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Superior Cell Isolation Using a Novel Microfluidics-based Cell Separation System for Leukocyte Radiolabeling*

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Background: Hydroxyethyl starch (hetastarch) augmented gravity sedimentation (conventional method) is commonly used for leukocyte isolation for white blood cell scintigraphy. The time required to separate leukocytes from whole blood using the conventional method is 1-2 hrs. Microfluidic cell isolation relies on microchannels and microstructures to fractionate blood into its constituents and can isolate leukocytes from 40-50 mL whole blood in 30 minutes or less. Data on labeling efficiency, label stability, and cell viability for microfluidic-isolated leukocytes are lacking. The aims of this institutional review board approved prospective investigation are to compare purity, labeling efficiency, label stability, and viability of leukocytes isolated with the conventional method to those isolated with an automated microfluidic method.

Methods: 80 mL peripheral blood was collected from 8 healthy donors (3 male, 5 female) on 2 separate occasions, 48 hours apart, once for labeling with ^{111}In-oxine and a second time for labeling with ^{99m}Tc-exametazime. From each blood draw, 40 mL was processed using the conventional method, including a fixed separation time of 90 minutes, and 40 mL was processed using microfluidic isolation. Leukocyte viability using trypan blue and leukocyte purity (percent of leukocytes in total cells in the isolate) using calcein AM staining were determined. Leukocytes were then labeled either with ^{111}In-oxine or ^{99m}Tc-exametazime. Labeling efficiency, leukocyte viability (immediately post labeling and 1, 2, 4 hrs. after labeling), and label stability of cells in plasma (1, 2, 4 hrs. after labeling) were determined. Two-tailed Student t-test was used to compare the two methods for each parameter evaluated. Significance was established as $p \leq 0.05$.

Results: Microfluidic isolation separated leukocytes from 40 mL whole blood in 23.0 ± 0.9 minutes vs. the fixed 90 minutes for the conventional method. Total processing time (time between blood draw and beginning radiolabeling) was 38 ± 6 minutes for microfluidic isolation vs. 127 ± 15 minutes for conventional method. Purity of microfluidic isolate, 96.2 ± 3.2 %, was significantly higher than that of the conventional method isolate, 8.3 ± 2.9 %. Majority of the impurities in the conventional method isolate were platelets. Labeling efficiency and leukocyte viability were comparable for the two methods, while label stability was improved in cells isolated with the microfluidic method compared to the conventional method (Table).

Conclusion: Microfluidic isolation is faster than the conventional isolation method, with comparable labeling efficiency and leukocyte viability, and significantly higher isolate purity and improved label stability. Despite similar labeling efficiency between the methods, the microfluidic approach results in cell isolates that are far superior in WBC purity. We hypothesize that using microfluidic isolation the radiopharmaceutical is concentrated in the leukocytes, while in the conventional method the radiopharmaceutical accumulates in red cells and platelets as well as leukocytes. Further experiments will be required to evaluate this hypothesis.

+Dr. Palestro receives research funding from MicroMedicine.

***First Prize – Dr. Hussein M. Abdel-Dayem Award**

Striatal Dopaminergic Neuronal Loss and the Neurovascular Unit in Parkinson Disease.*

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Background: Parkinson Disease (PD) is the second most common neurodegenerative disorder and the most common movement disorder. The pathophysiology of PD is related to loss of dopaminergic neurons in the substantia nigra. The neurovascular unit (NVU) is composed of endothelial cells, blood-brain barrier tight junctions, pericytes, and parenchymal cells such as astrocytes and neurons, and links vascular perfusion and neuronal function in the brain. NVU dysfunction, associated with a decrease in relative cerebral blood flow (rCBF), has been proposed as an early pathophysiologic mechanism in PD. In this project we investigated these pathophysiologic mechanisms using combined [C-11]-PE2i (N-(3-iodoprop-2E-enyl)-2b-carbomethoxy-3b-(4-methyl-phenyl)nortropane) (PE2i) PET and arterial spin labeling (ASL) MR imaging.
PE2i, a cocaine analog, binds dopamine transporters with high specificity, allowing for highly accurate and specific quantification of dopamine transporters. ASL allows non-contrast-MRI-based assessment of cerebral perfusion and is based on the principle of magnetically labeling protons in arterial blood prior to their entry into the tissue of interest. It allows estimation of cerebral blood flow and thus of NVU integrity.
Methods: 27 patients with an established clinical diagnosis of PD were enrolled in the study. All patients underwent 3D-pseudo-continuous ASL MRI on a 3.0 Tesla Siemens Prisma MRI scanner. Post-processed rCBF maps were aligned to the Montreal Neurological Institute (MNI) T1-weighted template, allowing for region-of-interest (ROI)-based rCBF analysis (Figure 1). A subcohort of patients (N=17) underwent PE2i PET/CT on a 64 slice Siemens Biograph mCT scanner per institutional research protocol following injection of 200 MBq/5.4 mCi PE2i. Processing in FreeSurfer 6.0 was performed for ASL and PET images in order to obtain mean PET standardized uptake values (SUV) for the same ROI (Figure 2). Pearson correlations and Mann-Whitney tests were performed for statistical analysis.
Results: We identified a trend for lower rCBF values and mean SUV in regions known to be affected in PD (putamen, caudate, globus pallidus) in patients with disease duration greater than 5 years. This trend was not apparent in reference regions (cerebral WM, cerebellar cortex, cerebellar WM) (Figure 3). Stratifying the patients based on MoCa scores (stratified into $\geq$27 vs <27), we identified a trend for higher rCBF values in patients with higher MOCA scores in 8/12 analyzed regions. There was statistically significantly lower PE2I avidity in the higher MOCA score group in the bilateral caudate and left putamen ($p < 0.05$). Supratentorial rCBF values additionally demonstrated a weak, negative correlation with striatal PE2 avidity (R = -0.49 to - 0.57).
Discussion: Our ROI-based analyses suggest that longer disease duration is associated with lower rCBF and lower PE2i mean SUV, implying greater NVU dysfunction and greater dopaminergic neuronal loss, respectively. Correlative studies of ASL and PE2i PET data further suggest that dopaminergic neuronal loss may precede or in fact be independent from cognitive impairment.
Conclusion: Combined ASL MRI and PE2i PET imaging could inform future prospective clinical trials providing an improved mechanistic understanding of the disease. Our findings suggest that this combined imaging can lay the foundation for the development of an early disease biomarker and a potential therapeutic target.
***Second Prize – Dr. Hussein M. Abdel-Dayem Award**

Utility of integrated 18F-FDG PET/CT in systemic staging of newly diagnosed stage IIA or higher breast cancer: a single institutional retrospective review*

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Background: National Comprehensive Cancer Network (NCCN) guidelines recommend CT chest abdomen and pelvis with contrast and bone scan (CTBS) for staging of patients with localized breast cancer (cT0-4N1-3 or T2-4N0) who are candidates for preoperative systemic therapy (PST), whereas 18FDG PET/CT (PET) is considered "optional" in circumstances where CTBS are equivocal or suspicious. Prior studies reported greater sensitivity of PET than CT for detection of locoregional lymph node (LN) and distant metastases (DM) (PMID 23640467) and greater accuracy than BS in detection of bone metastases (PMID 20516453). This study evaluates upstaging after PET in patients with cIIA or higher breast cancer, most of whom received PST.
Methods: In this Institutional Review Board-approved retrospective study, we performed medical record abstractions to identify all adult female patients with cIIA or higher breast cancer diagnosed at Montefiore Medical Center from January 1, 2014 to January 1, 2019 who underwent PET prior to PST or adjuvant therapy. The initial clinical stage was determined from physical exam, mammography, breast sonography and magnetic resonance imaging. PET was evaluated to identify unsuspected LN and DM. The proportion of patients upstaged overall stratified by stage was calculated. We also obtained the Medicare reimbursement (MR) rates of each scan from our institution patient financial office.
Results: A total of 283 patients including 3 with bilateral breast cancer who met the study inclusion criteria were evaluated. The mean age at diagnosis was 59.8±14.2 and the most common tumor histology was invasive ductal carcinoma (245, 86%). There were 124 (43%) ER+/Her2-, 95 (33%) ER-/Her2-, 37(13%) ER+/Her2+, and 30 (10%) ER-/Her2+ tumors. Most patients received PST after staging with PET scan and before surgery, including chemotherapy in 72% (plus anti-HER2 therapy in 24%) and endocrine therapy in 8%. The overall percentage of patients with upstaging based on LN and DM was as follows: cIIA-16/77 (21%) LN only; cIIB-28/108 (26%) LN and 12/108 (11%) DM; cIIIA-17/55 (31%) LN and 10/55 (18%) DM; cIIIB-5/36 (14%) LN and 6/26 (17%) DM; and cIIIC-3/10 (30%) DM. MR rate of PET is $1604.37 whereas CTBS is $1679.94.
Conclusion: Consistent with prior reports, we found that 20-50% of patients with localized cIIB-cIIIC breast cancer, most of whom subsequently received PST, were upstaged after PET. Advantages of PET include greater patient convenience, reduced procedure time, reduced radiation dose (14 mSv for base of skull to thigh PET/CT vs. 21 mSv for CTBS), avoidance of potentially nephrotoxic IV contrast, and comparable cost. These findings suggest that modification of NCCN guidelines to include PET as an alternative to CTBS for systemic staging in cIIB-cIIIC breast cancer rather than optional after CTBS is warranted, especially in patients who are candidates for PST and require an efficient and expeditious workup.
***Third Prize – Dr. Hussein M. Abdel-Dayem Award**

Diuretic Renal Scintigraphy Using High Dose Furosemide in a Patient with Renal Failure.

