The Use of Contrast Media in PET/CT Imaging

Alain S. Abi-Ghanem, MD, DABNM, DABR, American University of Beirut Medical Center, and Helen R. Nadel, MD, FRCP, DABNM, DABR, Stanford University Medical Center

Please Note: The lead article is now available for CE/SAM Credit at https://www.snmmilearningcenter.org/Activity/6539119/Detail.aspx, and it's free for PET CoE members!

Introduction: “To Enhance, or not to Enhance, that is the Question.”

Contrast agents are now an integral part of most imaging modalities in diagnostic radiology. They improve the visibility of normal anatomical and abnormal pathological structures in radiography, fluoroscopy, computed tomography, magnetic resonance imaging and, to a lesser extent, ultrasonography. Contrast agents have evolved over time and have become much safer and better tolerated by patients. One needs to be aware of their basic characteristics and be prepared to promptly recognize and treat their adverse effects [1].

18F-fluorodeoxyglucose (18F-FDG) positron emission tomography/computed tomography (PET/CT) is a hybrid modality combining the advantages of metabolic functional imaging provided by PET, and morphological imaging provided by CT. PET/CT using 18F-FDG exploits the increased glucose metabolism by the rapidly proliferating tumor cells, opening a new era in cancer imaging. It is widely used for staging, restaging, assessment of treatment response, and evaluation of prognosis in patients with several types of cancer. It has an edge over stand-alone CT and has been shown to improve the diagnostic accuracy in various malignant diseases [2-4].

Modern PET/CT scanners incorporate the latest CT technology, allowing the execution of high-quality multiphasic CT imaging. But do we really need contrast-enhanced PET/CT (PET/CECT), or is the usual low-dose, (Continued on page 2. See The Use of Contrast Media in PET/CT Imaging.)
So then, if our enemy is sickness, who are we? The PET CoE encompasses a diverse and multifaceted group of people of differing backgrounds and cultures. Can we stand united with our fellow medical professionals and sister societies as an army, working together towards common ideals? Can we rise above our differences and win as a team? As soon as we realize that we are fighting disease, not amongst each other, the answer is a loud and resounding, “Yes!”

In this issue of the PET CoE Newsletter, our lead article “To enhance, or not to enhance, that is the question” discusses the use of contrast to optimize PET/CT. For the first time, the lead article is available for CE/SAM credit, and it’s free for PET CoE members! Other articles look at the added value of PET/CT in neuroblastoma compared with conventional nuclear medicine imaging, and at harmonization of PET in simultaneous PET/MR – underlining the benefits of unifying imaging modalities.

So, on a lighter note, I conclude with a quote from Monty Python’s Life of Brian: “We mustn’t fight each other! Surely we must be united against the common enemy!” You can look up the rest.

---

Types of Contrast Agents and Technical Considerations

**Intravenous contrast:** Most intravenous contrast agents are iodine-based with variable iodine content per milliliter (mL). These agents are further classified into ionic (non-organic) and non-ionic (organic). Ionic agents were initially developed, and they have higher osmolality than normal plasma and more side effects. Non-ionic agents, which covalently bind to iodine, are water-soluble but do not dissociate in plasma, therefore have low osmolality and fewer side effects.

The use of positive contrast overestimates PET attenuation factors as a result of current CT-based algorithms for attenuation correction in present-day PET/CT scanners. These artifacts are correlated with Hounsfield Units (HU) on CT images and appear as areas of increased glucose metabolism on PET. Because artifacts are found in areas of high contrast concentrations, they rarely cause interpretation problems in the clinical setting because they can easily be attributed to the underlying vessel.

Practically, the following facts should be considered when using intravenous contrast:

- **a)** Contrast enhancement of visceral organs will slightly increase their measured physiologic activity. This could potentially decrease visualization of pathologic lesions in these organs on PET.
- **b)** Pathologic lesions that enhance may have artifically increased SUV values. Therefore, careful assessment of treatment response should be made when comparing with previous non-enhanced PET/CT exams.
- **c)** More intense activity in the thoracic veins and urinary tract from undiluted or concentrated contrast may obscure adjacent pathologic lesions. This can be minimized by scanning before renal contrast excretion, splitting the dose of contrast, using a saline chaser after each contrast administration and scanning caudocranially to minimize thoracic vein activity.

