>th</sup> birthday. However, the dream of imaging neuroendocrine malignancy with PET and using targeted radionuclide therapy to treat it is now a reality. Interestingly, the concept of machine learning is also not new. Although the stuff of science fiction, it is now closer to real applications today than it was when first conceived many years ago.

When we look back over history, many of the great characters of our time had a dream that they diligently pursued until it became reality.

(Continued on page 2. See **President's Report**.)

## FDG PET/CT for Infection Imaging

Gad S. Abikhzer, MDCM, FRCPC, ABNM, Jewish General Hospital and McGill University, Montreal, Canada, and Zohar Keidar, MD, PhD, and Ora Israel, MD, Rambam Health Care Campus and Rappaport School of Medicine, Technion, Haifa, Israel

$^{18}\text{F}$ -Fluorodeoxyglucose (FDG) PET/CT is routinely used in oncological imaging. The use of FDG imaging has also expanded beyond oncology to include cardiac viability studies, assessment of neurological diseases including dementia and epilepsy, and evaluation of infection and inflammation. This article briefly summarizes the utility of FDG PET/CT for infection imaging.

### Background

The basis for FDG uptake in infectious processes is related to the high expression of glucose transporters (GLUT1 and GLUT3) and increased hexokinase activity in activated granulocytes involved in the infectious/inflammatory response<sup>1</sup>. Advantages of FDG PET/CT for infection imaging include excellent image resolution and lower radiation exposure compared to other radiotracers, lack of blood manipulation, and a shorter procedure for both the patient and technical staff, with results available in less than two hours after injection. FDG-PET/CT is especially useful in patients with renal failure or those who are allergic to contrast media.

FDG imaging has, however, a few limitations: The radiotracer is nonspecific for infection with the differential diagnosis of increased uptake, including inflammatory and malignant processes. Its use is limited in the early post-operative period, when it may concentrate in post-surgical inflammatory changes. Recent studies demonstrate that diabetes and hyperglycemia<sup>2</sup>, as well as antibiotic use<sup>3</sup>, do not have a clinically significant impact on the diagnostic accuracy of FDG PET/CT in the assessment of infection.

In Europe, FDG PET/CT is often used for infection imaging, but its use for this purpose in North America has been limited due to reimbursement issues and prioritization of PET/CT devices for oncology imaging.

(Continued on page 2. See **FDG PET/CT for Infection Imaging**.)

### In this Issue

PET in the News	4
Pediatrics Corner	6
Tech Corner	7
Machine Learning and PET: A Good Match?	8
Philadelphia: Site of SNMMI's Annual Meeting and a Great City to Explore	9
PET CoE News	9
SNMMI Speaks Out on PET	10
Calendar of Events	11

However, even they had to remember what was real and what was fiction. Indeed, there are many stories of those who tried to make us believe what was not real and never would be. If science teaches us anything, it is to treat data with respect, prejudice aside.

Recent publications throw a spotlight on the need for a rigorous scientific method and peer review process to ensure adherence to reality. In 2017, *The Journal of Clinical Oncology* published an article “A risk of hematologic malignancies after radioiodine treatment of well-differentiated thyroid cancer.” This caused quite a stir in our community, as the methodology was questioned and the conclusions were far reaching. Publications in *The Journal of Nuclear Medicine* have also caused a stir, although of a slightly different nature. For example, in 2017 the paper “Subjecting radiologic imaging to the linear no-threshold hypothesis: a non sequitur of non-trivial proportion” highlights issues regarding the effect of radiation exposure—what is real, what is imagined and what the data show. Questions remain: Is our system of data review and dissemination flawed? When a mistake in scientific methodology is made, how should this be corrected? Where does science end, belief begin and what impact does this have on our patients?

In the last two issues of the *PET CoE Newsletter*, we first presented a practical-use guide to Axumin (co-authored by Ila Sethi, MD, and David M. Schuster, MD), followed by a guide to somatostatin receptor PET radiotracers (co-authored by Janet Pollard, MD, and Yusuf Menda, MD). Both papers provided a nuts and bolts approach that included imaging indications, protocol and tips for image interpretation on newly approved and available radiopharmaceuticals for PET. Both issues of the newsletter are available for review any time at [www.snmmi.org](http://www.snmmi.org).

This issue touches on aspects of FDG PET/CT for imaging infection. We anticipate our next issue will include a review of PET/CT in non-infectious causes of fever of unknown origin, as well as articles on issues related to clinical trials using PET/CT such as phantoms, dosimetry and an approach to PSMA image interpretation.

It seems we just welcomed 2018; now it's already March, and we're looking ahead to the SNMMI Annual Meeting, June 23-26 in Philadelphia, Pennsylvania! On Saturday, June 23, the PET CoE is co-hosting a categorical session with the Pediatric Imaging Council and the Computer and Instrumentation Council on PET/CT and PET/MR for Adults and Children: Fundamental and Evolving Practices. During this session, we will cover an array of topics from machine learning, instrumentation and technological issues to advances in pediatric and adult PET/CT and PET/MR image acquisition and interpretation. We will also host CE sessions on PET/CT in therapy response assessment; PET/CT before, during and after tumor ablation; PET/CT in precision medicine in the setting of breast cancer; PARPi; and immunotherapy.

Finally, in other news, we wish to congratulate the winner of the PET CoE Valk Award for 2018: Peter S. Conti, MD, PhD, FSNMMI, for his contributions to PET over the years.

Our world moves forward, spurred by those who live in the now wishing for a better tomorrow. Our foundation is built on a wealth of research and experience of what works and what doesn't or, in other words, challenges met and overcome. And so, although it has been said many times and many ways, no matter your age, may you continue to dream and I hope your dreams come true!

## (FDG PET/CT for Infection Imaging. Continued from page 1.)

### Protocol

Uptake time and acquisition parameters of FDG PET/CT are similar to standard protocols used in oncological imaging. The extremities should be included in the imaging field-of-view in specific clinical settings. In cases such as the assessment of diabetic foot infection, acquisition of a limited field-of-view may be used. If cardiac or pericardiac infections are suspected, a high-fat/low-carbohydrate diet for the day before the PET study and a minimum 12-hour fast are recommended.