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Introduction: Diuretic renal scintigraphy is used for the assessment of renal outflow obstruction. With normal renal function the recommended dose is 20-40 mg of intravenous furosemide. In cases of renal failure, the renal response to diuretics is blunted and an effective dose is difficult to determine[1]. Higher doses of furosemide (up to 80 mg) have been used successfully[2]. We present a case of a diuretic renal scintigraphy study performed with a very high dose of furosemide in a patient with renal failure.
Methods: The patient is a 73 year old male with a history of chronic hydronephrosis felt to be secondary to urinary retention caused by benign prostatic hypertrophy. The patient presented with acute on chronic renal failure with a serum creatinine of 5.7 mg/dL compared to a baseline value of 3.3 mg/dL. Renal scintigraphy was performed to determine if outflow obstruction contributed to the recent decompensation. As the standard dose of 20-40 mg of furosemide was felt to be an inadequate challenge, the renal service was consulted and a challenge dose of 200 mg of furosemide (described previously as the ceiling dose in CKD)[3] was recommended. Following injection of 11.2 mCi of 99mTc-MAG3, posterior images were acquired for 30 minutes. A subsequent 60 minute acquisition was

started at the same time as a slow intravenous administration of 200 mg of furosemide over 30 minutes. Bilateral renal uptake of MAG3 was then plotted for both portions of the study.
Results: The renal scintigram prior to administration demonstrates markedly reduced uptake of MAG3 in the left kidney and somewhat reduced uptake in the right kidney.
Over the course of the 30 minutes of imaging there was no nuclide seen in the left renal pelvis; by 14 minutes nuclide is seen in the right renal pelvis.
Neither kidney demonstrates washout (clearance) of nuclide over the 30 minutes.
With the subsequent infusion of 200mg of furosemide the half-time of washout of nuclide from the right kidney was 55 minutes with no appreciable response from the left kidney by 60 minutes.
Bilateral nephrostomy tubes were then placed with a subsequent drop in the patient's serum creatinine level from a high of 7.7 mg/dL to 4.22 mg/dL several days later.
Discussion: Furosemide causes diuresis by blocking Na^+ and Cl^- re-absorption in the thick ascending limb of the loop of Henle[3]. Furosemide is an organic acid that reaches the lumen of the tubule after secretion by the organic anion transporter of the proximal tubule. Patients with acute or chronic renal insufficiency often demonstrate a blunted response to furosemide. This is due to reduced delivery to the tubular lumen secondary to reduced renal blood flow and reduced secretion from the proximal renal tubules cells that results when endogenic organic acids accumulate and compete with furosemide for transport [4,5].
The blunted response can be overcome by increasing the dose of furosemide, in this case to 200 mg. For administration of a dose of this magnitude supervision by the renal service is recommended and the infusion should be performed over 30-60 minutes to avoid ototoxicity.

SPECT/CT evaluation **of a Meckel's Diverticulum in an Elderly Patient**

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Background: Meckel's diverticulum (MD) is a common congenital malformation of the gastrointestinal tract that presents in the antimesenteric margin of the ileum. It largely affects children and has an estimated prevalence of 0.3 to 2.9 percent in the general population. Approximately, 9 to 71.1 percent of patients with MD present symptomatology and over 50 percent of these are younger than 10 years of age (, while affected adults usually present during the fourth decade of life. The likelihood of complications during a lifetime is an estimated 4.2 percent, decreasing zero in elderly patients. Complications are more common in males and usually present as obstruction in children, or bleeding in adults. A Meckel's diverticulum is lined by the same intestinal mucosa as the ileum, however, it frequently presents ectopic tissue, commonly gastric mucosa, with a frequency of 24.2 to 71 percent, and pancreatic tissue in 0 to 12 percent. While this disease rarely affects the elderly, one case series described 7 patients over 65 years of age, presenting with acute abdominal pain, peritonitis, or rectal bleeding secondary to MD. Diagnosis is achieved with a ^{99m}Tc pertechnetate scan, which has a sensitivity and specificity of 85 to 97 percent in children. However, the accuracy decreases in adults with a sensitivity of 62%. In elderly patients, diagnosis is further complicated by the non-specificity of the symptoms and low incidence of MD in this age group. A 74-year-old female patient presented to our institution for follow-up 2 weeks after resolution of a spontaneous small-bowel perforation. At that time, an abdominal CT scan revealed an area of inflammation in the distal ileum, precisely where an older CT scan had shown a fluid-filled diverticulum suspicious for MD.
Methods: The patient received approximately 10 millicuries of ^{99m}Tc pertechnetate, after which whole-body images were obtained in anterior and posterior projections. After an initial negative result on planar scintigraphy, additional images of the abdomen were obtained with single-photon emission computed tomography with anatomical CT (SPECT/CT).
Results: Attenuation-corrected images with SPECT/CT revealed an area of increased radiotracer uptake, consistent in morphology and location with the lesion described on the prior CT imaging, and imperceptible on planar scintigraphy.
Conclusions: The initial false-negative result on planar images is consistent with the lower accuracy of scintigraphy reported in adult patients and may be associated with higher tissue attenuation. In these cases, initial evaluation with SPECT, particularly SPECT/CT, may significantly improve accuracy, as opposed to using only planar

scintigraphy. When SPECT is unavailable, the addition of cimetidine or ranitidine may improve the accuracy of planar scintigraphy by increasing retention of pertechnetate in the gastric mucosa.

Utility of Perfusion-only Scanning in Patients with Clear X-ray and High Probability Pattern

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Background: Most V/Q interpretations are based on comparison of ventilation and perfusion scans. Previous papers have demonstrated the adequacy of a normal perfusion scan for excluding the presence of pulmonary embolism without the need for a comparative ventilation sca . Other studies have demonstrated that a ventilation scan has little additive value in a high probability perfusion scan in a patient with a normal chest x-ray (2,3). Finally, one study has shown that a perfusion scan with a normal chest x-ray can be diagnostic in patients who present with signs and symptoms suspicious for pulmonary embolus. This poster demonstrates that a ventilation scan is not necessary in patients with a clear chest x-ray and high probability pattern.
Methods: We present two patients with high pre-test probability of pulmonary embolism with negative chest x-rays for whom a perfusion-only scan was performed. Patient A is a 55 year old man who presented with new onset of exertional dyspnea for the past week. Due to a sudden decrease in renal function a CTPA could not be performed and the patient was sent for a perfusion scan. A ventilation scan was not performed due to unavailability of the equipment needed to aerosolize 99mTc-DTPA.
Patient B is an 89 year old man who presented with shortness of breath, SaO2 70% on room air. A perfusion-only scan was performed instead of a CTPA due to decreased renal function. A ventilation scan could not be obtained due to equipment malfunction and patient's inability to cooperate.
Results: For Patient A the perfusion scan (below) demonstrated multiple bilateral segmental defects. A chest x-ray was clear. The patient was treated with IV heparin and warfarin. For Patient B the perfusion lung scan demonstrated no activity in the left lung and wedge-shaped peripheral abnormalities in the right lung. A chest x-ray obtained at the time of the V/Q scan was clear with fully expanded lungs. A CT scan obtained the next day demonstrated a near occlusive embolus in the left main pulmonary artery. The patient was treated with heparin and apixaban; treatment was then withdrawn due to co-morbidities and the patient passed away 10 days later.
Discussion: A paper by Sostman et al. using the modified PIOPED II criteria demonstrated that perfusion scintigraphy combined with chest radiography can provide diagnostic accuracy similar to both CTA and ventilation–perfusion scintigraphy, at lower cost and with lower radiation dose. Stein et al demonstrated that a high-probability perfusion scan has no less diagnostic validity in acute PE than does a high probability ventilation and perfusion scan. Miniati et al demonstrated that clinical evaluation combined with a perfusion-only scan can establish or exclude a pulmonary embolus. It is well -known that perfusion-only scans are an effective means to rule out a pulmonary embolus in pregnant women without a history of asthma or chronic lung disease and a clear chest x-ray.
The present cases demonstrate the efficacy of perfusion-only scanning in patient with a normal chest x-ray and high probability perfusion scans.

