President’s Report

Katherine Zukotynski, MD, FRCP
PET CoE President

Dear Friends and Colleagues,

I have been reflecting on the relationship between balance and change in the context of medicine. Balance implies a weighing of variables to find the perfect blend, while change is one of the few dependable things in life. As such, I suspect maintaining balance is an ongoing endeavor that is likely both a science and an art, and it’s indispensable to governing those forces swirling around us.

The concept of balance in medicine is ancient. Indeed, Asclepius, the Greek demi-god of medicine was killed by a thunderbolt from Zeus because his medical skills posed a threat to the balance between man and god. Today, his staff remains one of the best-known symbols of medicine, although it is often confused with the caduceus, or staff, of Hermes. Interestingly, the staff of Asclepius is a rod entwined by a single snake, while the staff of Hermes is a rod with two snakes that may suggest balance within the realm of commerce and negotiation.

Balance manifests in medicine in ways I cannot begin to explain. At the most basic level, there is work-life balance, financial balance, and balance with family, friends and colleagues. Then, of course, there is the weighing of new versus old equipment, the relative values of SPECT versus PET for a particular patient, the benefits of treatment versus the effects of toxic side effects on quality of life, and even the roles of radiology versus nuclear medicine.

For example, in the October issue of The Journal of Nuclear Medicine, two articles are devoted to the future of nuclear medicine education. Questions remain: Should nuclear medicine be incorporated into medicine, radiology, both or go it alone? What will result in

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Somatostatin Receptor PET Radiotracers

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Introduction

$^{68}$Ga-DOTATATE ($[^{68}$Ga-DOTA$^0$-Tyr$^3$]-octreotate) or NETSPOT® (Advanced Accelerator Applications, Saint-Geny-Pouillet, France) is one of a group of “DOTA-peptides” for PET imaging that includes $^{68}$Ga-DOTATOC and $^{68}$Ga-DOTANOC. The DOTA-peptides are $^{68}$Ga-labeled DOTA-chelated somatostatin-receptor-agonist radiotracers used for PET imaging of somatostatin-receptor-positive tumors. $^{68}$Ga-DOTATATE is the first in that group to achieve FDA approval (in 2016), and is indicated for localization of somatostatin-receptor-positive neuroendocrine tumors in adult and pediatric patients. $^{68}$Ga-DOTATOC and $^{68}$Ga-DOTANOC are investigational at this time.

Imaging with these radiotracers capitalizes on the high density of somatostatin-receptor (SSTR) expression on the cell surface of neuroendocrine cells. Gastroenteropancreatic neuroendocrine tumors (GEP-NETs) comprise the largest subgroup of neuroendocrine tumors (NETs).(1)

The first widely available functional imaging agent tailored for these tumors was the γ-emitter SSTR analog $^{111}$In-pentetreotide (Octreoscan®). The development of the $^{68}$Ga-labelled DOTA-peptides for PET has enabled higher resolution and higher sensitivity imaging, as well as faster imaging that is lower in radiation dose. An additional benefit is the radionuclide availability from a $^{68}$Ge/$^{68}$Ga generator rather than cyclotron.(2) PET also offers quantitative assessment of uptake. Receptor-based imaging plays an essential role in identifying eligible patients for peptide receptor radionuclide therapy (PRRT) with $^{90}$Y or $^{177}$Lu-labelled DOTA-peptides, as uptake of the diagnostic agent correlates with uptake of the therapeutic radiopharmaceutical and treatment outcome.

Biodistribution

Normal uptake of $^{68}$Ga-DOTATATE is seen routinely in the following

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The most innovative, capable practitioners and advance the field, improving the lives of more patients? What is the optimal course and length of study?

Winds of change swept through SNMMI this year. An example you will shortly see is our mid-winter meeting. Scheduled for January 25-27 in conjunction with the ACNM annual meeting in Orlando, Florida, SNMMI programming will be devoted to theranostics. A few additional CE sessions will be offered, and the PET CoE has organized a two-hour block of lectures on novel PET radiotracers including, somatostatin receptor PET in neuroendocrine tumor management and appropriate use criteria for somatostatin receptor PET in this setting, applications of PSMA imaging in prostate cancer and non-prostate malignancies and novel PET radiotracers for breast imaging. The AACR-SNMMI joint conference will be held soon after—February 14-17—in San Diego, California, and will focus on state-of-the-art molecular imaging in cancer biology and therapy. Both meetings promise to bring new experiences, and we hope to see you there!