**Oral contrast:** Oral contrast agents are positive or negative contrast agents. Positive contrast agents, such as iodine or barium sulfate, have a high atomic number and appear more radiopaque than the surrounding tissue. They increase CT attenuation values of the bowel lumen leading to its opacification and proper delineation from the adjacent structures. The use of positive oral contrast overestimates PET attenuation factors in the bowel. In cases where an artifact cannot be differentiated from pathology, non-attenuation-corrected (non-AC) images should be viewed. On these images, artifacts should disappear whereas true lesions remain avid.

Negative contrast agents have a low atomic number and appear radiolucent (0-20 HU) compared to the surrounding tissue. They include gases (air, oxygen, carbon dioxide) and fluids (water, mannitol, sorbitol, polyethylene glycol). Negative oral contrast agents provide delineation of bowel loops by causing bowel distention rather than opacification. Based on their low CT attenuation, they do not cause artifacts or inaccuracies in tracer quantification (SUV value) on PET. However, application of water alone does not usually provide satisfactory bowel...
of these lesions are greatly facilitated by the use of intravenous and with hepatic and peritoneal metastases. The localization and delineation colon with SUVmax 4.9 (C and D, white arrows). These are consistent Another soft tissue lesion is seen more inferiorly along the descending lobe measuring 1.4 x 1.1 cm with SUVmax 5.3 (A and B, red arrows). CECT shows an FDG-avid hypodense lesion in the right inferior hepatic tumor post surgical debulking and chemotherapy. Follow-up FDG PET/CT shows an FDG-avid hypodense lesion in the right inferior hepatic lobe measuring 1.4 x 1.1 cm with SUVmax 5.3 (A and B, red arrows). Another soft tissue lesion is seen more inferiorly along the descending colon with SUVmax 4.9 (C and D, white arrows). These are consistent with hepatic and peritoneal metastases. The localization and delineation of these lesions are greatly facilitated by the use of intravenous and positive oral contrast.

**Figure 1**: 29-year-old man with desmoplastic peritoneal small round cell tumor post surgical debulking and chemotherapy. The colon is usually well delineated by its larger size and stool content. The colon is ideally imaged in the late venous phase in the cranial direction from the thighs to the head is suggested. The application of oral contrast must be timed to provide homogeneous distribution. One protocol suggests using 1.5 L of water-containing mannitol and LBG. In this protocol, patients are instructed to ingest 1.3 L over the course of 50 minutes starting directly after the intravenous administration of PET radiotracer. The remaining 200 mL are administered immediately before positioning the patient on the examination table to ensure gastric distention [14].

### Contraindications for Contrast Agents and Adverse Reactions

The use of contrast agents mandates proper training of physicians, nurses and technologists to promptly recognize and manage adverse reactions. Contraindications for the application of intravenous contrast agents may arise from known allergic reactions to iodinated contrast, hyperthyroidism or decreased renal function. Barium must not be used in patients with known or suspected bowel perforation/obstruction or in patients undergoing bowel surgery.

A detailed history of each patient should be taken to rule out any contraindication. Risk factors include a history of previous allergy-like reaction to contrast media. Such patients have a 5-fold increased likelihood of experiencing a subsequent reaction. Also, patients with significant allergies, such as a major anaphylactic response to any allergen in the past, need special attention. Atopic patients with a history of allergy to food products (e.g., dairy products) are also at a 2 to 3-fold increased risk for a contrast reaction. Patients with asthma or multiple myeloma and those with renal insufficiency are also at increased risk.

When contrast reactions occur, they may be divided into mild, moderate and severe. Mild reactions are the most common and include itching, flushing, pallor and rash. These usually require observation and reassurance. Moderate reactions like tachycardia, hypotension, bronchospasm and laryngeal edema require urgent treatment and close observation. Rarely, severe life-threatening reactions may occur like progressive laryngeal

(Continued on page 4. See The Use of Contrast Media in PET/CT Imaging.)
edema, profound hypotension, cardiopulmonary arrest and convulsions. These require hospitalization and immediate intervention [1].