Recurrence of tumor-induced osteomalacia detected by Ga68-DOTATOC PET/CT: a case report

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Background: Tumor-induced osteomalacia (TIO) is a rare paraneoplastic syndrome usually caused by small mesenchymal tumors. Patients can present hypophosphatemia, hyperphosphaturia and low or normal levels of vitamin D.

PET/CT with Ga68- DOTATOC may play an important role, because these tumors express somatostatin receptors. This case report highlights the importance of Ga68-DOTATOC PET/CT in localizing suspected recurrence of TIO in patients with refractory and resistant osteomalacia.
Methods: A female patient of 77 years old had her first diagnosis of TIO in 2005; at that time she was treated with surgical resection of the tumor localized in the left anterior chest wall.
This woman was admitted to our Centre for suspected recurrence of disease, because she had hypophosphatemia with no response to phosphate and vitamin D supplementations; she also reported asthenia and pain to the limbs. We finally decided to perform a Ga68-DOTATOC PET/CT scan in order to identify the sites of recurrence of this disease.
Results: The PET/CT scan showed intense uptakes of the radiotracer to the anterior tract of the second left rib, to two parasternal nodulations and to a single pulmonary nodule in the medium lobe.
Conclusions: The suspected recurrence of tumor-induced osteomalacia is a diagnostic challenge. Ga68-DOTATOC PET/CT in this patient was an important tool in the detection of the sites of recurrence of TIO.

Rare case of a primary extranodal subcutaneous diffuse large B-cell lymphoma with recurrence as a primary skeletal muscle lymphoma.

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Background: Non-Hodgkin's lymphoma (NHL) is the most common form of lymphoma; diffuse large B-cell lymphoma (DLBCL) is the most common form of NHL. DLBCL usually occurs in lymph nodes, but can manifest in extranodal sites such as: intestine, bone, breast, liver, skin, lungs and central nervous system. Primary skeletal muscle lymphoma is a rare disease that accounts for 0.5% of all extranodal lymphomas; 5% of all primary extranodal NHL; less than 1% of DLBCL. Herein we present a 61-year-old male with no significant medical history who presented with a right upper thigh mass. Initial MRI of the pelvis showed a lobulated subcutaneous lesion. Pathology confirmed DLBCL. 6 cycles of R-CHOP (rituximab, doxorubicin, cyclophosphamide, vincristine, and prednisone) was given. Subsequent [^{18}F] fluorodeoxyglucose (FDG) PET/CT showed complete resolution of the lesion. The patient remained disease free for nearly three years until he presented with pain and swelling of the right lower extremity. MRI showed enlargement and diffuse muscle edema of the tibialis anterior muscle. Pathology confirmed recurrence of DLBCL. The patient received one cycle of R-ICE therapy (rituximab, ifosfamide, carboplatin and etoposide) and underwent post-treatment FDG PET/CT which didn't show improvement. Subsequently, the patient received one round of radiation therapy to the right lower extremity and is pending a post treatment FDG PET/CT following a second round of R-ICE therapy.
Methods: Initial evaluation was with imaging using a multiplanar multi-sequence MRI before and after intravenous administration of gadavist contrast. Biopsy of the lesion was obtained via a needle core biopsy. The specimen was analyzed with flow cytometry and fluorescent in situ hybridization (FISH). Initial staging and response to treatment was assessed with FDG PET/CT.
Results: On presentation, MRI of the pelvis showed a lobulated enhancing lesion with surrounding inflammatory changes. Pathology showed a high grade DLBCL, germinal center B-cell-like subtype, CD 20+, CD10+, BCL2+, BCL6+, MCY+. Initial staging FDG PET/CT showed an FDG avid soft tissue mass in the right lateral subcutaneous tissue of the pelvis. Post-treatment FDG PET/CT showed a complete resolution of the FDG avid mass. Three years later, the patient presented with pain and swelling of the right lower extremity. MRI showed enlargement and diffuse muscle edema of the tibialis anterior muscle. Pathology showed DLBCL, compatible with non-germinal center B-cell-like subtype CD20+, CD79a+, PAX5+, BCL6+, MUM1+, MYC+, BCL2+. Initial staging FDG PET/CT showed activity within

muscles in the anterolateral aspect of the right lower extremity. Post-treatment FDG PET/CT showed no improvement, with new foci of uptake.
Conclusion: Extranodal manifestations of DLBCL are uncommon; primary skeletal muscle DLBCL is a rare entity that occurs among elderly adults. Imaging is useful in identifying the location and size of the mass, with MRI as the most useful modality for assessment of muscular lymphomas [2,8,9]. However, definitive diagnosis can only be made by biopsy. The response to treatment can be assessed with post-treatment imaging using FDG PET/CT.

Past Medical History Can Be a Fountain of Knowledge: Case of a Patient With Prior Fontan Procedure Presenting With Hypoxia.

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Background: Past medical history can be a fountain of knowledge and the key in a puzzling case. A 25 year old patient presented to the Nuclear Medicine department for a VQ scan due to shortness of breath and hypoxia; raising concern for pulmonary emboli. The initial VQ scan was obtained instead of CTA because of patient's complex surgical anatomy. As usual, a right upper extremity IV line was placed for the perfusion portion of the study. This study revealed complete lack of perfusion to the left lung with normal ventilation imaging. The results of this initial scan prompted an exhaustive search through the patient's medical record to elucidate the explanation for such a puzzling imaging finding. Review of the patient's chart revealed she had a remote history of cardiac surgery for repair of tricuspid atresia and univentricular heart.
Methods: A thorough chart review was performed via our EMR system. This included the review of cardiology consult notes, prior cardiac MRI report/imaging and the medical history section provided by our workflow software. This revealed a prior history of cardiac surgery for repair of tricuspid atresia and univentricular heart (Fontan Procedure). In turn, this led to the recommendation of a repeat study with the IV to be placed in one of the lower extremities. The IV was inserted in the right foot and a repeat perfusion scan was performed. The ventilation portion was not performed for patient comfort.
Result: The Fontan procedure is a common procedure performed in child with univentricular heart. Usually the superior vena cava(SVC) is anastomosed to the right main pulmonary artery with little flow from the SVC reaching the left pulmonary artery. The changes in cardiac flow dynamics after a fontan procedure explain the lack of perfusion to the left lung on initial study. On the repeat exam, the perfusion scan was with symmetric flow to both lungs and the scan was read as very low probability for PE thus avoiding unnecessary anticoagulation in this patient.
Conclusion: The VQ scan is important for clinicians to rule out a potentially deadly diagnosis: pulmonary embolism, however, patients with congenital heart repair can present a unique dilemma for the unsuspecting interpreting physician. The medical history of these patients and knowledge of the surgical repair can prove invaluable to troubleshoot any pitfalls seen on nuclear medicine imaging. Placing an IV in a lower extremity can be a quick solution in patients with congenital heart repairs such as a Fontan and can save the patient from additional medical intervention and discomfort. Had the clever radiologist not looked deeply into the patient's past medical history, suspecting that the patient had a very specific type of cardiac surgery done, and found that the patient had a previous Fontan procedure, the resolution to this case would never have come to pass.