In this issue of our newsletter, we emphasize neuroendocrine imaging, a rapidly changing area where PET plays a central role. Moving forward, we plan to discuss advancements in PET with a practical and, hopefully, balanced approach to make it easier for you to incorporate change in your practice.

Change requires us to continually reevaluate and reset our balance point. That’s a good thing. The PET CoE strives for innovation, balance and inclusivity. We welcome input and feedback from everyone in the field. I am deeply grateful for those around me who share their perspectives and insights. They help me weigh factors and make decisions with a clearer eye. Please do not hesitate to reach out should you wish to be more active in our community!

Somatostatin Receptor PET Radiotracers (Continued from page 1.)

organs: pituitary (mild/moderate); thyroid (mild); liver (mild/moderate); adrenal glands (moderate); spleen (intense); pancreatic uncinate process (mild/moderate); pancreatic body, tail, head (mild); bowel (mild); and urinary system (intense). Excretion occurs almost entirely through the kidneys.(3)

Indications for Use

Somatostatin receptor PET/CT is indicated for imaging of NETs arising from the gastroenteropancreatic, bronchial, and sympathoadrenal tissues. GEP-NETs have been classified by the WHO into three histologic grades based on cellular differentiation, mitotic rate, and proliferation (represented by Ki-67 index): Grade 1 (G1) tumors are well-differentiated and slow growing (Ki-67< 2%, mitotic count < 2); G2 tumors are well-differentiated but show more heterogeneity and aggressiveness (Ki-67 between 2% and 20%, mitotic count of between 2 and 20); and G3 tumors are poorly differentiated, aggressive, and confer poor survival (Ki-67 > 20%, mitotic count> 20). G3 tumors are often so dedifferentiated that they lose SSTR expression and the ability to take up the SSTR analog radiotracer. G3 tumors are, therefore, better imaged with FDG, a “flip flop” phenomenon.(4) Functional imaging characteristics of tumors are thus predictive of tumor grade, even when the histology is unknown.(5)

Appropriate use criteria for SSTR PET imaging were recently published. (6) The use of SSTR PET/CT is considered appropriate and recommended for initial staging of NETs, including localization of unknown primary tumor, selection of patients for PRRT and restaging of patients at the time of clinical progression or new indeterminate lesions on conventional imaging. Evaluation of patients with biochemical evidence and symptoms of NETs without prior NET diagnosis. Negative conventional imaging is also considered appropriate, although the yield of somatostatin receptor PET imaging in this scenario is low.(6) More research is needed to address the use of somatostatin receptor PET in monitoring of NET patients with disease visible on conventional imaging.

Nuclear imaging for pediatric neuroblastoma staging is first performed with 123I-MIBG. However, when tumors dedifferentiate to the point of losing norepinephrine (NE) transporters and their ability to take up 123I-MIBG, these tumors may be imaged with 68Ga-DOTA-peptides. Medullary thyroid carcinoma is rare compared with other forms of cancer arising from the thyroid. Due to its origin from parafollicular calcitonin-secreting cells, the tumor notably lacks the ability to take up radioiodine. Cellular expression of NE transporters and SSTRs is high, lending itself to functional nuclear imaging for staging and detection of recurrence.(7)

Protocol

The recommended dose for 68Ga-DOTATATE in adults is 2 MBq/kg of body weight up to 200 MBq. The radiotracer is intravenously injected with a 60-minute uptake period. The patient is typically scanned from skull vertex to midthigh. Controversy persists over temporary discontinuation of “cold” octreotide therapy before the scan. However, the SNMMI 68Ga-DOTAXXXX Positron Emission Tomography (PET) for Diagnosis, Staging and Measurement of Response to Treatment in Somatostatin Receptor-Positive Neuroendocrine Tumors Imaging Manual (2014) advises scheduling scans at the end of the monthly long-acting octreotide treatment cycle and at least 12 hours after the last injection of short-acting octreotide.(8) There are no dietary or activity/exercise restrictions as there are for FDG PET. Anxiolytics such as alprazolam may be given for anxiety.