IV Contrast in Adult PET/CT Imaging

Contrast-enhanced PET/CT provides additional information when compared with non-enhanced PET/CT. Because CT data supply anatomic background for PET, the most important benefit of contrast agents relates to more precise anatomic localization of a pathology by differentiation of the lesion from its surrounding structures. In addition, the lesion is better characterized once it is detected.

Pfannenberg et al. compared low-dose non-enhanced CT with standard dose CECT in combined PET/CT for staging and therapy planning in patients with non-small cell lung cancer (NSCLC). They concluded that in patients with advanced NSCLC, PET/CECT more accurately assessed the TNM stage in approximately 8 percent more patients than non-enhanced PET/CT.

In addition, for radiotherapy and surgical planning, PET/CECT proved to be indispensable owing to its precision in delineating the tumor. Similarly, PET/CECT has been shown to be superior to non-enhanced PET/CT for preoperative nodal staging in rectal cancer [13] and for assessing recurrence of ovarian cancer [9, 17], colorectal cancer [18, 19], uterine cancer [10, 20] and pancreatic cancer [21]. A similar report of the superiority of PET/CECT over non-enhanced PET/CT was reported for assessing the resectability of pancreatic cancer [12]. PET/CECT allows a more precise assessment of distant metastasis, scalene node metastasis and peritoneal dissemination in patients with pancreatic cancer [22].

In malignant lymphoma, Morimoto et al. concluded that PET/CECT improves the diagnostic accuracy in evaluating the nodal status of pelvic and retroperitoneal stations in a cohort of 66 patients [23]. In HPV-positive squamous cell carcinoma of the tonsils, Haerle et al. showed that PET/CECT outperforms PET/CT in detecting cystic lymph node metastasis [24].

Some malignant tumors do not demonstrate increased FDG uptake or only express a mild increase in glucose utilization compared with surrounding tissues. If a tumor or its metastases turn out to be FDG PET-negative, the use of CT contrast agents in PET/CT can increase attenuation differences between anatomical structures. Lesion detection will be enhanced, and the pattern of contrast-enhancement can aid lesion characterization.

The problem of lesion delineation and localization relates to all body regions but is most pronounced in the head and neck, as well as the abdomen and pelvis. In the head and neck, intravenous contrast agents provide differentiation of malignant lesions from adjacent blood vessels, thyroid gland, major salivary glands and muscles. In the abdomen and pelvis,
intravenous and oral contrast agents are used to accurately delineate lesions adjacent to bowel loops, stomach, mesenteric and iliac blood vessels and parenchymal organs.

**IV Contrast in Pediatric PET/CT Imaging**

To our knowledge, there is limited use of PET/CECT in the pediatric population. In general, the comments made above regarding PET/CECT also apply to children. Limitations to performing the CECT examination with the PET study have to date been more related to reimbursement issues and the need for more sedation possibly due to the additional requirement for indwelling IV after injection of radiotracer.

In addition, children may not tolerate the subjective “feelings” of heat and metallic taste caused by the injected iodinated contrast as well as adults can. Most pediatric institutions routinely utilize low osmolar non-ionic IV contrast agents. Children, in general, have a very low rate of contrast reactions to IV-administered low osmolar iodinated contrast with less than 0.5 percent adverse reactions reported [1].

IV contrast can help reduce the total radiation absorbed dose by using a lower kVp in association with dose modulation. This is because the relative attenuation of IV contrast is increased at lower kVp and the signal-to-noise ratio can be maintained [25].

PET/CECT can be used for both the attenuation scan and the diagnostic scan, thus potentially reducing the number of CT acquisitions that may be required. Positive oral bowel contrast can be helpful in children and teenagers due to their reduced body fat. However, adequate bowel opacification in children may be hampered by the difficulty of delivering/tolerating the oral contrast administration [26].