### Fever of Unknown Origin (FUO)

Fever of unknown origin is a challenging clinical scenario. It is defined as fever greater than 100.9°F (38.3°C) on several occasions, lasting for more than three weeks with failure to reach a diagnosis.

FDG PET/CT has become the gold standard in imaging of FUO due to its ability to diagnose infection, inflammation (Figure 1) and malignancy—all three potential causes of FUO—in a single whole-body study.

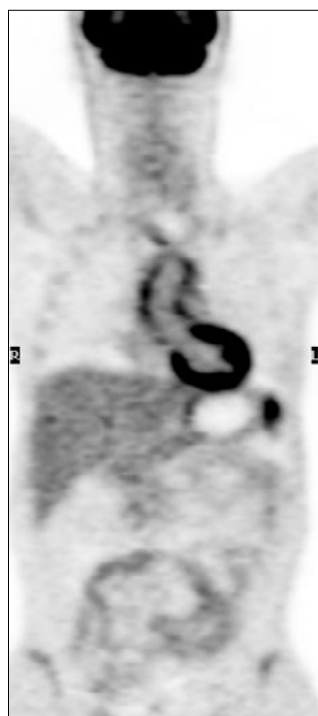


Figure 1 – FUO. Diffuse moderate hypermetabolism in the ascending aorta, consistent with vasculitis in a patient presenting with FUO

(Continued on page 3. See **FDG PET/CT for Infection Imaging**.)

If performed early in the diagnostic workup, FDG imaging can reduce costs and hospitalization time, and lead to more rapid diagnosis without performing unnecessary and, at times, invasive tests<sup>4</sup>.

Many studies have demonstrated the value of FDG PET/CT in the investigation of FUO, with a meta-analysis showing a pooled sensitivity of 86%, specificity of 52% and diagnostic yield of 58%<sup>5</sup>. Abnormal findings, present in two thirds of cases, are strongly associated with a high rate of definitive diagnosis, increasing from 36% in negative cases to 83% when FDG PET/CT is positive<sup>6</sup>.

### Spondylodiscitis

FDG PET/CT is the nuclear medicine gold standard for diagnosis of spondylodiscitis, with results superior or comparable to MRI<sup>7,8</sup>, while providing the benefits of routine whole-body imaging. By combining the strengths of both modalities, PET/MR has been reported to have a sensitivity of 100% and specificity of 88%<sup>9</sup>, and it can overcome the relative weakness of FDG PET/CT in detecting epidural abscesses. In a meta-analysis of 12 studies, FDG PET/CT was found to have a sensitivity, specificity, positive predictive and negative predictive values of 97%, 88%, 96% and 85% respectively<sup>10</sup>. FDG PET/CT has also been useful in assessing response to therapy<sup>11</sup>.

### Vascular Graft Infections

Vascular graft infection, an uncommon but severe complication, is associated with nonspecific and variable clinical presentations. CT angiography is the initial test of choice; its sensitivity, however, may be limited. In a prospective study of 39 patients, the sensitivity and specificity of FDG PET/CT in

diagnosing vascular graft infection were 93% and 91% respectively<sup>12</sup>, findings that have been further reproduced by several studies<sup>13</sup>.

It is important to note that non-infected vascular grafts can demonstrate physiological linear, diffuse, mild to moderate homogeneous FDG uptake, which varies according to the graft material but not timing since surgery<sup>14</sup>. Pathological FDG uptake is characterized by focal or heterogeneous intense uptake along the graft, sometimes associated with additional sites of uptake in adjacent soft tissue collections.

### Infective Endocarditis

Infective endocarditis (IE) is associated with a high mortality and is diagnosed by a combination of clinical, microbiological and echocardiogram criteria (modified Duke criteria). Transthoracic and transesophageal echocardiography are the standard imaging tests, although assessment of prosthetic valves is limited.

In prosthetic valve endocarditis (PVE), FDG PET/CT is recommended for the diagnosis of suspected infection in cases for which surgery was performed at least three months prior. Non-infected prosthetic valves may show mild homogeneous uptake. Infected prosthetic valves demonstrate focal and/or heterogeneous uptake along the valve plane, better visualized when physiological myocardial uptake is suppressed following cardiac diet preparation.

A number of studies have demonstrated the role of FDG PET/CT for the diagnosis of PVE. The sensitivity of FDG imaging in cases of native valve endocarditis is lower. In a recent meta-analysis of 10 studies<sup>15</sup>, the overall pooled sensitivity of FDG PET/CT for the diagnosis of IE is 81%, with a specificity of



Figure 2 – Vascular graft infection. Heterogenous, intense uptake in an infected right femoral graft

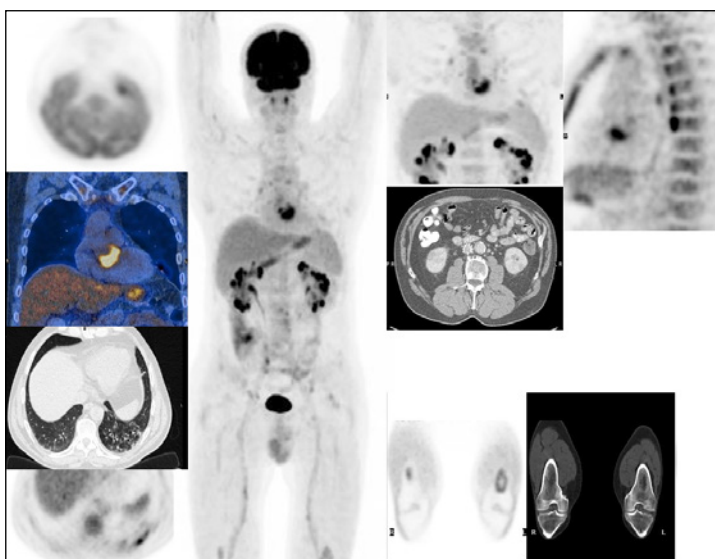


Figure 3 – Endocarditis with septic emboli. Patient with native aortic valve endocarditis and extensive embolic disease. Septic emboli are present in the left temporal lobe, lungs, kidneys, prevertebral soft tissues and bones.