89Zr-Df-IAB2M And 68Ga-PSMA-11 Imaging In Localized Pre-Prostatectomy Patients

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Background: Due to the high expression of Prostate Specific Membrane Antigen (PSMA), it's an excellent target for molecular imaging. IAB2M is an 85kD minibody derived from J591 and PSMA-11 is a PSMA small molecule ligand.
Methods: Patients with clinically significant (defined as: ≥ 0.5 cm3 with Gleason pattern ≥ 4) localized prostate cancer(PCa) on conventional imaging modalities who planned to undergo surgery were imaged by PET/CT 90 -120 minutes after 5±2mCi of 68Ga-PSMA-11 injection and 2-4 days after 10mg IAB2M labeled with 2.5 mCi of 89Zr injection. Image results were read and mapped by a Nuclear Medicine MD without knowledge of the surgical pathology. Mapped findings were later compared with a surgical pathology map.
Results: 20 Pts with median age 64.5(46-79) and PSA 7.5(1.6-36.56) were enrolled in 2 groups. In group 1, eleven patients were imaged with IAB2M only while in group 2, nine patients were imaged with both PET agents. For validation, surgical path was available for 19 pts (1 declined surgery). Amongst **clinically significant** PCa lesions, in group 1, surgical path identified 15 lesions, with median GS 7(6-9) with detection rates for IAB2M and mpMRI were 87% and 67%, respectively with median SUVmax 2.6 on IAB2M and median MR PIRADS 4.5(4-5). Smallest imaged lesion was 8mm on both. In group 2, surgical path identified 14 lesions with median GS 7 (6-9) and detection rates of IAB2M, PSMA-11 and mpMRI were 64%, 71% and 57%, respectively with median SUVmax 3.1 on IAB2M and 4.3 on PSMA-11 and median MR PIRADS = 4 (4-5). Smallest lesion imaged was 8mm on all. Amongst **clinically non-significant** PCa lesions, in group 1, surgical path identified 6 lesions, all 3+3 and detection rate was 33% for both IAB2M and MRI. In group 2, surgical path identified 4 lesions, all 3+3. Neither of the PET agents nor MRI detected any of these 4 lesions. For **extra-prostatic lesions**, in group 1, surgical path identified 8 lesions, all LNs. IAB2M detected 5/8; MRI detected 1/6 (2 para-aortic LNs were not detected as MR was not done for that region) and in group 2, four lesions in 1 patient were detected by both PET agents, 3 confirmed by surgical pathology (2 pelvic LNs and 1 sacral lesion); 1 confirmed by bone scan 2 months post-op (clavicle). MR detected 3, while for clavicular lesion, MR was not preformed. In group 1: 10 FPs lesions were detected on IAB2M (8 prostatic, 2 nodal) and in group 2: 5 FPs on IAB2M (3 prostatic, 2 nodal) and 4 prostatic FPs on PSMA-11. In group 1: IAB2M missed 8 lesions: four GS 3+3, one GS 4+3 (all less than 7mm) and 3 nodal (2mm, 5mm, 15mm) and in group 2: both IAB2M and PSMA-11 missed 8 low grade lesions: six GS 3+3 and 2 GS 3+4, all were less than 7mm.
Conclusions: In this small series, the performance of both PET agents was similar. An advantage of IAB2M is its hepatobiliary rather than renal/urinary clearance, which makes it potentially easier to visualize the PCa and/or pelvic disease; an advantage of PSMA-11 is the ability to image within 1-2 hours.

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Department of Urology, Weill Cornell Medical College, New York
Conflict of Interest:
Dr. Bander is an inventor on patents related to PSMA antibodies that are assigned to Cornell Research Foundation ("CRF"). Dr. Bander is a paid consultant to and owns stock in BZL Biologics, LLC, the company to which the patents were licensed by CRF for further research and development.

Focal Acetabular Fossa FDG Uptake in a Patient with Non-Hodgkin's Lymphoma: A Potential PET Imaging Pitfall

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Background: FDG PET in oncology is sensitive for the staging and re-staging of many malignancies, which often have an over-expression of glucose transporters. However, increased FDG activity on PET is not tumor specific. Inflammatory cells such as activated macrophages and neutrophils at sites of active infection/inflammation also accumulate FDG, as cytokines are hypothesized to increase the affinity of GLUT transporters for FDG. It is important to be aware of benign causes of FDG uptake on PET scans in Oncology patients to avoid additional imaging, biopsies, as well as unnecessary surgery. At times, we have encountered focal FDG uptake in the acetabular fossae in our oncology patients, which has been coined in the literature as the Acetabular Focal Hot Spot (AFHS). AFHS is a rare benign cause of musculoskeletal FDG uptake on Pet at the intra-articular acetabulum, which can mimic malignancy in oncology patients. However, intra-articular metastases are overall a very rare entity. We describe a case of AFHS from our institution and will present the PET imaging findings and subsequent patient course. We will review the current understanding of the pathophysiology of AFHS, and also present companion cases.
Methods: The patient is a 69-year-old male with Non-Hodgkin's Lymphoma who presented for follow-up FDG Pet scan after two cycles of chemotherapy. Whole body PET scan revealed resolution of previous hypermetabolic adenopathy in the chest, abdomen, and pelvis with new focal uptake at the right acetabulum, which localized on fusion imaging to the right acetabular fossae. The maximum SUV value was 5.0. The patient was asymptomatic at the right hip.
Results: The unexpected FDG uptake at the right acetabular fossae was reported on PET as most likely benign and a normal variant, which was confirmed on subsequent PET imaging. AFHS is a benign musculoskeletal cause of focal intra-articular FDG uptake that can mimic malignancy. We will review AFHS and its imaging findings, propose etiologies, and present companion cases of potential PET pitfalls for focal intra-articular FDG uptake, including localized Pigmented Villonodular Synovitis and Adhesive Capsulitis at the shoulder.
Conclusions: Incidental focal FDG uptake at the acetabular fossa, so called Acetabular Focal Hot Spot, is a rare entity with focal FDG uptake localizing to the acetabular fossa. Patients are most commonly asymptomatic, and intra-articular uptake at this region is most commonly benign and does not progress to malignancy. It is important to accurately diagnose this entity to avoid unnecessary follow-up imaging, intervention, and patient anxiety.

Dynamic Gallium-68-DOTATATE PET/MRI in the Diagnosis and Management of Recurrent and Progressive Intracranial Meningiomas.

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Background: Meningiomas are the most common primary intracranial tumors. Contrast enhanced MRI is the gold standard for diagnosis and treatment planning of meningioma. However, MRI can have limited accuracy in distinguishing recurrence from treatment effect in the postsurgical and post-radiation setting. Meningiomas express high levels of somatostatin receptor 2 (SSTR2) and [68]Ga-DOTATATE is a PET radiotracer targeting SSTR2 with high affinity. The purpose of our study was to evaluate static and dynamic [68]Ga-DOTATATE PET/MRI in a prospective clinical cohort of patients with meningioma.
Methods: 18 patients with clinically-suspected or pathology proven meningioma were imaged over a time period of 6 months. [68]Ga-DOTATATE-PET/MRI was acquired in 3D list mode over 50 minutes, beginning 5-15 minutes post injection. Maximum SUV values were obtained based on static PET data. The pituitary gland and superior sagittal sinus (SSS) were analyzed as reference regions. Target lesions were classified based on pathologic and/or

imaging outcomes, the latter based on the PET/MRI and subsequent MRI follow up at 3/6/9 months. Based on our previous work, we classified lesions with maximum SUV values of greater than 3 x the SSS background as meningioma, lesions with SUV values similar to SSS as post-treatment change, and lesions with intermediate avidity relative to SSS as indeterminate. In target and reference regions, dynamic activity data was obtained on a voxel-by-voxel basis through a volumetric analysis of the PET/MRI, and time-activity and time-SUVmean curves binned into 5-minute frames were generated individually as well as across the cohort. Finally, we used the standard Patlak graphical analysis to generate voxel-wise measurement of the [68]Ga-DOTATATE macro parameter of Ki, denoting the net influx rate constant in target lesions.
Results: Across the cohort, a total of 31 unique lesions were identified based on PET/MRI (19 meningiomas, 5 indeterminate lesions, 7 post-treatment change). In 14 patients PET favored recurrence, while in 4 patients low avidity suggested a diagnosis of post-treatment change or indeterminate lesion. [68]Ga-DOTATATE PET provided improved extent of disease visualization and confirmed parenchymal and osseus invasion. Dynamic PET data demonstrated unique kinetic uptake patterns for meningiomas, pituitary glands and post-treatment change across the cohort. The mean static SUVmax of target lesions normalized to SUVmax of SSS was 27.0 for meningiomas (range: 3.59-136.1), 6.10 for indeterminate lesions (range: 2.18-10.9) and 2.21 for post treatment change (range: 0.95-4.50) ($p = 0.0004$). The mean Ki was 0.086 for meningiomas (range: 0.0042-0.30), 0.042 for indeterminate lesions (range: 0.0085-0.0867) and 0.0085 for post-treatment change (range: 0.0001-0.028) ($p = 0.0035$).
Conclusion: [68]Ga-DOTATATE PET/MRI is a promising tool that allows improved diagnosis and extent of disease evaluation in the assessment of meningiomas. In addition to static PET, dynamic PET provides distinct kinetic uptake patterns and net influx rate constant of [68]Ga-DOTATATE, which may further aid in differentiating recurrence from post-treatment change. Our pilot study suggests that the incorporation of dynamic DOTATATE PET data into the imaging work-up of meningioma can provide additional valuable information in the differentiation of meningiomas and post-treatment change in the post-surgical and post-radiation setting and inform future prospective clinical trials.