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Interpretation, Pearls, and Pitfalls

Accurate interpretation depends on the origin and histology of tumors, familiarity with metastatic patterns, and awareness of causes of falsely positive and negative exams. (9) Knowledge of patterns of tumor spread can guide the search for metastatic lesions and unknown primary tumors. Gastrointestinal NETs frequently metastasize to the liver and regional lymph nodes, with metastasis to bone and lungs less common. Pulmonary carcinoids frequently metastasize to lymph nodes, liver, and bones. (10)

Increased focal uptake outside the normal distribution of the $^{68}$Ga-DOTATATE is considered positive for NETs. False-positive uptake can occur in the setting of inflammation due to SSTR expression on white blood cells. (4) Osteoblasts express SSTRs, so the osteoblastic activity associated with degenerative bone disease, fractures, hemangiomas, and growth plates show uptake. (4)

Islet cells of the pancreas express SSTR subtype 2 receptors in variable amounts with highest concentration in the uncinate process. Prominent uncinate uptake can be seen in up to a third of patients. (4) This finding can be a potential pitfall for imagers less familiar with SSTR PET imaging, as it is rare on SSTR SPECT imaging. (4) The SUVmax in normal pancreatic uncinate process can be as high as 17. (11) In ambiguous cases, correlation with good cross-sectional imaging, such as contrast CT or MRI, is essential to exclude tumor. Splenules and splenosis show intense uptake and can complicate interpretation, particularly when the splenic tissue is in an unusual site or is intrapancreatic. (4)

Knowledge of non-neuroendocrine tumors that express SSTRs is important for accurate study interpretation. Meningiomas are relatively common and can be identified incidentally, with even greater sensitivity than MRI (4). There is an increasing role for $^{68}$Ga-DOTATATE in delineating the boundaries of aggressive meningiomas. (4) Some lymphomas express SSTRs, which can complicate interpretation, particularly when disease patterns overlap with that of NETs. Mild SSTR expression is also known to occur in breast and prostate cancer, as well as some other types of tumors. (9)

False negatives occur due to small lesion size (less than 5-7 mm), effects of recent cytotoxic treatment, and receptor-negative disease (such as G3 NETs). The high physiologic uptake of some organs can obscure pathologic uptake. (3) A significant portion of pancreatic insulinomas, particularly those with more benign features, have been reported to evade detection by SSTR imaging. (3, 4)

What the ordering physician needs to know

The sensitivity of the SSTR PET/CT is quite high ranging from 82-100%, higher than for γ-emitter SPECT imaging. (5) Where possible, SSTR PET/CT should be pursued over γ-emitter imaging, as a change in management in over 70% of patients has been reported with PET-based imaging. (5) Given the inherently higher sensitivity, care must be taken in declaring new or progressive disease when comparing to prior SPECT or other conventional imaging. (1)

References:

Pediatrics Corner

Pediatric Malignant Granular Cell Tumor Characterized Using FDG PET/CT: A Case Study

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History

A 17-year-old male presented with swelling and pain in his left foot. Previously, this patient had several surgical resections performed outside of the country for what had been thought to be a benign tumor in his left foot. A chest, abdomen, and pelvis CT scan revealed multiple bony lesions throughout the skeleton, and biopsy confirmed a malignant granular cell tumor (GCT). A staging FDG PET/CT then showed multiple metastatic bony and soft tissue lesions, with the left foot being the most likely site of primary disease (Figure 1).

Other significant findings included lymphadenopathy in the left lower thigh, an expansile lytic lesion in the left anterior sixth rib, and multifocal skeletal lesions throughout the skeleton (Figure 2). He was then treated with chemotherapy that was tailored based on a personalized oncogenomics trial.

Subsequent PET/CT scans were performed throughout the patient’s treatment to assess response. Unfortunately, the patient showed continual disease progression throughout treatment (Figure 3) and was eventually placed on palliative care.