**Conclusion**

PET/CECT looks promising and provides not only excellent anatomic details but also information on tumor vascularization. CT contrast agents can be of additional value in FDG PET-negative tumors. Moreover, equivocal readings and the need for additional diagnostic imaging modalities are reduced, thereby saving time, which may have an impact on patient management and clinical outcome.

**References**

History

A previously healthy 3-year-old boy presented with constipation, palpable hepatomegaly, and a 3-month history of intermittent abdominal cramps. A CT scan of the chest, abdomen, and pelvis showed a right-sided mass separate from the liver, without metastatic disease. Biopsy later confirmed the diagnosis of stage IV neuroblastoma with MYCN gene amplification, a well-characterized genetic indicator of poor prognosis in neuroblastoma [1]. The bone marrow biopsy was negative.

Staging evaluation with whole-body, contrast-enhanced PET/CT confirmed the primary tumour and also revealed many intensely FDG-avid bony metastases throughout the skeleton that were not previously identified (Figure 1).

For comparison, a staging mIBG study was performed, which indicated the intensely avid mass but showed only a few faintly avid bony lesions (Figure 2). Multiple bony lesions identified on the PET/CT were not at all visualized on the staging mIBG study.

The patient underwent high-dose chemotherapy, autologous stem cell transplant, immunotherapy, tumour resection, and radiation. PET/CT scans were performed throughout treatment and demonstrated good response to therapy. The patient is now in remission and mIBG/CT scans were used in post-treatment follow-up.

Discussion

Neuroblastoma is one of the most common childhood extracranial solid tumours and the leading cause of death in pediatric cancers [1,2]. Originating from neural crest cells, the most common presentation of neuroblastoma consists of an adrenal mass and often features metastases at diagnosis [2]. High-risk patients have a low survival rate of less than 50 percent, compared to the more favourable prognosis of low- and intermediate-risk patients, who have an 80-95 percent survival rate [1].

Amplification of the MYCN oncogene occurs in about 25 percent of neuroblastoma cases and is strongly correlated with an undifferentiated, aggressive phenotype and poor prognosis[1,2]. In these high-risk patients, such as the patient in this study, management typically involves multimodality treatment and targeted therapeutics [2].

(Continued on page 10. See Pediatrics Corner.)
Harmonization of PET in Simultaneous PET/MRI

Richard Laforest, PhD, Washington University Medical School, St. Louis, and John Sunderland, PhD, University of Iowa

Introduction

Combined PET/MRI imaging systems were introduced commercially nearly a decade ago, and currently more than 70 PET/MRI scanners are installed worldwide by two manufacturers. Their use has seen a growing acceptance in many areas: neurology, oncology (notably for the evaluation of brain and abdominal cancers), and cardiology for a comprehensive protocol to evaluate myocardial viability and function, in addition to perfusion assessment and scar tissue imaging with late enhancement MRI. PET/MRI also shows a clear benefit in pediatric imaging from reduced radiation dose and the advantage of a single point of examination.

It is uncertain whether a single clinical application will emerge that will justify PET/MRI as an indispensable clinical tool, but the simultaneous dual modality platform has clear clinical and research roles to play in a spectrum of diseases. As PET/MRI applications evolve and its use becomes more ubiquitous, important questions are arising regarding the accuracy, reproducibility, and multi-center site comparativeness of the quantitative PET data generated from PET/MRI.

To address some of these concerns, research is currently underway investigating quantitative harmonization and standardization strategies for acquiring and reconstructing PET data within the context of PET/MRI. The primary motivation is to assure quantitative comparability of PET data both between PET/MRI scanner models and between PET/MRI and PET/CT.

Strategies to achieve this end include identification of acquisition protocols, attenuation correction strategies, and associated reconstructions that would validate meaningful quantitative comparison. Harmonization and standardization initiatives would result in reducing bias and variance and generate confidence that PET data generated from the two devices are truly comparable. Further, this would generate a paradigm whereby multicenter clinical trials with quantitative endpoints could use pooled data from multiple institutions, even combining PET/MRI and PET/CT data.