Enlarged Atria in The Right Hemithorax and Heart to Contralateral Ratio:
A ^{99m}Tc-PYP Imaging Potential Pitfall in the Evaluation of Transthyretin Cardiac Amyloidosis

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Background: Amyloidosis is a systemic disease characterized by the accumulation and deposition of misfolded abnormal proteins (amyloid fibrils) in various organ systems. One of these systems is the heart, and patients may present with heart failure and preserved ejection fraction. Of the different types of amyloidosis, AL amyloidosis (deposition of light chains) and transthyretin amyloidosis (deposition of either mutant or wild-type transthyretin protein) are the most common and cardiac involvement is often underdiagnosed. Recent advances in imaging have helped identify patients with this disorder so that timely and appropriate interventions may be initiated. One of the imaging modalities is ^{99m}Technetium-pyrophosphate (^{99m}Tc-PYP) imaging which uses visual cardiac uptake compared to bone as well as Heart-to-Contralateral Lung (H/CL) ratio as criteria for diagnosing transthyretin cardiac amyloidosis (ATTR-amyloidosis). Recent ASNC guidelines recommend planar and SPECT imaging at one hour with at least 750,000 counts obtained. A H/CL ratio >/= to 1.5 is considered to be positive for ATTR cardiac amyloidosis, and H/Cl <1.5 as negative. However, to our knowledge, potential imaging quantitative criteria pitfalls have not been described. This case report highlights a potential pitfall in the quantitation of H/CL ratio in diagnosing ATTR amyloidosis due to elevated blood pool activity in the right hemithorax.
Methods: A 65-year-old male patient with a history of preserved ejection fraction heart failure (60-65%), restrictive type without definitive etiology, was found to have elevated kappa and lambda light chains during his

most recent hospitalization. He was referred by his cardiologist for a ^{99m}Tc-PYP amyloid scan. Planar and spect images were obtained at 1 and 3 hours, including SPECT-CT, and quantification. The patient has had multiple echocardiograms and computerized tomographic imaging studies of the chest in the past, all of which have revealed moderately enlarged right and massively enlarged left atria of the heart.
Results: ^{99m}Tc-PYP imaging quantification was limited as there was increased radiotracer uptake localizing to the medial right hemithorax. This activity was diffuse and decreased from 1 to 3 hours, consistent with blood pool activity from significant atrial enlargement. This is the first case we are aware to describe abnormal uptake in the contralateral hemithorax which could potentially reduce H/Cl ratios and reduce sensitivity for ATTR amyloidosis.
Conclusion: Tc-99m PYP imaging to diagnose ATTR cardiac amyloidosis is being increasingly utilized. This is the first report to our knowledge of marked bi-atrial enlargement that could potentially reduce sensitivity of H/Cl in the diagnosis of ATTR amyloidosis.

Estimation of the Chest Wall Attenuation of the Emissions From Iodine-123 in the Instance of Substernal Goiter.

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Objective: The underestimation of thyroid uptake measurements with iodine isotopes has been a generally accepted theory in patients with substernal goiter due to attenuation by the chest wall. In this study, we calculate the attenuation utilizing a cadaver chest wall and mathematical models in order to better understand the severity of this underestimation.
Methods: Attenuation was calculated by two methods. A capsule of 300 microCuries (mCi) of iodine-123 was measured using a thyroid probe (Biodex) directly and unattenuated, in a standard neck phantom and behind a cadaveric chest wall which included the soft tissues and bony structures (sternum). The chest wall was then imaged with computed tomography (CT, GE Definition). Attenuation was calculated based on the tissue composition of the cadaveric chest wall as measured depth and CT numbers (Hounsfield units).
Results: Attenuation of the iodine capsule by the neck phantom was 18% while attenuation by the chest wall was 35%. Attenuation measured by CT was 27%.
Discussion: Attenuation by the chest wall in the case of substernal goiter may be substantially underestimated by standard techniques using a neck phantom. While the amount of bony structure between patients may not have much variability, the soft tissue composition of the chest wall and substernal extent of the goiter would be difficult to calculate with a high level of accuracy on a routine basis. Direct comparison with a cadaveric specimen leads to similar issues but does give us a rough estimation of the extent of the issue. Individually calculating chest wall attenuation by performing CT on patients would increase radiation dose to the patient and introduce new costs to the system.
Conclusion: Although the attenuation of thyroid uptake in the case of a substernal goiter cannot be calculated with a high level of accuracy due to the variables that must be considered on an individual basis, it is suggested by this study that the attenuation by chest wall soft tissues can be substantial. Knowledge of the extent of the substernal component and the chest wall composition and thickness may be useful if the uptake measurement is used to calculate doses for the treatment of hyperthyroidism in substernal goiter patients.

Scoring the Z-scores – A Novel Approach to Distinguish Alzheimer Disease and Frontotemporal Lobar Degeneration with Statistical Parametric Mapping

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Background: Distinguishing frontotemporal lobal degeneration (FTLD) and Alzheimer Disease (AD) with [18F]-FDG-PET presents a diagnostic challenge. The purpose of this study is to develop a Statistical Parametric Mapping (SPM)-based scoring method and apply it to a retrospective clinical cohort of patients with clinically suspected dementia.

Methods: Sixty-five subjects with clinically suspected dementia were retrospectively identified. PET data were processed with Siemens syngo.via software using a dataset of 33 healthy controls, and region-specific output Z-scores were generated. A scoring method using multiple Z-score cutoffs (-2.0, -3.0, or -4.0) and normalization approaches (whole brain vs. cerebellar) was applied (see Figure). The concordance rate, sensitivity, and specificity of the qualitative read and the SPM-based scoring methods was evaluated, with the clinical diagnosis as gold standard. Readers were predominately neuroradiologists and nuclear radiologists with an average post-fellowship experience of 7.9 years.

Additionally, Z-scores of each region of interest were compared among patients with a neurologic diagnosis of FTLD, PPA, AD, and MCI using the Kruskal-Wallis test and Dunn's test for multiple comparisons.

Results: Whole brain normalization (WBN) with Z-score cutoff of -3.0 had the highest concordance rate with clinical diagnosis (71%), outperforming cerebellar normalization (66%) and qualitative reads (66%). WBN had a sensitivity of 81.5% and specificity of 72.7%, compared to qualitative reads (sensitivity of 55.6%, specificity of 81.8%). Furthermore, SPM-based scoring methods reduced misclassification of AD patients by 17.7%.Patients with a neurologic diagnosis of FTD had significantly lower Z-scores than normal patients in the left anterior temporal lobe, and Z-scores in the anterior cingulate were significantly lower in PPA patients than normal and MCI patients. Z-scores were significantly lower in the posterior parietal cortex in patients with AD compared to MCI and normal patients, and patients with AD consistently had significantly lower Z-scores in the precuneus and posterior parietal cortices relative to patients with FTD.

Conclusion: An SPM-based scoring system using WBN and a Z-score cutoff of -3.0 outperformed scoring with cerebellar normalization and qualitative reads. While there are notable limitations (i.e., suboptimal gold standard, retrospective analysis), this study preliminarily validates a readily deployable scoring system that could be applied in prospective studies and potentially in the clinic.

Pulmonary Tumor Embolism from Anal Cancer Detected on ^{18}F-FDG PET/CT scan

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Background: Pulmonary tumor embolism has been described as a significant source of morbidity and mortality in cancer patients. Patients can develop dyspnea and cor pulmonale signs. With advanced PET imaging, several reports attempted to describe this entity and differentiate it from thromboembolism. We describe a patient with metastatic anal cancer who developed tumor embolism identified on ^{18}F-FDG PET/CT scan.

Methods: A 49-year old male patient with history of advanced anal squamous cell carcinoma, for which he underwent chemotherapy. At some point during the course of his disease, the patient failed to follow-up and subsequently presented with an infected large right groin mass requiring hospitalization and treatment with antibiotics. Patient underwent a restaging ^{18}F-FDG PET/CT scan. Following a minimum four hours fasting, the patient received an intravenous injection of 10.0 mCi ^{18}F-FDG. Following approximate 45 minutes images were acquired.