Discussion

GCTs are rare soft tissue neoplasms of neural origin. They are typically benign and seldom found at the extremities. Malignant GCTs, such as the one described above, tend to have poor prognosis and high chance of recurrence and metastasis. Due to the aggressive nature of malignant GCTs, it is important to differentiate between malignant and benign GCTs early on to improve prognosis. The literature suggests that FDG PET/CT may be a good candidate for this evaluation, as it has been able to correctly identify and characterize metabolic activity of malignant GCT. However, current information regarding use of PET/CT on pediatric granular cell tumors is minimal, and frontline management typically includes CT scans, biopsy, and wide-local excision.

In this case, PET/CT accurately identified the primary site of disease and characterized metastases. It also provided valuable insight into response to different treatments over time and helped inform changes to therapy, thereby improving efficiency and efficacy of patient care.

References

Neuroendocrine cells produce hormones that regulate numerous important physiological processes. Although early detection of neuroendocrine tumors (NETs) is still difficult and conventional therapies have had limited success, the recent development of new detection methods, particularly those utilizing positron emission tomography (PET), has resulted in improved diagnostic and therapeutic strategies.

NETs overexpress somatostatin receptors, so targeted therapies with somatostatin analogues offer an effective strategy for treatment of NETs patients. Peptide-receptor radionuclide therapy (PRRT) using somatostatin analogues radiolabeled with lutetium-177 (177Lu) has shown great promise by increasing progression-free survival. However, access to this treatment is still limited and varies based upon location and institution. The hope is that as more trials are carried out and minimal toxicity and efficacy are demonstrated, this treatment will become the standard of care.

**Practical Aspects of Therapy: The Hamilton Health Sciences Experience**

The Hamilton Health Sciences Nuclear Medicine Department, which administers 177Lu therapy treatment, is equipped with three cameras, a hot-lab and a multi-purpose, non-imaging room. Prior to enrollment, patients undergo a gallium-68 (68Ga)-PET scan to identify those with somatostatin positive NETs. Creatinine and bloodwork are also done to evaluate kidney function, as kidney and bone marrow are the critical organs.

Qualifying patients are informed about the therapy and what to expect before signing their consent for treatment. Patient preparation includes stopping somatostatin analogues. Hydration is encouraged prior to the procedure to facilitate venous access and clearance of radioactive materials. There are no food restrictions and patients take prescribed anti-nausea medication.

Two IV lines are set up, and patients are pretreated with lysine and arginine prior to administration of therapy, which is infused over 4 hours. Minimizing radiation exposure to others by maintaining strict access and following time guidelines ensures that everyone is safely below the allowed exposure limits. Patients are isolated from caregivers for most of the day during therapy. They are, therefore, encouraged to bring entertainment in the form of books, music with ear phones, etc.

After the procedure, patients are instructed to maintain some distance from others, including family members (for example, sleeping in a different area and using a separate washroom). While in the department, and for days when imaging takes place, patients undergoing imaging/radiotherapy are given a dedicated radioactive washroom to minimize exposure to other patients. Active monitoring is performed throughout the day, and all patient-used facilities are frequently checked for contamination. Studies have shown that the caregiver remains within the public limit of 1 mSv per year. Radioactive waste is stored and allowed to decay prior to disposal per CNSC guidelines.

For patients, the main concern is the dose to bone marrow and kidneys. The half-life of 177Lu is 6.73 days, with an effective half-life of 4.2 days. Doses are set to keep within exposure limits for kidneys and bone marrow. Patients are kept in the department for 3 hours after injection. This ensures the allowable release limit, which was found to be ≤ 25 mSv/h at 1 m, reached in a mean time of 2.6 h (Bakker et al., Q. J. Nucl. Med. Mol. Imaging, 2006; 50(4): 265–71). Imaging is done at 4, 24, and 72 hours to coincide with 177Lu clearance. They are imaged using a SPECT/CT camera, which needs to be calibrated and peaked based on 177Lu prior to imaging. Four doses are

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AUC Update: Two new Appropriate Use Criteria

SNMMI has published two more appropriate use criteria (AUC) as part of a series of new AUC developed by the society in its role as a qualified provider-led entity (PLE) under the Medicare Appropriate Use Criteria Program for Advanced Diagnostic Imaging. The new AUC are for

- **FDG PET/CT restaging and response assessment of malignant disease** and,
- **Somatostatin receptor PET imaging**, which addresses several clinical scenarios for diagnosing neuroendocrine tumors (NETs).