Sources of Quantitative Variability in PET/MRI

PET data are often expressed in terms of standard uptake value (SUV), for which accuracy and reproducibility are affected by multiple factors, including differences in patient preparation, imaging protocols across centers, different technologies from different vendors, as well as biological (body size, blood glucose, diet, breathing, uptake time) and technical factors (scanner calibration, quality control, image reconstruction algorithm, choice of parameters and scatter correction). These variables are common to both PET/MRI and PET/CT platforms.

Attenuation correction measurement in PET/MRI is a source of potential quantitative error that is specific to the PET/MRI platform. In PET/CT, attenuation correction is well established from scaling the CT images to appropriate attenuation coefficients for PET annihilation photons. In MRI, no such direct transformation is possible. In PET/MRI, the current commercial approaches use the DIXON sequence, which provides adequate attenuation in the soft-tissue of the body but neglects bone and has problems in the lung. Alternative techniques, such as UTE or ZTE, are now being tested along with numerous algorithms based on either using more advanced MRI techniques or using atlases and machine-learning algorithms.

At this time, optimized attenuation correction in PET/MRI appears to be a patchwork of different components [1-4]: DIXON for soft-tissue segmentation, ZTE or UTE for bone in the head or other limited areas of the body, or atlas-based for skull and major bones. MLAA or HUGE algorithms [5] are used to extend the MRI axial field of view to match the PET counterpart. No single/simple solution is integrated in a consistent manner by manufacturers. Additionally, the MRI phased-array coils, although made of low-attenuation material, are typically not included in the attenuation correction, which may affect PET quantitation accuracy.

Standardization Initiatives for PET/MRI

In the context of PET/CT and PET/MRI, imaging standardization is the process of implementing a series of prescriptive quality control, patient preparation and image acquisition steps designed to minimize quantitative and qualitative variance in PET image data. To this end, SNMMI, EANM, and RSNA’s Quantitative Imaging Biomarkers Alliance (QIBA) have generated best-practices documents for FDG-PET/CT imaging [6-12].

Despite the existence of multiple guidance documents, attempts have been made to assure that these documents are generally consistent with one another. Only recently have projects been initiated to apply and validate these standardization initiatives to PET/MRI. Through a recently funded NIH grant (R01CA212148), Thomas A. Hope, MD, and Richard Laforest, PhD, initiated a multi-center test-retest oncology FDG PET/MRI project implementing QIBA FDG PET/CT standardization requirements to validate reproducibility of PET/MRI FDG measurements. Laforest is also heading an initiative within QIBA to modify the current published FDG PET/CT oncology profile to include PET/MRI technology.

(Continued on page 8. See Harmonization of PET.)
Harmonization Initiatives for PET/MRI

Harmonization initiatives for PET/CT have been underway for several years. The goal of harmonization within the context of PET/CT refers to implementation of post-acquisition strategies (reconstruction or analyses strategies) to generate quantitatively similar (SUV) PET image data regardless of the model or vintage PET system the data were acquired on. Both SNMMI and EANM are involved in initiatives to prospectively identify scanner model-specific reconstruction parameter sets to generate quantitatively similar images across PET/CT vendor and models, and the Alzheimer’s Disease Neuroimaging Initiative (ADNI) has been doing this for many years. Commercial vendors are also now offering approaches for post-reconstruction Gaussian filtering capabilities in analysis software to achieve this end.

Only recently have efforts been initiated to identify PET/MRI reconstruction parameter sets that will allow harmonization with PET/CT systems and across the two available PET/MRI systems. Preliminary efforts and results using a modified NEMA Image Quality phantom and pre-calculated attenuation maps were reported at the SNMMI annual meeting. More sophisticated and PET/MRI specific phantoms are now under development.

Need for a PET/MRI Compatible Standardized Phantom

Proper testing of PET imaging equipment requires the use of appropriately designed phantoms. Typical phantoms used in PET/CT generally do not work in the MRI environment: water shows uniformity artifacts, and standard construction materials such as plastic/acrylic typically give no signal. Phantoms are in development with materials that have tissue-equivalent MRI properties, ideally with tissue-similar PET attenuation properties (Hope and Laforest, R01CA212148). Bone-like materials are particularly challenging, but progress is being made.