(Continued on page 4. See **FDG PET/CT for Infection Imaging**.)



# 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 proves value in cardiac sarcoidosis detection](#)

**Aunt Minnie Europe**

[Whole-body imaging links heart, brain inflammation after MI](#)

**Cardiovascular Business**

[FDG-PET/CT predicts outcomes in pediatric osteosarcoma](#)

**Aunt Minnie**

[Researchers find a way to 'starve' cancer](#)

**MedicalXpress**

[Alzheimer's Disease Variants Linked to Brain Amyloidosis](#)

**Physician's Weekly**

[An Innovative PET Tracer Can Measure Damage from Multiple Sclerosis in Mouse Models](#)

**Science Newsline—Medicine**

[Artificial intelligence guides lower PET tracer dose](#)

**Aunt Minnie**

[The Utility of PET/CT in External Radiation Therapy Planning of Prostate Cancer](#)

**UroToday**

[Advances in brain imaging settle debate over spread of key protein in Alzheimer's](#)

**MedicalXpress**

[Baby cured of rare disease goes home for Christmas](#)

**[<sup>18</sup>F DOPA]**

**NBCDFW.COM**

## **(FDG PET/CT for Infection Imaging. Continued from page 3.)**

85%. Detection of PVE is superior to detection of native valve endocarditis<sup>16</sup>.

WBC SPECT/CT is an alternative nuclear medicine modality with advantages related to its infection-specific properties and is the preferred test in the early post-operative period. FDG PET/CT and labeled WBC scintigraphy have been incorporated in the European Society of Cardiology 2015 guidelines<sup>17</sup> for the diagnosis of infective endocarditis.

There has been a paradigm shift in the evaluation of IE, with increasing awareness of the systemic nature of the disease, with whole-body PET/CT detecting septic emboli in up to 58% of cases<sup>18</sup>. Incidental malignancy was diagnosed in 10% of cases. FDG PET/CT also provided alternative diagnoses in 11 of 80 patients<sup>19</sup>.

While FDG PET/CT provides excellent whole-body staging, detection of cerebral emboli is likely limited, and MRI may still be required for this indication. Detection of septic emboli is an important prognostic factor and, following the use of FDG PET/CT, relapse rates decrease significantly, from 9.6% to 4.2%<sup>20</sup>. FDG PET/CT is included in the algorithm for detection of embolic events in both native and prosthetic valves in the European guidelines.

## **Cardiovascular Implantable Device Infections**

FDG PET/CT is indicated in the diagnosis of cardiovascular implantable electronic device (CIED) infections to differentiate superior and generator-pocket infections and to identify suspected lead infections. Both the non-attenuated and attenua-

tion-correction images need to be reviewed to ensure that focal uptake in the device or lead is not related to metal artifacts.

In a recent meta-analysis, FDG PET/CT had a pooled sensitivity of 87% and specificity of 94% for detecting CIED infections<sup>21</sup>. Echocardiography is limited in the detection of lead vegetations. Despite CIED and lead extraction, there is a high mortality rate in these patients, likely related to the presence of systemic infection, which is often undiagnosed or underestimated—thus limiting appropriate treatment. In a prospective study of 35 patients with lead endocarditis, FDG PET/CT detected septic emboli in 10 patients (29%), most diagnosed with spondylodiscitis. Detection of septic emboli guided appropriate and more prolonged therapy<sup>22</sup>.

## **Bacteremia**

In patients with gram-positive bacteremia, routine FDG PET/CT has been reported to be cost effective, reducing morbidity and mortality from 32% in the control group to 19% in the FDG PET/CT group<sup>23</sup>. In patients with staphylococcus aureus bacteremia, metastatic infectious foci were detected in 74% of high-risk patients, leading to treatment modifications and a decrease in three-month mortality when compared to the control group<sup>24</sup>.

## **Osteomyelitis**

FDG PET/CT is an accurate modality for the diagnosis of post-traumatic osteomyelitis, with a sensitivity range of 86 to 94% and specificity of 76 to 100% in a recent systematic review<sup>25</sup>.

*(Continued on page 5. See [FDG PET/CT for Infection Imaging](#).)*

Excellent results have been also obtained for the diagnosis of diabetic foot osteomyelitis<sup>26</sup>.

## Conclusion

FDG PET/CT plays an important role in the evaluation of infectious processes and has proven to be of particular value in the work up of fever of unknown origin, spondylodiscitis, vascular graft and cardiac infections. Results are available within two hours, and whole-body imaging allows the systemic staging of the disease.

The excellent image quality provided by PET/CT scanners, which can detect small infectious foci (occurring for example, in pacemaker lead infections and septic emboli), facilitates image interpretation and improves diagnostic confidence. A number of studies have demonstrated that the use of FDG PET/CT for the diagnosis of infection reduces the overall amount of testing and hospitalization time, is cost effective and cuts relapse and morbidity/mortality rates. In the future, FDG PET/CT will likely play an even more important role in the diagnosis and management of infectious diseases.

