Background: Myocardial perfusion scintigraphy (MPS) is a robust imaging technology, in terms of prognostic value, for patients with known or suspected coronary artery disease (CAD).

Objective: To determine the value of MPS in patients with no significant obstructive CAD on invasive coronary angiography.

Design: Retrospective review of patient database.

Participants: 118 patients with a normal angiogram within 3 months of MPS were included. This group was 65% male and 13% diabetic, and it had a mean age of 61 years. Exclusion criteria were previous revascularization, infarction, valvular heart disease, left bundle branch block, or cardiomyopathy.

Methods: Significant CAD was excluded when there was no lesion on angiography or when all lesions identified had <50% diameter stenosis on visual analysis. Stress MPS was performed with Tc-99m sestamibi or tetrofosmin. Scans were quantified using a fully automatic operation mode giving summed scores. Follow-up was for at a minimum 4.5 years (mean, 6.3 years). End points were (1) death; (2) a composite of major adverse events (MAEs) including death, myocardial infarction, bypass surgery, or percutaneous coronary intervention; and (3) occurrence of symptoms.

Results: There were 16 deaths, 29 patients with MAEs, and 76 patients with either an MAE or significant symptoms. Statistically significant differences in the summed stress score (SSS) were found between patients who died (SSS, 9.5 ± 6.9) versus those who did not (5.4 ± 5.6), between patients with an MAE (8.7 ± 7.2) versus those who did not have an MAE (5.2 ± 5.0), or between those who had either an MAE or significant clinical symptoms (7.2 ± 7.1) versus those who did not (4.6 ± 6.2). Logistic regression analysis found the SSS to be a predictor of death and MAEs.

Conclusions: In patients without significant angiographic CAD, MPS is a predictor of long-term prognosis.

Reviewer's Comments: Multivariate analysis found that the only predictor of death was the SSS. The only predictors of an MAE were diabetes and the SSS. (Reviewer-Thomas F. Heston, MD).

© 2009, Oakstone Medical Publishing

Keywords: Coronary Artery Disease, Myocardial Perfusion Scintigraphy, Prognosis

Print Tag: Refer to original journal article
Lasix is useful for reducing iodine in the body, leading to a greater likelihood of successful thyroid remnant ablation.

**Background:** Thyroid remnant ablation remains an important part of the postoperative care for patients with well-differentiated thyroid carcinoma. For years, there has been disagreement regarding the proper dosage of I-131 for this purpose. In addition, the value of iodine depletion using Lasix and lithium to enhance iodine retention in remnants and tumor has received interest in recent years.

**Objective:** To evaluate the added value of Lasix and lithium for remnant ablation.

**Design:** Prospective study.

**Methods:** rTSH (Thyrogen) in the usual protocol was used for all subjects to elevate TSH levels. The authors treated stage I-II patients with 30 mCi of I-131 and stage III-IV patients with 100 mCi. Within each of these dosing groups, there were 3 subgroups: group 1 had T4 withheld for 4 days; group 2 had T4 held plus 3 days of Lasix before treatment; and group 3 had T4 held plus 3 days of Lasix plus lithium therapy. All patients underwent low-iodine diet for 2 weeks prior to radioiodine. The control group was treated with 30 mCi with no additional intervention.

**Results:** 201 subjects participated in the study. In the 30-mCi group, withholding T4 and using Lasix were additively and significantly effective in improving the likelihood of successful ablation. In the 100-mCi group, although there was improvement in outcome with Lasix, it was not statistically significant (increase from 90% to 95% in ablation success rate). Lithium did not seem to add to the outcome success rate in either dosage group.

**Conclusions:** The use of Thyrogen was very effective for remnant ablation. When using 30 mCi of I-131, the addition of Lasix plus discontinuation of T4 was highly beneficial.

**Reviewer's Comments:** T4 contains a significant amount of “cold” iodine, and the benefit of withholding this hormone for 3 to 4 days before therapy has been demonstrated by others. My approach is to start a low-iodine diet, begin Lasix therapy, and discontinue T4, all at the same time 4 days prior to therapy with I-131. Most patients are unable to follow a strict 2-week low-iodine diet. I use Lithium only when treating stage IV patients. Remember that the most important aspect of postthyroidectomy I-131 therapy is the prevention of tumor recurrence. Consequently, elimination of micrometastases is the ultimate goal of this treatment. As such, in higher-risk patients, I prefer using 100 mCi even though 30 mCi may well eradicate the actual thyroid remnant. (Reviewer-David Bushnell, MD).