The other recently released AUC are for **bone scintigraphy in prostate and breast cancer; ventilation/perfusion (V/Q) imaging in pulmonary embolism**, which is endorsed by the American College of Emergency Physicians; and **hepatobiliary scintigraphy in abdominal pain**.

The new AUC are intended to assist referring physicians and ordering professionals in fulfilling the requirements of the 2014 Protecting Access to Medicare Act (PAMA). Current regulations call for PAMA to require referring physicians to consult AUC developed by a PLE beginning January 1, 2018, to ensure cost-effective and appropriate utilization of advanced diagnostic imaging services. However, the Centers for Medicare & Medicaid Services has proposed pushing back the start date for when providers will be required to consult AUC to January 2019.

The FDG PET/CT Workgroup consisted of expert representatives from SNMMI, the European Association of Nuclear Medicine (EANM) and the American Society of Clinical Oncology (ASCO).

To develop the somatostatin receptor PET imaging AUC, SNMMI worked collaboratively with EANM, the European Neuroendocrine Tumor Society (ENETS), the American Gastroenterological Association (AGA), the American Society of Clinical Oncology (ASCO), the American College of Radiology (ACR), the National Comprehensive Cancer Network (NCCN), the American Joint Committee on Cancer (AJCC), the North American Neuroendocrine Tumor Society (NANETS), the National Cancer Institute (NCI), the Endocrine Society, the American Association of Engineering Societies (AAES), and the Society of Surgical Oncology (SSO).

The workgroups reviewed the scientific literature and developed consensus recommendations for the clinical use of these technologies. The Oregon Health Science University’s (OHSU) Evidence-based Practice Center conducted a systematic review of existing evidence based on the scope and parameters set by the workgroups, which the workgroups then used to make their recommendations for clinical use.

The SNMMI Guidance Oversight Committee is also developing AUC for gastrointestinal transit, infection imaging, PET myocardial perfusion imaging, prostate cancer imaging, and thyroid imaging and therapy.

For background and a detailed explanation of the AUC development process, click here. An abbreviated version of the FDG-PET/CT AUC will be published in the December 2017 issue of *The Journal of Nuclear Medicine*, and the somatostatin receptor PET imaging AUC will be published in the January 2018 issue.

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administered 6 to 12 weeks apart with 200 mCi to start, and subsequent doses are calculated based on individual dosimetry, up to a max of 300 mCi.

Staff also receive training in handling, preparation and administration of therapies. Personnel are thoroughly monitored and ALARA is practiced by maintaining distance and shielding. Beta emissions are blocked by the patient, while gamma exposure is minimized by distance. Ring- and whole-body dosimeters are worn at all times. Dose rates in the preparation and administration of 400 mCi treatments – 7.4 GBq – have been reported to be below 10 percent of annual dose limits (Bakker et al.).

The challenge is to keep the flow of the department going around these studies. A dedicated space is optimal, but not always possible when hospital real-estate, including rooms and hot-lab, are limited. Ideally, patients are coming at a time when volume is low. Scheduling is typically affected, as rooms adjacent to the therapy room are not booked to prevent exposure to other patients.

Doses for other studies should be drawn up earlier, or a separate shield should be used to minimize contamination risk and exposure. It’s also important to ensure that amino acids arrive on time, and the dose is ready for administration. The reality is that these patients could potentially be so ill that they are unable to come in for their injection. This plays havoc with scheduling and cost concerns. Multi-disciplinary teams need to track patients carefully and try to anticipate adverse circumstances.

Centers with a dedicated therapy space may not encounter some of the above issues, but those that are integrating $^{177}$Lu therapy into their practice using existing facilities may need to juggle resources.

These studies take considerable co-ordination among multi-faceted teams that include oncologists, research staff, pharmaceutical suppliers, radiation safety officers, nuclear medicine physicians and technologists. These collaborations are vital, as recent technological advances have resulted in a shift towards individualized, precision medicine. As care providers, we need to adapt to such advances in order to provide the best possible care for our patients.
Neuroendocrine tumors (NETs) are a heterogeneous group of malignancies characterized by high disease complexity (1). Each year an estimated 8,000 individuals are newly diagnosed with NETs in the United States, and the annual incidence is rising; there has been a five-fold increase since 1973 (2). NETs arise from neuroendocrine cells that are distributed throughout the body. Aggressive forms of NETs are uncommon; the tumors are mostly well-differentiated and slow-growing (3).