## References:

1. Vaidyanathan et al. FDG PET/CT in infection and inflammation-current and emerging applications. *Clinical Radiology* 2015;70:787.
2. Rabkin et al. Do hyperglycemia and diabetes affect the incidence of false-negative <sup>18</sup>F-FDG PET/CT studies in patients evaluated for infection or inflammation and cancer? A comparative analysis. *J Nucl Med* 2010;51:1015.
3. Kagna et al. Does antibiotic treatment affect the diagnostic accuracy of <sup>18</sup>F-FDG PET/CT studies in patients with suspected infectious processes? *JNM* 2017;58:1827.
4. Balink et al. FDG PET/CT in inflammation of unknown origin: a cost-effectiveness pilot-study. *EJNMMI* 2015; 42:1408.
5. Takeuchi et al. Nuclear imaging for classic fever of unknown origin. *Meta-analysis. JNM* 2016;57:1913.
6. Besson et al. Contribution of FDG PET in the diagnostic assessment of FUO: a stratification based meta-analysis. *EJNMMI* 2016; 43 1887.
7. Stumpe KD et al. FDG PET for differentiation of degenerative and infectious endplate abnormalities in the lumbar spine detected on MR imaging. *AJR*. 2002 Nov;179(5):1151-7.
8. Fuster et al. Prospective comparison of WB FDG PET/CT and MRI of the spine in the diagnosis of haematogenous spondylodiscitis. *EJNMMI* 2014.
9. Fahnert et al. Use of simultaneous <sup>18</sup>F-FDG PET/MRI for the detection of spondylodiskitis. *JNM* 2016;57:1396.
10. Prodroumou et al. FDG PET/CT is a robust tool for diagnosis of spondylodiscitis. A meta-analysis of diagnostic data. *CNM*. 2014;39:330.
11. Nanni et al. FDG PET/CT is useful for the interim evaluation of response to therapy in patients affected by haematogenous spondylodiscitis. *EJNMMI* 2012;39:1538.
12. Keidar et al. Prosthetic vascular graft infection: The role of <sup>18</sup>F-FDG PET/CT. *JNM* 2007;48:1230.
13. Keidar Z, Nitecki S. FDG PET in prosthetic graft infections. *Semin Nucl Med* 2013;43:396.
14. Keidar et al. <sup>18</sup>F-FDG uptake in noninfected prosthetic vascular grafts: Incidence, patterns and changes over time. *JNM* 2014;55:392.
15. Juneau D. et al. Molecular imaging for the diagnosis of infective endocarditis: A systematic review and meta-analysis. *Int J Cardiol* 2017; <https://doi.org/10.1016/j.ijcard.2017.10.116>.
16. Granados et al. Diagnostic accuracy of <sup>18</sup>F-FDG PET/CT in infective endocarditis and implantable cardiac device infection: A cross-sectional study. *JNM* 2016;57:1726.
17. Habib et al. 2015 ESC Guidelines for the management of infective endocarditis: The Task Force for the Management of Infective Endocarditis of the European Society of Cardiology (ESC). *Eur Heart J*. 2015;36(44):3075.
18. Salomaki et al. <sup>18</sup>F-FDG PET/CT in infective endocarditis. *J Nucl Cardiol*. 2017;24:195.
19. Granados et al. Diagnostic accuracy of <sup>18</sup>F-FDG PET/CT in infective endocarditis and implantable cardiac device infection: A cross-sectional study. *JNM* 2016;57:1726.
20. Kestler et al. Role of FDG PET in patients with infectious endocarditis. *JNM* 2014;55:1093.
21. Juneau D. et al. Positron emission tomography and single-photon emission computed tomography in the diagnosis of cardiac implantable electronic device infection: A systemic review and meta-analysis. *Circ Cardiovasc Imaging*. 2017; 10:e005772.
22. Amraoui et al. Contribution of PET imaging to the diagnosis of the septic embolism in patients with pacing lead endocarditis. *J Am Coll Img*. 2016;9:283.
23. Vos et al. Cost-effectiveness of routine <sup>18</sup>F-FDG PET/CT in high risk patients with gram-positive bacteremia. *J Nucl Med* 2011;52:1673.
24. Berrevoets et al. <sup>18</sup>F-FDG PET/CT Optimizes Treatment in Staphylococcus Aureus Bacteremia and Is Associated with Reduced Mortality. *J Nucl Med* 2017;58:1504.
25. Govaert G. et al. Accuracy of diagnostic imaging modalities for peripheral post-traumatic osteomyelitis – a systematic review of the recent literature. *Eur J Nucl Med Mol Imaging* 2017;44:1393.
26. Kagna et al. FDG PET/CT imaging of the diagnosis of osteomyelitis in the diabetic foot. *Eur J Nucl Med Mol Imaging*. 2017; 44:1393.

# Pediatrics Corner

## Pediatric NUT Midline Carcinoma Characterized Using FDG PET/CT: A Case Report

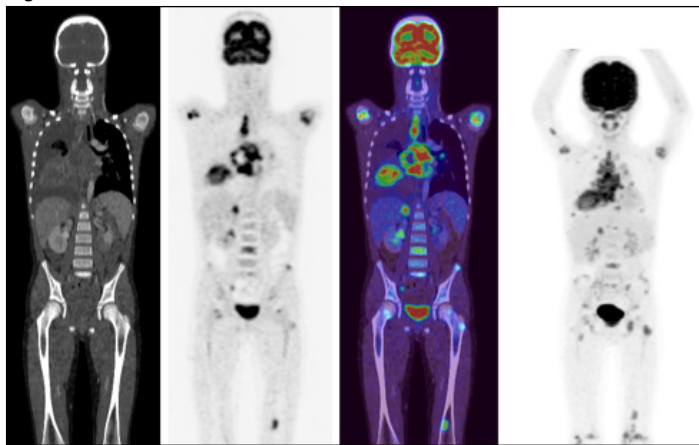
Melissa C. Kong and Helen R. Nadel, MD, FRCPC, British Columbia Children's Hospital, University of British Columbia, Vancouver, British Columbia

### History

A previously healthy eight-year-old male presented with three weeks of limping due to left knee pain without clear traumatic etiology. He was also experiencing wheezing, weight loss, and nonspecific bilateral arm pain. X-ray and MRI of the left knee demonstrated cortical irregularity of the knee and multiple osseous metaphyseal lesions of the distal femur and proximal tibia. A chest x-ray showed mediastinal lymphadenopathy with right lower lobe collapse and pleural effusion, and abdominal ultrasound suggested a possible adrenal lesion as well.