Conclusions

PET/MRI technology is still evolving and, in particular, the methodologies for attenuation correction measurement are rapidly progressing. Along with this development, standardization of image acquisition and image reconstruction strategies will help harmonize PET/MRI quantitation between PET/MRI platforms and between PET/MRI and PET/CT systems. These efforts should help PET/MRI integrate into mainstream clinical practice and help for inclusion of PET/MRI in multicenter clinical trials along with their PET/CT siblings.

References

PET CoE News

Peter E. Valk, MD, Memorial Lectureship and Award

Congratulations, again, to Peter Conti, MD, PhD, FSNMMI, 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 Keck School of Medicine, University of Southern California. His lecture, presented during the SNMMI Annual Meeting in Philadelphia, was titled “PET – The Final Frontier or a Stepping Stone?”

Peter Conti, MD, PhD, FSNMMI (left), was presented the award by PET CoE Vice President Michael V. Knopp, MD, PhD.

Nominations Open for 2019

The PET Center of Excellence is now accepting nominations for the 2019 Peter E. Valk, MD, Memorial Lectureship and Award, which honors the memory of Peter E. Valk, MD, a pioneer in the establishment of PET as an important clinical study. This award recognizes individuals who have made significant contributions to the advancement of PET, including PET/CT, PET/MRI and other emerging technologies, as well as those individuals who are dedicated to the PET Center of Excellence.

Although all individuals are eligible for this award, nominations will only be accepted from PET Center of Excellence members. The nomination process requires:

1. A letter written on behalf of the nominee, stating the individual’s qualifications (submitted by a PET Center of Excellence member)
2. The curriculum vitae of the nominee

The nomination package should be sent to K. Malaika Walton, SNMMI associate director of Governance (mwalton@snmmi.org), by November 1, 2018. The winner of the Peter E. Valk, MD, Memorial Award will be notified in early February and will be expected to present during a continuing education (CE) session at the 2019 SNMMI Annual Meeting in Anaheim, California, June 22-25. The award carries with it an honorarium of $1,000, which is sponsored by the PET Center of Excellence.

PET Center of Excellence 2018-2019 Board of Directors

Congratulations to Medhat M. Osman, MD, ScM, who began his term as a PET CoE Board member during the 2018 SNMMI Annual Meeting. The board thanked David Dick, PhD, for his service as his term on the board ended. The full list of the Board of Directors is at the end of this newsletter.

Call for Volunteers

The PET Center of Excellence seeks volunteers for two key initiatives (see below). If you are interested in participating in one of these working groups, please email K. Malaika Walton (mwalton@snmmi.org) and include a one-paragraph statement of interest along with your CV:

PET/MRI Working Group

The PET Center of Excellence has launched 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 this 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, as well as 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.

Theranostics Task Force

The purpose of this committee is to focus on the utility of PET for therapy—specifically, to evaluate and promote the use of PET as an adjunct for therapies and to provide educational materials on theranostics. While the primary therapeutic focus is targeted radionuclide therapies (TRT), this working group will focus more largely on any role of PET related to therapies (i.e., patient selection and/or radiation treatment planning). Current projects are examining the role of 68Ga-DOTATATE for 177Lu-DOTATATE therapy in NETs and the role of 18F-FDG in radiation treatment planning.
Of the scans performed, PET/CT provided the most sensitive and comprehensive scan for detecting and characterizing disease in this patient, followed by mIBG. The findings from the PET/CT scan upstaged the patient to high-risk, allowing him to receive the necessary treatment early on in his management. This case suggests that PET/CT may be a key modality for staging neuroblastoma patients and assessing response to treatment. However, mIBG was also able to detect some bony metastases at diagnosis and provided adequate follow-up assessment of the patient in remission.

The literature shows varying results in terms of PET/CT vs. mIBG sensitivity in the detection of neuroblastoma, and it is unclear whether one modality is superior to the other for all cases [3-6]. In future staging evaluations of neuroblastoma, the extent of the disease may be best characterized using both modalities in conjunction for comparison, as was done with this patient.