Patients may present with symptoms related to inappropriate peptide or amine hypersecretion, but the majority of NETs are nonfunctioning. This characteristic can delay diagnosis and increase the likelihood of the disease only being discovered at an advanced stage (4).

The most common type of NETs originates in the gastroenteropancreatic tract (GEP-NETs), but a large number of subtypes exist, including pheochromocytomas, paragangliomas, medullary thyroid cancer, Merkel cell cancer, and bronchial carcinoids (5).

Somatostatin receptors are high-affinity G-protein-coupled membrane receptors expressed in neuroendocrine cells (6). Since it was discovered that well-differentiated NETs express high levels of somatostatin receptor (SSTR), specifically subtype 2 (7), interest in SSTR-targeted imaging has increased. SSTR scintigraphy imaging, first with iodine-123 (123I) labeling, followed by indium-111 (111In) and Tc-99m (99mTc) labeling, has been used for more than 20 years. Different studies have reported various tumor-detection rates ranging from 50 percent to 100 percent (8). Gallium-68 (68Ga)-DOTA peptides (eg, DOTATATE, DOTANOC, and DOTATOC) selectively bind SSTR receptors and, among them, DOTATATE has the highest in vitro affinity for SSTR type 2 (9).

Recent studies have demonstrated the high sensitivity and specificity of 68Ga-DOTATATE for imaging neuroendocrine tumors and higher accuracy compared with 111In-pentetreotide scintigraphy (10-12). Furthermore, the additional information provided by 68Ga-DOTATATE PET/CT has been shown to alter management of patients with neuroendocrine tumors (13,14).

Usually, when there is suspicion of NETs, the diagnostic workup involves morphologic imaging such as CT, ultrasonography, or MRI. Even though CT is widely available and less expensive than MRI, it exposes patients to ionizing radiation and is less sensitive than MRI in NET imaging in solid organs (7,15).

Within the last few years, integrated PET/MRI scanners have become available for clinical use. Hybrid PET/MRI is a promising diagnostic tool in this setting, having the ability to combine the high sensitivity and specificity of PET SSTR-specific radiotracers with the equally important MRI image resolution and great soft tissue contrast. In addition, administration of an MRI contrast agent such as gadoxetate disodium greatly increases the sensitivity of the examination.

Figures 1 and 2 below show two cases of metastatic GEP-NETs with involvement of liver and retroperitoneum. They illustrate why hybrid PET/MRI should be routinely performed in cases of liver dominant NETs.

![Figure 1](https://example.com/figure1.png)  
**Figure 1.** Case 1: A 64-year-old woman with well-differentiated, functional, mesenteric carcinoid (Ki-67: 7 percent) and metastatic disease at diagnosis (liver, lymph nodes, bone and mid-esophageal involvement). She was treated with octreotide and PRRT. 68Ga-DOTATATE PET/CT followed by PET/MRI were done for evaluation of extent of disease. PET/MRI MIP (A), PET/CT MIP (B), transaxial PET images (C), transaxial T1 LAVA-Flex MRI images (D) and transaxial fused PET/MRI (E) showed markedly increased 68Ga-DOTATATE uptake throughout the liver and multiple sites of retroperitoneal lymphadenopathy. Transaxial low-dose non-contrast-enhanced CT (F) did not identify liver metastases.

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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. Additional news articles can be found online at www.snmmi.org under “MI: Making a Difference.”

Subjective Cognitive Decline Associated with Tauopathy and Global β-Amyloid Burden
Neurology Advisor

PET study shows oxytocin failing to aid serotonin in the autistic brain
Health Imaging

Promising new prostate cancer test developed
MedicalXpress

Brain Inflammation Tied to Depression, Suicidal Thoughts
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Menopause can cause changes in brain linked to Alzheimer’s
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Imaging agents developed to better monitor growth of tumours
Phys.org

PSMA-PET Agents Poised to Advance Imaging in Prostate Cancer
Onclive

Positron Emission Tomography Offers Diagnostic Value in Myocardial Ischemia
Cardiology Advisor

Fluciclovine (18F) PET/CT scan led to change in treatment plan for 61 percent of patients: Blue Earth Diagnostics
DOTmed – Healthcare Business News

PET/CT a dependable differentiator of types, origins of space-occupying brain lesions
Health Imaging

(PET/MR Corner. Continued from page 7.)