Staging evaluation with PET/CT not only confirmed these findings, but also further revealed the extent of soft tissue disease in the chest and indicated numerous intensely FDG-avid bony metastases throughout the skeleton (Figure 1). Very little focal skeletal abnormality was seen on the CT scan to correspond with these bony lesions (Figure 1). The patient underwent biopsy and was diagnosed with NUT midline carcinoma after cytogenetic testing. He was treated with chemotherapy.

Figure 1

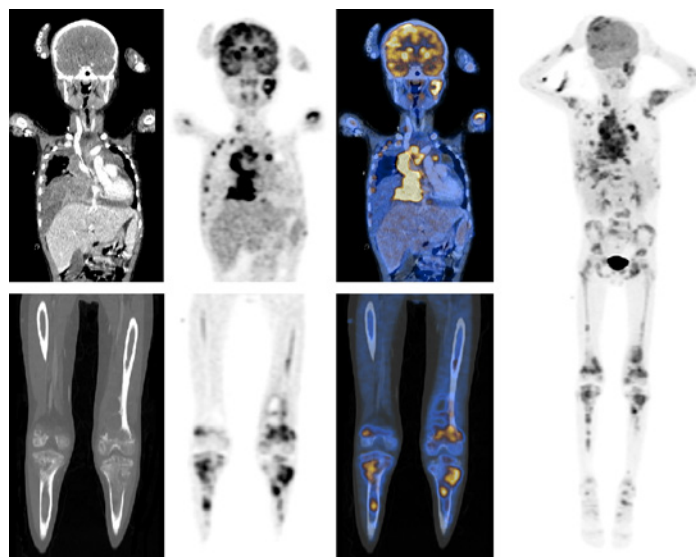


Follow-up PET/CT scans revealed initial minimal response with persistent disease, and later progressive disease (Figure 2). Unfortunately, the patient eventually succumbed to his disease.

### Discussion

NUT midline carcinoma (NMC) is a rare and highly aggressive cancer with no curative therapy. It is caused by rearrangements in the NUT gene on chromosome 15q14.<sup>1</sup> NMC presents as a poorly differentiated carcinoma, often with squamous differentiation.<sup>1,2</sup> The most common rearrangement involves translocation and fusion of NUT with the BRD4 gene (19p13),

Figure 2



which was the case for this patient.<sup>1,2</sup> About a third of NMC is caused by rearrangements of NUT with other genes, termed NUT variants.<sup>3</sup>

The course of treatment typically involves intensive chemotherapy and radiation.<sup>1,2</sup> However, prognosis for this type of cancer is very low, with typical survival below one year.<sup>1</sup> Literature suggests that patients with NUT-variant carcinoma may survive longer than those with BRD4-NUT carcinoma, but more research is needed to confirm this.<sup>1,2</sup>

In this case, PET/CT evaluated disease extent and indicated the best site for tissue biopsy. Notably, PET revealed a large amount of FDG-avid metastatic disease that was not marked on CT. PET thus allowed for a better understanding of the extent of disease early on, with localization using CT. Later PET/CT scans allowed for accurate assessment of treatment response over time and indicated a need for modifications to therapy. PET/CT was valuable in that it accurately characterized this aggressive tumor and dynamically helped shape treatment plans. This case suggests PET/CT may be instrumental in the management of future NMC patients.

### References

1. French CA. NUT Midline Carcinoma. *Cancer Genet Cytogenet.* 2010;203:16-20.
2. French CA, Kutok JL, Faquin WC, Toretsky JA, Antonescu CR, Griffin CA, et al. Midline Carcinoma of Children and Young Adults With NUT Rearrangement. *J Clin Oncol.* 2004;22:4135-39.
3. Mills AF, Lanfranchi M, Wein RO, Mukand-Cerro I, Pilichowska M, Cowan J, et al. NUT Midline Carcinoma: A Case Report with a Novel Translocation and Review of the Literature. *Head Neck Pathol.* 2014;8:182-6.

# TECH CORNER

## Radiation Safety Considerations in PET/CT

Mark Weir, PET/CT technologist, St. Joseph's Healthcare, Hamilton, Ontario, Canada

Nuclear medicine has long been an invaluable contributor in diagnosing disease. In the last decade however, it has seen its role reduced somewhat as isotope shortages and booms in other imaging modalities like CT have encouraged clinicians to look elsewhere to get answers for their patients. Despite this, the future of nuclear medicine is bright. In a world where hybrid imaging has become the norm, PET/CT will undoubtedly be key.

$^{18}\text{F}$  is the  $^{99\text{m}}\text{Tc}$  of the PET world. It is manufactured using a cyclotron or linear accelerator, which means it doesn't rely on aging reactors for its production the way  $^{99\text{m}}\text{Tc}$  does. From there, it can be quickly synthesized into  $^{18}\text{F}$ -FDG, which has become an extremely important tool for the diagnosis and screening of lung, esophageal, colorectal, melanoma, and lympho-proliferative cancers. It also has a very desirable half-life of only 109 minutes, so patients and their waste remain radioactive for considerably shorter time periods than patients imaged with  $^{99\text{m}}\text{Tc}$ .

Although convenient for reducing scatter, the 511 keV positron annihilation photons create a much larger photon flux and are much higher in energy than the 140 keV photons typically found in general nuclear medicine procedures. Also, the short half-life of  $^{18}\text{F}$  makes using unit doses impractical, so extra manual manipulation is needed to draw and deliver patient doses from bulk vials. All of this results in a significantly higher equivalent dose for PET/CT technologists performing these exams. It is not unusual for PET/CT technologists to see body and extremity dosimetry readings 3 and 5 times higher respectively when compared to those of general nuclear medicine technologists<sup>1</sup>.

When we compare the half-value layers of lead for  $^{18}\text{F}$  (0.6 cm) and  $^{99\text{m}}\text{Tc}$  (0.027 cm), we see a greater than 20-fold difference. So, syringe shields used for manual injection work must be much more robust, although at the expense of being much heavier and cumbersome to work with than those used in nuclear medicine.