Results: The ^{18}F-FDG PET/CT images showed hypermetabolic circumferential soft tissue anal mass extending toward the perineum, the mesorectal fascia and base of the penis. Additionally, there was hypermetabolic right groin ulcerative mass with direct involvement of the femoral vessels, representing inguinal adenopathy. Furthermore, there were bilateral pulmonary FDG avid foci which were found to be associated with filling defects within multiple pulmonary arterial branches when correlated with contrast enhanced diagnostic CT performed separately, consistent with tumor emboli. Representative examples include foci in the right upper lobe (SUV 4.4) and in the lingula (SUV 2.1).
Discussion and Conclusion: The presence of clusters of tumor cells within the pulmonary arterial system is pathologically defined as pulmonary tumor embolism. The reported incidence of pulmonary tumor emboli exceeds 25% at autopsy. It is most commonly associated with stomach malignancy. These lesions are FGD avid which differentiates them from pulmonary thromboembolism. Proper recognition of these lesions with subsequent appropriate correlative imaging and treatment may lead to improved patient management and therefore optimize their ultimate outcome.

Xenon-133 Lung Scintigraphy (Xels) is a Safe Method to Screen Patients Prior to Hyperbaric Oxygen Therapy (HBOT).

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Background: HBOT is used to treat a number of diseases where hypoxia is an impediment to healing. These patients have a high prevalence of smoking and chronic lung disease; patients with bullae and severe COPD are at risk of barotrauma. Radiographic screening (chiefly CXR) has been performed to detect significant abnormalities prior to therapy; a single published abstract describes use of ^{133}Xe. We elected to retrospectively review our experience to understand how XeLS complements radiography for this purpose.
Methods: IRB approval was obtained with waiver of informed consent and HIPAA authorization. Screening XeLS between 7/12 and 12/18 were identified in PACS and NMIS. ~25 mCi of ^{133}Xe were administered by standard methods via double-trap closed ventilation system. Planar images were obtained at wash-in, equilibrium, and wash-out phases on a dual-head camera with LEHR collimation. The original imaging report was used to extract information regarding scintigraphic findings especially degree of focal or diffuse ^{133}Xe retention on washout. Images were re-reviewed by a nuclear medicine physician to clarify initial report when needed. Findings on XeLS studies were categorized as non-significant (nonexistent or mild), or significant (more severe), the latter representing areas of focal retention with washout times > 8 minutes. Contemporaneous CXR reports were reviewed. If unclear, CXR images were re-reviewed to extract relevant information. Radiographic abnormalities were subcategorized as significant or non-significant. HBOT outcomes were obtained by review of medical records. Outcome variables included cancellation or modification of HBOT parameters, and any reported complications. 23 cases of XeLS were performed for pre-HBOT screening during the 66-month accrual period. All patients were current or former smokers, with clinical evidence of COPD or asthma, or imaging evidence of COPD. 2 patients had an incomplete XeLS study due to refusal or inability to complete the scan. 2 patients did not proceed to HBOT following successful XeLS due to preexisting psychiatric or other issues; 19 patients were screened and treated.
Results: 2 patients had no radiographs performed; both had insignificant xenon findings and were treated without complications. Of 17 patients who underwent radiography, 8 exhibited significant X-ray findings. 3 of these patients also demonstrated focal xenon retention and were not treated by HBOT while 5 exhibited insignificant scintigraphic findings and were treated by conventional HBOT, without complication. Of 9 patients without significant radiographic findings, XeLS was insignificant in all cases. These 9 patients were treated by HBOT without complications, though time of decompression was increased in 2 subjects at the discretion of the

treating physician. Several patients were unable to complete their full course of HBOT due to non-pulmonary complications such as anxiety, uncontrolled HTN, severe ear pain, or lack of compliance however all patients were able to tolerate hyperbaric treatment without pulmonary barotrauma.
Conclusion: XeLS is a safe and less restrictive method than chest radiography for screening pre-HBOT patients which leverages functional information that standard radiographic imaging does not provide. In patients in whom CXR might preclude HBOT, functional imaging with xenon represents a safe and useful pathway to permit this important therapeutic modality.

Incidental Discovery of an Endobronchial Carcinoid on Cardiac Computerized Tomography

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Background: Cardiac computed tomography (CCT) techniques, coronary computed tomography angiography (CCTA) and coronary calcium scan, are of growing importance in noninvasive diagnosis of coronary artery diseases. Routine CCT images include portions of non-cardiovascular thoracic and upper abdominal anatomy, including the mediastinum, hilum, airway, lung parenchyma, pleura, chest wall, esophagus, stomach, liver, spleen, and colon. Review of all visible non-cardiovascular structures is important for 2 principal reasons: (1) recognition of primary and secondary comorbid pathology, and (2) identification of extracardiac findings (ECF) that lead to alternative non-cardiovascular diagnoses. In a systemic review conducted by Karius et al, the average prevalence of overall ECF was 41.0% during cardiac computed tomography and suspicious pulmonary nodules represented the vast majority of clinically significant ECF.
Methods: We present a case of 57-year-old woman who presented with complain of chest pain and shortness of breath and underwent cardiac computed tomography.
Results: CCTA revealed normal coronary arteries and whole heart. Agatston Score was 0 on coronary calcium scan. Notable significant extracardiac finding was focal opacification of anterior basal segment bronchus of the left lower lobe. Subsequent dedicated CT scan of the chest confirmed 5 mm x 7 mm endobronchial lesion involving the anterior basal segment bronchus of the left lower lobe. Bronchoscopy confirmed endobronchial lesion and excision biopsy revealed classic carcinoid neoplasm. She opted for serial imaging with Chest CT scans. CT scan of the chest 18 months later demonstrated interval increase in size of the endobronchial lesion, now measuring 9 x 6 mm. 68Ga DOTATATE PET/CT scan acquired for staging documented localized lesion in the anterior basal segment of the left lower lobe and no evidence of metastasis. Flexible bronchoscopy, left VATS, left lower lobectomy, mediastinal lymph node dissection. Endobronchial lesion was confirmed to be a 0.6 cm typical carcinoid and mediastinal lymph nodes were negative for tumor.
Conclusion: Lung cancer which is missed at CT scanning manifests in 67% of cases as a central endobronchial lesion, and this is difficult to distinguish from surrounding structures and sticky mucus. Although nonspecific, findings of bronchial obstruction or bronchial wall thickening and stenosis should not be overlooked. It is recommended that all structures within the reconstructed cardiac field of view be examined and that if abnormalities are noted, additional reconstructions, and if clinically necessary, bronchoscopy should be performed.

Demographic Influences on Cardiac Sarcoidosis

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Objective: To determine if there is a relationship between ^{18}F FDG-PET/CT (PET/CT) showing FDG-avidity consistent with cardiac sarcoidosis and demographic factors of sex and age.

Methods: Between 8/2016-10/2019, 62 patients (19 female; 43 male) with cardiac arrhythmias and/or non-ischemic cardiomyopathies underwent 81 combined PET/CT and ^{99m}Tc-MIBI myocardial SPECT/CT (SPECT/CT) studies to evaluate for cardiac sarcoidosis. For this IRB-approved retrospective study, patients on immunosuppressive therapy and patients with indeterminate scan results were excluded from analysis. For patients undergoing multiple scans, only the first scan was included. A total of 41 patients (13 female; 28 male) were included in the final analysis.Patients fasted for a minimum of 18 hours and followed a low carbohydrate, high fat diet on the day prior to the examination. Resting myocardial SPECT/CT was performed first, 45 minutes following injection of 370 MBq ^{99m}Tc-MIBI. PET/CT of the heart was performed 90 minutes following injection of 370-444 MBq ^{18}F FDG. A second PET/CT, including base of skull to mid-thigh, was performed 12-15 minutes later. A single reader interpreted PET/CT scans as positive (focal or focal on diffuse myocardial uptake of FDG greater than left ventricular blood pool activity), negative (myocardial FDG activity equal or less than left ventricular blood pool activity) or indeterminate (diffuse, uniform, segmental myocardial uptake of FDG, possibly related to incomplete suppression of physiologic myocardial glucose uptake or multiple granulomas) for cardiac sarcoidosis. Skull-to-thigh PET/CT was read as positive when extra-cardiac sites of hypermetabolism consistent with sarcoidosis were identified, and negative when only physiologic activity was seen. SPECT/CT was interpreted as normal (uniform myocardial perfusion) or abnormal (at least one area of decreased perfusion). Results of skull-to-thigh PET/CT and SPECT/CT were not included in this analysis. ANOVA analyzed whether there were significant differences with sex or age or positive readings. Logistic regression assessed whether age or sex were associated with positive readings. ROC analysis assessed efficacy of age to predict a positive reading, and if statistically significant, to establish the threshold for discrimination.