Figure 2, Case 2: A 47-year-old woman with a history of well-differentiated pancreatic neuroendocrine tumor with liver metastases. She underwent distal pancreatectomy + splenectomy + microwave ablation of hepatic lesions, followed by octreotide after surgery. Hepatic steatosis and fibrosis made it difficult to visualize liver disease on CT scan or MRI. 68Ga-DOTATATE PET/CT followed by PET/MRI were done for evaluation of extent of disease. PET/MRI MIP (A), PET/CT MIP (B), transaxial PET images (C) transaxial T1 LAVA-Flex MRI images (D) and fused PET/MRI (E) demonstrated multiple 68Ga-DOTATATE avid metastatic lymph nodes. Fused images also showed many foci of uptake throughout the liver (F). The liver metastases were not seen on transaxial low-dose non contrast-enhanced CT (G).

References
Clear communication between healthcare professionals is an irrefutable prerequisite for the provision of excellent and efficient care. Clinical information on requisitions for diagnostic imaging examinations is an integral part of communication between referring clinicians and diagnostic imaging physicians. An excellent requisition ensures a clear imaging study report with the necessary answers to the clinical questions posed, as well as adequate steps by the imaging team to deliver an optimized, tailored study in a timely manner.

Reasons for requisitions of poor quality include undisclosed details, clerical transcription errors in order-entry systems, lack of specificity, and overly specific acronyms or jargon (1). Inadequate requisitions are a growing problem in diagnostic imaging that is exacerbated by expanding lists of studies, increased study images and turn-around time requirements which exert increasing pressure on the imaging physician’s time (1). Despite this, a PubMed search for the terms “radiology” and “requisition” yielded only 12 results within the past 5 years, and only 4 were truly specific to the query terms. The search terms “nuclear medicine” and “requisition” yielded only 2 repeat results. Although by no means rigorous, given the potential for medical errors, unnecessary delays, and inappropriate examinations, this simple look-up exercise underpins a need for further work on this topic.

The importance of excellent clinical information on requisitions is even greater when the imaging scans requested enter the realm of costly, complex, and restricted. As the integration of PET/CT and PET/MRI becomes increasingly warranted for oncology, cardiac, and neurological patients (the three most popular application areas), it is even more imperative to tighten up efficiency and ensure appropriateness of scans ordered. Protocolling of requisitions is key to enabling triage and timely access with the best, cost-effective study for the clinical indication. Suboptimal protocolling can result from lack of adequate clinical information, which can, in turn, lead to numerous detrimental impacts, including delays in care, rescheduling call-back studies to complete assessment, loss of time for the healthcare system and the patient, increased costs, and potentially higher radiation exposure or medical risk (e.g. contrast media administration, sedation, etc.) among other detrimental impacts (2).

The need for improved quality of clinical information on requisitions is not exclusive to integrated imaging modalities; it’s crucial to all protocolled imaging studies. We must be proactive about providing clear communication and accurate, detailed requisitions.

References
Italian researches have demonstrated a better way of determining the aggressiveness of tumors in patients with advanced non-small-cell lung cancer (NSCLC). In a study presented in the featured clinical investigation article of the November issue of *The Journal of Nuclear Medicine*, they used 18F-fluorodeoxyglucose (FDG) PET/CT imaging to show that the amount of cell-free tumor DNA circulating in the bloodstream correlates with tumor metabolism (linked to cancer aggressiveness), not tumor burden (amount of cancer in the body).

According to the American Cancer Society, lung cancer is the leading cause of cancer death among both men and women, causing roughly 1 out of 4 cancer deaths. NSCLC represents approximately 85 percent of lung cancer cases. More than 22,000 new cases are expected this year in the United States, and the disease is expected to claim more than 155,000 lives.

“Despite the identification of circulating tumor cells (CTCs) and cell-free DNA (cfDNA) as biomarkers capable of providing clinically relevant information in cancer patients, at present their identification is not routinely used in clinical practice,” explains Silvia Morbelli, MD, PhD, of the IRCCS San Martino – IST National Cancer Research Institute and University of Genoa in Genoa, Italy.