A busy PET/CT department will typically have at any time, two or even three injected patients queued up waiting to be imaged. It's important to have a dedicated area away from staff and family members where the patients can wait. Lead-lined walls within the injection bays help further reduce dose to technologists working with patients in the vicinity and should really be an automatic part of any departmental design. Indeed, to use Canada as an example, when submitting a GD-52 design guide to the Canadian Nuclear Safety Commission, the federal regulator will

want to see proof that the shielding design will ensure inhabited public areas adjacent to the PET/CT department remain below 2.5  $\mu\text{Sv/hr}$ .

Like many things in life, if you have the money, you can really aim for the cream-of-the-crop PET/CT dose-reduction strategy, which is an automated patient dose infuser. Our department uses a Bayer Medrad Intego PET infuser. This is a mobile device loaded with a multi-dose stock vial of FDG, which is then literally driven to the patient bay. The dose savings here to the technologist are really two-fold. For starters, it totally eliminates manual drawing up of the patient doses by hand, which drastically reduces extremity dosage to technologists. Secondly, when patients are actually being injected, the technologist can stand back a couple meters, which greatly increases his/her distance from the source, while again basically eliminating direct handling of the isotope.

In our department, we found that the effective body dose of our PET technologists was reduced by up to 35 percent, and the extremity dose was reduced by up to 62 percent<sup>2</sup>.

The specialty of PET/CT is a fast growing and exciting branch of nuclear medicine. Certain considerations must be made to ensure good control of effective dose to staff and members of the public. It really just comes down to new ways of employing the same tried-and-true strategies of decreasing time, increasing distance, and incorporating shielding.

### References

1. St. Joseph's Healthcare Hamilton quarterly dosimetry dose report; 2016-2017
2. Validation of the MEDRAD Intego PET Infusion System in the Clinical Nuclear Medicine Setting; Mark Weir



# Machine Learning and PET: A Good Match?

*Vincent C. Gaudet, PhD, Chair, Department of Electrical and Computer Engineering, University of Waterloo, Ontario, Canada*

It seems like every conference these days has a special session on machine learning (ML). Indeed, ML has taken off in the past few years, and it is being applied to many domains, including medical imaging. A search on PubMed (Jan. 19, 2018) for the phrase “machine learning” returned 19,585 entries, of which 4,124 were published in 2017 alone. For comparison, “prostate cancer” returned 8,454 entries and “Alzheimer’s” returned 5,372 entries from 2017.

ML is not new: your email spam checker has used it for years, and your movie streaming service uses it to make recommendations. Within the medical domain, PubMed shows papers on ML going back to the mid-1960s. In the 1990s, there was a steady pace of around 20 articles each year, peaking in 1995 at 23. Growth clearly began around the turn of the millennium, and by 2013, there were over 1,000 articles per year on ML being indexed on PubMed.

Broadly speaking, ML refers to a family of computational techniques that learn from observations and that can subsequently make inferences based on what they have learned. Each observation should allow the ML algorithm to improve its performance. Contributions to ML are made by computer engineers and scientists, mathematicians, philosophers (including ethicists), as well as domain specialists (which is crucial for its adoption in PET).

How is ML different from traditional computing? A “classical” computer program must be explicitly written by a programmer, who specifies all aspects of the algorithm when writing the program. Therefore, the programmer must understand (i.e., have learned) all aspects of the algorithm. This is analogous to a cook (the computer) finding a recipe (the algorithm) in a book, and then following it (running the program). It is a static program, and nothing is learned that is not already in the recipe.

On the other hand, an ML algorithm has many parameters whose values are not known when writing the program. These parameters must be learned as the program is presented with observations. This is like a cook who wants to bake a cake but does not have a recipe. The cook must decide which ingredients to use and in what proportions (the parameters). Without a recipe, the cook must iterate, using different ingredients and amounts each time until achieving success. The key to success in ML is to have a sound way to improve the algorithm based on the observation. The starting point is key: an experienced cook might require fewer iterations than a novice. It also helps to know what a cake should look like. Imagine being asked to cook a “cake” without knowing what it is (in the ML world, we call this “unsupervised learning”)!

So, why is ML taking off? The answer is really two-fold: we now have better algorithms and better hardware. In the past decade, a subset of ML algorithms called “deep learning” has successfully tackled challenging problems such as natural language understanding and image recognition. Many of these deep learning techniques were already known, but required huge amounts of hardware resources, thus limiting their applicability. However, with the continued progress in semiconductor technologies and computing architectures, it has become feasible to implement these techniques.

Deep convolutional neural networks (one of the deep learning techniques) are formed of many computational layers, where each layer focuses on concepts at different granularity levels (e.g., edges and corners, shapes, tumors, disease), possibly combining information from several modalities. Thus, ML appears to be very well suited to hybrid imaging such as PET/CT or PET/MR. However, there remains a lot to be discovered!

A question that often comes up in ML sessions at conferences is: Will ML take away my job? Quite invariably, the response is that the short answer is “yes,” but that the long answer is, in fact, “yes, if you mean the exact job you are doing today, but you will have a rewarding job if you are willing to adapt.” ML algorithms work best when they are presented with high volumes of high-quality data. Clinical trial data with a few dozen samples are nowhere near sufficient. Also, it is easy for unrecognized biases in datasets to significantly skew the ML algorithms towards incorrect results. Therefore, at least for the time being, ML will continue to require very significant intervention by domain specialists who can pick out these biases. Indeed, truly unsupervised learning still has a long way to go before it takes away your job.

How can you get involved? Remember that the greatest advances in ML are being led by teams of scientists and engineers working with domain specialists such as yourselves. The scientists and engineers understand the algorithms and the theory, but you have access to the all-important data. So, if you want to succeed and to be at the forefront of this exciting revolution, reach out to others outside your field. We want to work with you!