References
Researchers have discovered a new nuclear medicine test that could improve care of patients with type 1 diabetes. The new positron emission tomography (PET) imaging method could measure beta-cell mass, which would greatly enhance the ability to monitor and guide diabetes therapies. This study is reported in the featured article of the month in The Journal of Nuclear Medicine’s August 2018 issue.

According to the American Diabetes Association, approximately 1.25 million American children and adults have type 1 diabetes. Jason Bini, PhD, at the Yale University PET Center in New Haven, Connecticut, explains the significance to patients of being able to track their beta-cell mass:

“Beta-cell mass includes both functional and non-functional beta cells. Many indirect methods to measure beta-cell function are influenced by factors such as glucose and insulin levels and are not able to measure non-functional (dormant) beta cells that may be responsive to treatments. This work is important for patients because uptake of a radiotracer measured on a PET scan could guide treatment options. For example, if a patient has low beta-cell function with high signal in the PET scan, this could represent a patient with dormant beta cells that could respond to a treatment targeting existing cells. If a patient has low beta-cell function and low signal in the PET scan (very few viable or dormant beta cells present), that individual may be a candidate for beta-cell transplantation.”

Beta cells and neurological tissues have common cellular receptors and transporters, so, the Yale researchers screened brain radioligands for their ability to identify beta cells. Then, 12 healthy control subjects and two subjects with type 1 diabetes mellitus underwent dynamic PET/CT scans with six tracers.

The dopamine type 2/type 3 (D2/D3)-receptor agonist radioligand carbon-11 (11C)-(+)-4-propyl-9-hydroxynaphthoxazine (PHNO) was the only radioligand to demonstrate sustained uptake in the pancreas with high contrast versus abdominal organs such as the kidneys, liver, and spleen.

The results provide preliminary evidence that 11C-(+)-PHNO is a potential marker of beta-cell mass with 2:1 binding of D3 receptors over D2 receptors. While further research is needed before clinical application, 11C-(+)-PHNO is a promising way to differentiate the beta-cell mass of healthy individuals from those with type 1 diabetes mellitus, as well as track and guide therapies for diabetes patients.

Bini also points out, “These findings could facilitate development and wider dissemination of novel imaging methods in molecular imaging and nuclear medicine to assess receptor/enzyme pharmacology in diabetes and other endocrine disorders.”


This study was supported by National Institutes of Health (NIH) grant 1DP3DK104092-01 and was also made possible by NIH grant 1S10OD010322-01 and by Clinical and Translational Science Awards (CTSA) grant UL1 TR000142 from the National Center for Advancing Translational Sciences (NCATS) at NIH.
Calendar of Events

International Conference on Advanced Microbiology and Research
September 19 – 20, 2018 • Amsterdam, The Netherlands
https://microbiology.pulsusconference.com/

Hong Kong Hybrid PET-Imaging Symposium and Workshop 2018
September 29 – October 1, 2018 • Hong Kong
http://www.diaradio.hku.hk/pet2018/

88th Annual Meeting of the American Thyroid Association
October 3 – 7, 2018 • Washington, DC
https://www.thyroid.org/88th-annual-meeting-ata/

Pharmaceutics & Novel Drug Delivery Systems 2018
October 4 – 6, 2018 • Moscow, Russia
https://novel-drugdelivery-systems.euroscicon.com/

The 18th International Cancer Imaging Society
October 7 – 9, 2018 • Menton, France
https://www.icimaging society.org.uk/

EANM’18: 31st Annual Congress of the European Association of Nuclear Medicine
October 13 – 17, 2018 • Dusseldorf, Germany
https://eanm18.eanm.org/

World Congress on Breast Cancer 2018
October 15 – 16, 2018 • Rome, Italy
https://breastcancer.pulsusconference.com/

7th European Clinical Microbiology Congress
November 1 – 2, 2018 • London, UK
http://clinicalmicrobiology.alliedacademies.com/

World Congress on Bio-organic and Medicinal Chemistry
November 12 – 13, 2018 • Dubai, UAE
https://bioorganic-medicinal.chemistryconferences.org/

Joint Meeting of the British Nuclear Medicine Society and Irish Nuclear Medicine Association
November 19, 2018 • Dublin, Ireland