Results: Among the 41 patients there were 19 positive & 22 negative PET/CT studies. Ages were normally distributed (Kolmogorov-Smirnov D = 0.08, $p > 0.10$), with mean age = 58±11 years, with similar ages for female and male patients (59±13 versus 57±9 years, $p = 0.66$). Logistic regression determined that sex was not a significant factor ($\chi^2 = 1.9$; $p = 0.17$), but that age was significantly associated with positive cases ($\chi^2 = 9.5$; $p = 0.002$). ROC analysis determined that age ≤ 58 years significantly ($p = 0.0003$) discriminated positive from negative readings (accuracy = 78±8%, sensitivity = 79%, specificity = 77%). Patients who had a positive PET/CT were significantly younger than patients with a negative scan (52±9 versus 62±10 years, $p = 0.003$).

Conclusions: When interpreting PET/CT for cardiac sarcoidosis, it is advisable to take into consideration that positive readings are more likely in younger patients than in older patients.

^{18}F FDG-PET/CT & ^{99m}Tc-MIBI Myocardial SPECT/CT to Assess Therapy Response in Cardiac Sarcoidosis

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Objective: Cardiac sarcoidosis is an increasingly recognized, potentially fatal condition that may be evaluated using ^{18}F FDG-PET/CT (PET/CT) and ^{99m}Tc-MIBI myocardial SPECT/CT (SPECT/CT). Patients with cardiac sarcoidosis may

present with nonspecific symptoms, such as palpitations or pre-syncope, or potentially fatal cardiac arrhythmias or non-ischemic cardiomyopathies. We reviewed our experience with cardiac sarcoidosis and PET/CT and SPECT/CT, before and after immunotherapy, to illustrate the value of imaging to assess therapy response.

Methods: Between 8/2016-10/2019, 62 patients (19 female; 43 male) underwent 81 combined PET/CT and SPECT/CT studies to evaluate for cardiac sarcoidosis. For this IRB-approved, retrospective review, we included untreated patients with no history of sarcoidosis at baseline who had PET/CT and SPECT/CT before and after immunotherapy. We identified 4 patients meeting these criteria.

Patients followed a low carbohydrate, high fat diet on the day prior to the exam and fasted for a minimum of 18 h prior to imaging. Resting myocardial SPECT/CT was performed first, 45 minutes following injection of 370 MBq ^{99m}Tc-MIBI. PET/CT of the heart was performed 90 minutes following injection of 370-444 MBq ^{18}F FDG. A second PET/CT, including base of skull to mid-thigh, was performed 12-15 minutes later. A single reader simultaneously interpreted PET/CT and SPECT/CT. Cardiac PET/CT was interpreted as positive (focal or focal on diffuse myocardial uptake of FDG greater than left ventricular blood pool activity), negative (myocardial FDG activity equal or less than left ventricular blood pool activity), or indeterminate (diffuse, uniform, or segmental myocardial uptake of FDG, possibly related to incomplete suppression of physiologic myocardial glucose uptake or multiple granulomas) for cardiac sarcoidosis. SPECT/CT was interpreted as normal (uniform myocardial perfusion) or abnormal (at least one area of decreased perfusion). Skull-to-thigh PET/CT was read as positive when extra-cardiac sites of hypermetabolism consistent with sarcoidosis were identified, and negative when only physiologic activity was seen.

Results: For 3 of 4 patients, baseline PET/CT showed cardiac and extra-cardiac foci of hypermetabolism consistent with sarcoidosis; 1 patient had isolated cardiac disease. One patient subsequently had an ultrasound-guided percutaneous biopsy of a 1 cm FDG-avid liver lesion which confirmed sarcoidosis. Despite the presence of an accessible percutaneous biopsy site, one patient had a non-diagnostic endobronchial ultrasound-guided biopsy of mediastinal nodes, followed by mediastinoscopy, which confirmed sarcoidosis. For 2 patients, a biopsy was not performed, and the diagnosis was made clinically. All 4 patients had abnormal myocardial perfusion at baseline. Repeat studies following immunosuppressive therapy showed resolution of myocardial FDG avidity for 3 patients, and persistent, unchanged myocardial FDG uptake for 1. Extracardiac disease resolved for 2 patients and improved for 1 patient. For 1 patient, new liver lesions were seen. Myocardial perfusion normalized for 1 patient, improved for 2, and was unchanged for 1 patient.

Conclusion: This small series suggests that serial ^{18}F FDG-PET/CT and ^{99m}Tc-MIBI myocardial SPECT/CT may be useful for guiding immunosuppressive therapy in patients with cardiac sarcoidosis. Identifying responders may facilitate tapering of therapy and identifying non-responders may lead to change in therapy.

18F-FDG PET/CT as an Imaging Surrogate Marker for Paraneoplastic Leukocytosis

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Introduction: Paraneoplastic leukocytosis (PL) is a phenomenon that can occur with any neoplasm but is most frequently found in lung cancer. Leukocytosis has historically been associated with a poor prognosis in patients with solid tumors. The mechanisms of tumor-related leukocytosis may be driven by secretion of hematopoietic growth factors like granulocyte-colony stimulating factor (G-CSF), cytokines (interleukin-6) or tumor microenvironments. FDG-PET/CT may serve as an imaging surrogate marker for PL.

Methods: We reviewed initial staging FDG-PET/CT scans of three cases with PL. All the scans were performed on the GE IQ PET/CT scanners. At approximately 60 minutes following intravenous tracer administration, positron emission tomography was performed from the base of the skull through the mid-thigh. Non-contrast low-dose helical CT imaging was performed over the same range without breath-hold for attenuation correction of PET images and anatomic correlation. Pathology and laboratory investigations were reviewed to document the diagnosis, complete blood count and differential white blood cell count.

Results: Case 1 was an 80-year-old man diagnosed with poorly differentiated invasive adenocarcinoma with gene for murine granulocyte-colony stimulating factor (G-CSF) cloned from the lung tissue. Case 2 was a 66-year-old woman diagnosed with metastatic SMARCA4 deficient undifferentiated carcinoma from the right iliac mass biopsy with primary in the lung. Case 3 was a 55-year-old woman with sarcomatoid-type malignant pleural mesothelioma. Markedly increased and diffuse FDG uptake in the bone marrow and spleen was seen in all three cases on FDG-PET/CT. Laboratory evaluations showed marked leukocytosis in all three cases with WBC counts ranging from 29 K/µL to 79 K/µL, with differential counts showing primarily neutrophils.
Conclusion: It is possible that FDG-PET/CT, in combination with laboratory assessment, may be an imaging biomarker of PL and underlying disease for monitoring disease progression, response to treatment and development of new therapeutic strategies.

Ga-68 DOTATATE (SSTR) in the Evaluation of Sinonasal Neuroendocrine Neoplasms

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Background: Neuroendocrine neoplasm are a heterogeneous group of lesions that occur across almost all visceral subsites in the body, including the head and neck. Sinonasal tumors with neuroendocrine differentiation comprise neoplasms of neuroectodermal and epithelial origin, consisting of olfactory neuroblastomas (ONBs) and neuroendocrine carcinomas (NECs). The ONBs constitute the neuroectodermal group, while the NECs are divided into SNEC (including carcinoids and atypical carcinoids), small cell carcinoma, neuroendocrine type, and large cell carcinoma, neuroendocrine type. ONBs account for approximately 3% of all sinonasal tumors, while SNEC accounts for about 5% of sinonasal malignancies.
Methods: Two cases of sinonasal neuroendocrine tumors who underwent Ga-68 SSTR for staging are presented. Important SSTR and MR imaging findings are discussed.
Results: Case 1: 55 y.o. Male who presented with new-onset of nasal congestion and right-sided epistaxis. MR demonstrated an enhancing polypoid mass in the right upper/middle nasal cavity without evidence of intracranial or infraorbital extension (A, B). Pathology was consistent with a low-grade neuroendocrine tumor; immunostains were positive for CAM 5.2, AE1/AE3, and synaptophysin and negative for CD34, S-100, HMB-45, beta-catenin, Bcl-1, and actin. Ga-68 SSTR MIP and fused PET/MR (C, D) showing SSTR avid mass in the right nasal cavity.
Case 2: 48 y.o Male with nasal congestion left>right for more than one year. He initially saw an allergist who noted a nasal polyp and was treated with topical sprays without improvement. The patient went for a second opinion where he got a biopsy of the polyp that was negative for carcinoma, and the patient was started on steroid trial. MR was obtained that showed a lesion in the nasal cavity with extension into anterior cranial fossa. The patient underwent endoscopic endonasal resection of mass that was consistent with ONB. Ga-68 SSTR showing tracer avid mass in the left nasal cavity with intracranial extension and no evidence of distant metastasis.
Conclusion: Immunohistochemical characterization of sinonasal neuroendocrine neoplasms as well as their markers is paramount to improved understanding of the biology of these tumors, assess prognosis, and to promote a more individualized treatment approach that could prolong patient survival and improve quality of life. On the presented cases of well-differentiated neuroendocrine tumors, abundant expression of SSTR in their cell surface can be used for imaging with Ga-68 SSTR that have been proven helpful for staging, post-treatment follow-up and surveillance. Furthermore, Ga-68 SSTR PET has value for treatment planning particularly in the field of theranostics to plan PRRT for somatostain receptor-expressing tumors refractory to convectional therapies or

in delineating tumor extend prior to radiotherapy or accurate delineation after surgery where it can be challenging on MRI alone.