# Philadelphia: Site of SNMMI's Annual Meeting and a Great City to Explore

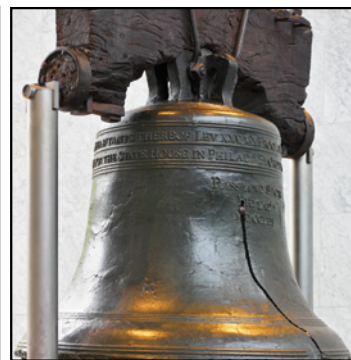
*Rania Arabi, CNMT, MRT(MR), MBA, Hamilton Health Sciences, Hamilton, Ontario, Canada*

As a generation Xer, when I think of Philadelphia, I first think of the Fresh Prince of Bell Air theme song “In West Philadelphia Born and Raised.” Secondly, I obviously think of the upcoming SNMMI Annual Meeting in June!

A few years ago, I attended a great meeting in Philly, and look back with fond memories on the City of Love. People were friendly, and there was so much to fit in around the conference. The Penn Convention Center is convenient to all the bustling downtown life and just a short walk to many hotels and restaurants.

I found the best way to see the city is via a hop-on/hop-off tour bus, easily accessible from most hotels. The tours usually hit the main landmarks, including the Liberty Bell; Liberty One observation deck overlooking the city; Philadelphia Museum of Art, where you can make your way up the “Rocky Stairs;” and stops in unique neighbourhood with great street art and history. LOVE Park is also a must-stop for a photo-op with the LOVE sculpture, which was just renovated and should be back in place by June.

As for exploring, I especially enjoy discovering great food! An authentic Philly steak is a must-do; Pat’s King of Steaks, Geno’s Steaks, and Jim’s Steaks are just a few of the options. Also check out the Reading terminal, a hub for different cuisines, delis, and markets within walking distance of the Penn Center. Another treat is South Street with its mix of culture, food and shopping. So, make some time in your schedule and check out all that Philly has to offer!



## PET CoE News

### SNMMI 2018 Annual Meeting

The Annual Meeting will be held June 23-26 in Philadelphia, PA. Registration details can be found at [www.snmmi.org/AM2018](http://www.snmmi.org/AM2018). Early-bird registration ends on April 19.

### Peter E. Valk, MD Memorial Lectureship and Award

The PET Center of Excellence is pleased to announce that Peter Conti, MD, PhD, FSNMMI, is the recipient of the 2018 Peter E. Valk, MD Memorial Lectureship and Award. Conti is director of the Molecular Imaging Center and the PET Imaging Center at the Kerk School of Medicine, University of Southern California. He will receive his award and present a lecture on Monday, June 25, at 10 AM during the SNMMI Annual Meeting.

### PET/MRI Working Group

The PET Center of Excellence is launching a PET/MR working group that will bring together members from across SNMMI. PET/MRI is an emerging imaging modality that requires significant development to realize its full potential in research and clinical care. The objective of the SNMMI PET/MRI working group is to support the development of PET/MRI and to educate physicians, researchers and technologists. It will support educational activities at the annual meeting, webinars and workshops jointly sponsored with other organizations.

PET/MRI is truly an intersociety modality requiring input from multiple organizations to help accelerate its development and clinical adoption. The new PET/MR group will work with the SNMMI community to address member needs and help advance PET/MRI. If you are interested in joining the PET/MRI Working Group, please complete this survey: <https://www.surveymonkey.com/r/PETMRIWG>

## PSMA PET/CT Visualizes Prostate Cancer Recurrence Early, Impacts Radiation Therapy

*Earlier pinpointing of prostate cancer recurrence locations after radical prostatectomy means that PSMA PET/CT could help guide salvage radiotherapy, resulting in more effective treatment for many patients.*

A nuclear medicine scan may locate prostate cancer recurrence after radical prostatectomy early after disease recurrence and could help guide salvage radiotherapy, according to new research from the University of California Los Angeles (UCLA). The study, which utilizes PET/CT with gallium-68 prostate-specific membrane antigen (<sup>68</sup>Ga-PSMA-11), is documented in the [featured article](#) in the February issue of *The Journal of Nuclear Medicine*.

Prostate cancer biochemical recurrence occurs in 20 to 80 percent of patients within 10 years after radical prostatectomy and is difficult to treat. Salvage radiotherapy is the main option for treatment, but the imaging modalities currently used are not sensitive enough to identify the location of recurrence until it is too late, leading to a “best-guess” approach for targeting the radiotherapy.

“Based on European data, we believe that PSMA PET/CT, an imaging technique that is not yet approved by the U.S. Food and Drug Administration, is sufficiently sensitive to detect and localize the recurrent prostate cancer early enough to potentially guide salvage radiotherapy,” explains Jeremie Calais, MD, at UCLA. “The first sign of prostate cancer recurrence is a rising PSA. For salvage radiotherapy to be successful, it should be initiated before the PSA rises above 1 ng/mL, and ideally, closer to 0.2 ng/mL or lower.”

The study included 270 well-documented patients from databases established at four institutions (UCLA and three in Germany: Technical University of Munich, Ludwig-Maximilians-University of Munich, and University of Essen). All patients had a biochemical recurrence of prostate cancer after radical prostatectomy but had not received prior radiotherapy. They underwent PSMA PET/CT at a serum PSA level of less than 1 ng/mL.

Nearly half (132 patients or 49 percent) had a positive PSMA PET/CT, and 52 (19 percent) had at least one PSMA-positive lesion that was not covered by the consensus clinical target volume (CTV). The two most common PSMA PET-positive lesion locations outside the consensus radiation fields were bone (23/52, 44 percent) and perirectal lymph nodes (16/52, 31 percent).

Calais points out, “Salvage radiotherapy is only curative if recurrent disease is completely encompassed by the radiotherapy fields. Therefore, in almost 20 percent of these patients, the addition of PSMA PET/CT would have a potentially major impact on the outcome of salvage radiotherapy.”

He elaborates, “Visualizing sites of prostate cancer recurrence accurately, and early enough to guide therapy, enables truly precision radiation therapy. This is, in fact, the definition of individualized medicine. We believe that PSMA PET/

CT imaging will ultimately be incorporated into the standard of care for prostate cancer patients with biochemical recurrence.”

Toward that end, the suggested next step is a randomized imaging trial of salvage radiotherapy with or without PSMA PET/CT to investigate further its potential beneficial impact on treatment outcome.