This study of 37 patients (24 men and 13 women, ages 51 to 80) who had never been treated with chemotherapy found direct correlation of the amount of cfDNA with tumor metabolism (based on PET-derived parameters), but not with metabolic tumor volume. These results suggest that cfDNA might better reflect tumors’ biological behavior and aggressiveness than tumor burden in metastatic NSCLC.

The researchers noted that a subgroup of 13 patients had metabolically active bone lesions and also higher levels of cfDNA. In addition, while cfDNA correlated with tumor metabolism, no association was found with circulating tumor cells (CTCs). Previous investigations have suggested that cfDNA and CTCs might provide complementary information about tumor biology. The small size of this study means that no definitive conclusions could be made regarding the role of CTCs in NSCLC metabolism.

Morbelli points out, “Our findings illustrate the prognostic value of 18F-FDG and provide a deeper understanding of clinically reliable, noninvasive biomarkers that may help identify potential unresponsive NSCLC patients before treatment and limit unnecessary toxicity.”

*The authors of “Circulating tumor DNA reflects tumor metabolism rather than tumor burden in chemotherapy-naive patients with advanced non-small cell lung cancer (NSCLC): 18F-FDG PET/CT study” include Silvia Morbelli, Giulia Ferrarazzo, Francesca Bongioanni, Roberta Piva, Alberto Nieri, Matteo Bauckneht, and Gianmario Sambuceti, IRCCS San Martino – IST National Cancer Research Institute and University of Genoa, Genoa, Italy; Angela Alama, Simona Coco, Carlo Genova, Erika Rijavec, Federica Biello, Maria Giovanna Dal Bello, Giulia Barletta, Irene Vanni, and Francesco Grossi, IRCCS AOU San Martino – IST National Cancer Research Institute; and Michela Massollo, EO Galliera Hospital, Genoa, Italy.*

Figure: Representative examples of two patients enrolled in present study. (A and B) Two coronal and transaxial sections of 18F-FDG PET/CT scan of 73-y-old woman with stage IV NSCLC (adenocarcinoma; free circulating tumor DNA (cfDNA) level, 462 hTERT copy numbers; 3 CTCs/3 mL). (A) Primary lesion that highly concentrated 18F-FDG in left lung (maximum diameter [dmax], 49 mm; SUVmax, 7.2; MTV, 82.4 mL). (B) Small bone lesion in left scapula (dmax, 10 mm; SUVmax, 5.7; MTV, 5 mL). (C and D) 18F-FDG PET/CT scan of 70-y-old man with stage IV NSCLC (adenocarcinoma; cfDNA level, 113 hTERT copy numbers; 3 CTCs/3 mL). (C) Primary lesion that moderately concentrated 18F-FDG in left lung (dmax, 83 mm; SUVmax, 4.9; MTV, 193.2 mL). (D) Multiple mediastinal and cervical lymph nodes (dmax of largest lymph node, 30 mm; SUVmax, 3.2; MTV, 65 mL). Patient shown in A and B had lower tumor burden (as expressed by MTV) but higher SUVmax and cfDNA levels than patient shown in C and D. Credit: Silvia Morbelli, et al., San Martino Hospital, University of Genoa, Italy.
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Calendar of Events
2018 SNMMI Mid-Winter Meeting & ACNM Annual Meeting
January 25 – 27, 2018 • Orlando, Florida
http://www.snmmi.org/mwm2018

EANM Focus Meeting 1 - The International Conference on “Molecular Imaging and Theranostics in Prostate Cancer”
February 1 – 3, 2018 • Valencia, Spain
http://focusmeeting.eanm.org/

AACR-SNMMI Joint Conference on State-of-the-Art Molecular Imaging in Cancer Biology and Therapy
February 14 – 17, 2018 • San Diego, California
http://imagecancer2018.org/

MediSens Conference 2018 – The European Medical Imaging Conference
February 26 – 27, 2018 • London, England
http://medisens-conference.com/

2018 High Country Nuclear Medicine Conference
March 3 – 7, 2018 • Sun Valley, Idaho
http://www.hcnmc.org/

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