A Case Based Review of the Future of Clinical Metabolic Versus Receptor Based Imaging

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Background: As clinical oncologic PET imaging diversifies, there are currently 2 strategies that are being used for the evaluation of patients: metabolic versus receptor based imaging. Metabolic imaging has been present from the beginning, classically with FDG, which single handedly changed the management of oncologic patients, and was the first of tracers available for molecular imaging. Another metabolic agent that is available for general use is the metabolic amino acid analogue ^{18}F-Fluciclovine (FACBC) for prostate cancer imaging.
A receptor binding imaging agent, which is becoming more widely used, is the neuroendocrine tumor somatostatin receptor (SSTR) imaging agent ^{68}Ga-DOTATATE. Prostate Specific Membrane Antigen (PSMA) receptor imaging will likely soon be available for general use.
Although the receptor-based tracers seem more promising as the standard evaluation modality respectively in Neuroendocrine (NET) and Prostate malignancies, there is still a role of metabolic imaging with FDG, and possibly FACBC.
Methods: We are presenting 2 case studies which show the ongoing usefulness of metabolic imaging despite potentially better receptor based diagnostic imaging agents, and theoretically may have an important role to play in the future of molecular imaging.
Patient 1: A patient with a high grade, poorly differentiated ovarian NET had both SSTR and FDG imaging during the course of her evaluation and treatment.
Patient 2: A patient with prostate cancer who was treated with pembrolizumab was followed with FACBC imaging. The cases highlight the time sequence of the scans in relation to chemotherapy and external radiotherapy, and other areas that are potential weaknesses for receptor based imaging.
Results: Patient 1 demonstrated diminished FDG uptake following both external beam and chemotherapy with evidence of residual disease. Conversely, SSTR imaging showed no evidence of therapeutic response. Patient 2 demonstrated diminshed FACBC uptake following pembrolizumab administration with evidence of residual disease, but also suggestive of favorable metabolic response to treatment.
Discussion: Usually, FDG is the preferred tracer for imaging high grade NETs for the purposes of staging and subsequent therapy. Patient 1 demonstrates that even though SSTR was adequate to stage the disease, metabolic imaging was more useful than receptor based imaging in following the patient's treatment response following with external radiation and chemotherapy, as is well known to happen in general oncologic imaging. Likewise, patient 2 demonstrated a metabolic therapeutic response using FACBC. In both cases, a metabolic response better guides active clinical therapeutic decisions, whereas it is theorized that receptor based imaging may not be able to provide the same clinical information as the former tracers.
Conclusion: Receptor based imaging is proving to be superior for staging, as well as invaluable for planning theranostic treatment in NET and Prostate cancers; however, these 2 cases demonstrate molecular imaging also has an ongoing role in evaluating treatment response. Hence, there will likely continue to be a role of metabolic tracers in the management of NET and Prostate cancers, even if receptor based imaging provides superior diagnostic information. Clinical trials are warranted to explore these ideas further.

Nuances in the Interpretation of Gastric Emptying Study: A Case Report

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Objective: Gastric Emptying studies performance and interpretation have been standardized based on meals and retention criteria. Although the recommendations are still straightforward, there are still some nuances that are less well understood, and it is important to perform quality control and ancillary studies to get a definitive diagnosis. Furthermore, it is important to understand the key timepoints in gastric emptying that provide more definitive diagnostic data. This case study will review the finer points of gastric emptying beyond simply reading the numbers so as to assist in coming to a correct diagnosis.
Background: 36 year old female with a 2 year history of bloating after eating and feeling extremely full, abdominal pain. She subsequently underwent an esophagogastroduodenoscopy, which noted retained food and mild reflux. She was referred to evaluate for gastroparesis.
Methods: The patient underwent an initial gastric emptying study performed with 8 oz of Ensure Plus. Subsequently 17 days later she underwent an ancillary repeat study, but with a standard meal of 4oz egg white, 2 pieces toast with jelly and 4 oz water. Each study was processed twice to verify results.
Results: The Ensure Plus study demonstrated high normal emptying rates on both initial and re-processed retention times. Although technically in the normal range, the study was read as borderline/low normal emptying rate. Subsequent standard meal emptying study showed borderline delayed emptying at 2 and 3 hours. Both the studies were reprocessed using new regions of interest, as well as slightly different intensity settings to determine anatomic contours, and the compared to the original processing. The Ensure Plus study showed slightly increased rates, whereas the Standard Meal study showed increasingly abnormal rates, compared to the original processing. Based on the clinical data and the study results the final interpretation was that the patient had delayed gastric emptying.
Conclusion: Slight changes in processing - even when it looks visually valid, and especially in borderline cases – can significantly change the diagnosis. In this case, an astute following of quality control was followed, and diligently followed up with a supportive study to demonstrate the final diagnosis. Furthermore, there are key points in gastric emptying that should be paid attention to that may assist in making the diagnosis in borderline cases. Additionally, although the 2 studies have been shown to be congruent in results, it is again important to note that incongruent results, although rare, are possible, and an overall assessment must be made to arrive at a valid clinical diagnosis.

Variable Patterns of Lymphatic Drainage Observed on Lower Extremity Lymphoscintigraphy Performed to Assess for Lymphedema.

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Background: Lymphedema is defined as the abnormal accumulation of interstitial fluid resulting from injury, infection, or congenital abnormalities of the lymphatic system. Lymphedema can be primary or secondary depending on etiology and presentation.
Lymphoscintigraphy images the flow of subcutaneous/intradermal injected radioactive colloid and interstitial fluid from the skin to the lymph nodes (1).
Methodology: Whole body images were obtained immediately after one or two intradermal injection of 0.1 mCi of Tc99m-tagged filtered sulfur colloid in the dorsum of the foot on each side; transmission scan was also

obtained. Delayed mages were obtained at 2-hours and 4-hours after the injection; if needed, further delayed images were also obtained. Imaging was performed on dual head gamma cameras.

Results: Normal lower extremity lymphatic drainage is seen in the first two cases (Cases 1 and 2) and is characterized by visualization of lymphatic channels, symmetric bilateral inguinal, iliac and retroperitoneal lymph nodes. In some cases, lymphatic channels are not seen. Lymph nodes may not be visualized until 45- minutes to 1-hour post injection. Delayed images obtained at 2-hours and 4-hours post injection may show more proximal lymph nodes in a normal study. In some instances, a left supraclavicular lymph node is visualized as in Case 2. Once the tracer reaches systemic circulation from lymphatic circulation by the time delayed images are obtained, there is visualization of the tracer in the liver and in some instances, the spleen.

Presence of lymphedema on lymphoscintigraphy is characterized by decreased number or non-visualization of lymph nodes by 2-hours post injection. Demonstration of dermal backflow is considered definitive for presence of lymphedema.

Visualization of popliteal lymph nodes may reflect an alternative pathway of drainage as this lymph node is part of the deep lymphatic system (2). However, this can depend on the injection technique. A deep injection can result in visualization of this lymph node and this finding alone does not indicate lymphedema. Rather, it is best to consider it an ancillary finding that when seen with other findings, can indicate lymphedema.

Discussion: Lymphoscintigraphy is usually performed in patients with lower limb edema and rarely for upper limb edema. Other less common indication for lymphoscintigraphy is for assessment of possible lymphatic leak. Lymphoscintigraphy has a sensitivity of 96% and specificity of 100% (3) for diagnosis of lymphedema. It is useful in patients in whom it is difficult to characterize the extremity swelling as vascular or lymphatic in origin. It is also useful in patients whose swelling is deemed of vascular etiology based on clinical and ultrasonographic evaluation and surgical procedures are planned for management; in these patients, lymphoscintigraphy can exclude lymphatic component and to help assess prognosis. It can also be used to assess the severity of lymphedema as seen by delayed transit and dermal backflow of the tracer, as patients with these findings have worse prognosis and need stringent compliance with compression therapy to prevent further extremity enlargement (1).

Conclusion: Lymphoscintigraphy is a relatively easy to perform and useful non-invasive diagnostic imaging test. Awareness of variable patterns of lymphatic drainage that can be observed in lower extremity lymphoscintigraphy is helpful in establishing or excluding the diagnosis of lymphedema.