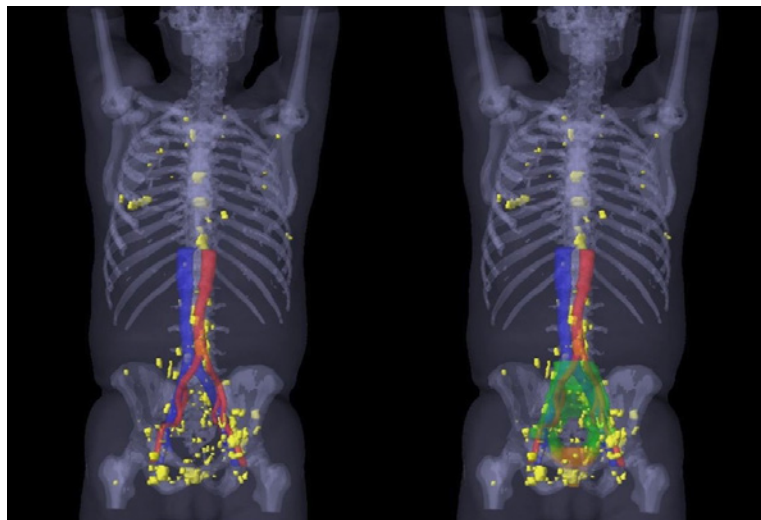


FIGURE: A 3-dimensional map of the PSMA-positive lesions outside the standard radiation fields

[Click here](#) for a video of Jeremie Calais, MD, and Nicholas G. Nickols, MD, PhD, at UCLA explaining their research and the potential benefits of PSMA PET/CT for prostate cancer patients with biochemical recurrence after radical prostatectomy.

*Authors of “<sup>68</sup>Ga-PSMA-11 PET/CT Mapping of Prostate Cancer Biochemical Recurrence After Radical Prostatectomy in 270 Patients with a PSA Level of Less Than 1.0 ng/mL: Impact on Salvage Radiotherapy Planning” include Jeremie Calais, Johannes Czernin, Minsong Cao, Amar U. Kishan, John V. Hegde, Narek Shaverdian, Kiri Sandler, Fang-I Chu, Chris R. King, Michael L. Steinberg and Francesco Ceci, UCLA, Los Angeles, Calif.; Isabel Rauscher, Technical University of Munich, Munich, Germany; Nina-Sophie Schmidt-Hegemann, University Hospital, LMU Munich, Munich, Germany; Thorsten Poeppel and Philipp Hetkamp, Universitätsklinikum Essen, Essen, Germany; Ken Herrmann, UCLA and Universitätsklinikum Essen; Wolfgang P. Fendler, UCLA and Ludwig-Maximilians-University, Munich, Germany; Matthias Eiber, UCLA and Technical University of Munich; and Nicholas G. Nickols, UCLA and VA Greater Los Angeles Healthcare System, Los Angeles, Calif.*

## Calendar of Events

### Central Chapter Annual Spring Meeting

March 23–25, 2018 • Ann Arbor, Michigan

[www.ccsnmml.org](http://www.ccsnmml.org)

### 48<sup>th</sup> Annual Spring Mid-Eastern Chapter Meeting & Exhibition

April 13–15, 2018 • Hanover, Maryland

[www.mecsnm.org/index.html](http://www.mecsnm.org/index.html)

### British Nuclear Medicine Society Spring Meeting 2018

April 14–16, 2018 • Birmingham, West Midlands, England

[www.bnms.org.uk](http://www.bnms.org.uk)

### 8<sup>th</sup> International Symposium of Sentinel Node Biopsy in Head & Neck Cancer

April 20–21, 2018 • London, England

<https://eighthsnb.com>

### 12<sup>th</sup> Congress of the World Federation of Nuclear Medicine and Biology

April 20–24, 2018 • Melbourne, Australia

<https://wfnmb2018.com>

### SNMMI 2018 Annual Meeting

June 23–26, 2018 • Philadelphia, Pennsylvania

<http://www.snmmi.org/AM2018>

### 2<sup>nd</sup> World Congress on Radiology and Oncology

July 16–17, 2018 • Dubai, United Arab Emirates

<https://radiology-oncology.annualcongress.com/>

## VIEW THE FIRST ISSUE OF THE Annual Meeting Preview Magazine



## PET Center of Excellence Newsletter

*The PET Center of Excellence Newsletter is a quarterly member information service published under the direction of the PET CoE leadership and SNMMI.*

### PCoE Newsletter Editorial Board

Alain S. Abi-Ghanem, MD

Delphine L. Chen, MD

James R. Crowley, BS, CNMT

Patrick Colletti, MD

David W. Dick, PhD

Thomas Hope, MD

Frédéric Lacroix-Poisson, MD, FRCPC

Helen R. Nadel, MD

Alan Packard, PhD

Gabriel Soudry, MD

Jian (Michael) Yu, MD, FACNM

Katherine Zukotynski, MD, *Editor*

### PCoE Board of Directors

Katherine Zukotynski, MD

*President*

Michael V. Knopp, MD

*Vice President*

Helen R. Nadel, MD

*Secretary/Treasurer*

Ryan Niederkoher, MD

*Immediate Past President*

Twyla B. Bartel, DO, MBA, FACNM

Delphine L. Chen, MD

David W. Dick, PhD

Bennett S. Greenspan, MD, FACNM, FACR

Thomas Hope, MD PhD

Maria Liza Lindenberg, MD

Erik Mittra, MD, PhD

Todd E. Peterson, PhD

Gary Ulaner, MD, PhD

Chadwick L. Wright, MD, PhD

Jian Q. Yu, MD, FRCPC, FACNM

Shelley Nicole Acuff, CNMT, RT(R) (CT), Intern

Sonya Youngju Park, MD, Intern

### SNMMI Chief Executive Officer

Virginia Pappas, CAE

Managing Editor

Laurie Callahan

Graphic Designer

Laura Reyes

©2017 SNMMI, Inc.