© 2009, Oakstone Medical Publishing

Keywords: Remnant Ablation, Lasix, Lithium

Print Tag: Refer to original journal article
The standard uptake value is influenced by patient preparation, acquisition timing, and the selection of regions. Meaningful SUV results require attention to details and compliance among the participating sites.

**Background:** Standard uptake values (SUVs) in F-18 FDG PET studies that are used to monitor response to therapy may be limited by measurement variability.

**Objective:** To assess the reproducibility of F-18 FDG SUVs obtained in a multicenter phase I trial when quality assurance routines were followed.

**Participants:** 62 patients sequentially enrolled in a clinical trial with 8 participating institutions.

**Methods:** Two baseline F-18 FDG PET studies were acquired within 14 days of therapy initiation and within a 7-day window of each other. Visualized tumor uptake was monitored with SUV determined in 4 different ways based on mean, 70% threshold mean or maximum region counts, or by peak volume value. The reproducibility of the SUV measurements was evaluated from absolute differences between the 2 studies. The effects of compliance with the imaging and analysis protocol were investigated. The site-generated results for the entire subject group were compared with (1) the subgroup that complied with the study quality assurance (QA) procedures and (2) the compliance subgroup in which all SUVs were generated by a single individual. Statistical evaluations of the SUV results included repeatability coefficients and intra-subject coefficients of variation along with confidence intervals of the mean differences.

**Results:** The mean difference between the repeated individual SUV measurements varied from -2% to 1.9%. The intra-subject coefficient of variation was best for the single observer SUVs (10.7%), was slightly worse for the multiobserver QA group (12.7%), and was 16% for the entire set. The reproducibility of the SUV measurements was fairly independent of the SUV method.

**Conclusions:** The reproducibility of the SUV from repeated F-18 FDG scans was improved in clinics that complied with QA procedures. These results indicate that SUV can be used to monitor tumor FDG uptake in multicenter oncologic clinical trials.

**Reviewer’s Comments:** Although SUV has been used for at least 2 decades as a means of quantifying tumor metabolism in F-18 FDG studies, the PET community has been slow to adopt a standard SUV method. This creates obvious problems when SUVs obtained at different sites are compared. This paper is one of several recent studies to show that SUVs can be reliably used when all sites use the same image acquisition protocol and SUV method. It also points out the need for standard imaging protocols and the advantage of having a centralized analysis group for obtaining the SUVs. (Reviewer-Mark T. Madsen, MD).

© 2009, Oakstone Medical Publishing

Keywords: SUV Repeatability, FDG PET, Quality Assurance

Print Tag: Refer to original journal article
CCTA Reduces Need for ICA After Equivocal Stress Results

Clinical Effectiveness of Coronary Computed Tomographic Angiography in the Triage of Patients to Cardiac Catheterization and Revascularization After Inconclusive Stress Testing: Results of a 2-Year Prospective Trial.

Abidov A, Gallagher MJ, et al:

J Nucl Cardiol 2009; 16 (September-October): 701-713

Coronary CT angiography reduces the rate of invasive coronary angiography in patients with an equivocal stress imaging study.

**Background.** Patients with an inconclusive stress imaging tests frequently undergo invasive coronary angiography (ICA). Coronary CT angiography (CCTA) may help define risk in this patient population, thus reducing the need for ICA.

**Objective:** To determine the incremental value of CCTA in patients with an equivocal or inconclusive stress imaging test (stress myocardial perfusion imaging [MPI] or stress echocardiography).

**Participants:** 199 patients with suspected coronary artery disease, equivocal stress MPI or stress echocardiography within the previous 90 days, and age ≥25 years.

**Methods:** Referring physicians completed a structured questionnaire to help researchers identify a "planned catheterization" group of patients (those who would undergo ICA if CCTA were not available). Patients underwent CCTA within 90 days of a prior equivocal stress MPI or stress echocardiography test. Patients were followed up for ±2 years. CCTA studies were classified as normal (no obstructive disease), mild (stenosis ≤50%), or abnormal (>50% stenosis).

**Results:** Of the 199 patients, there were no deaths, no myocardial infarctions, no acute coronary syndromes, and 3 unique late revascularizations. Eighteen patients underwent percutaneous coronary interventions (PCI). None of the 93 patients with a normal CCTA underwent ICA, and no major adverse cardiac events occurred in any of these patients. Of the 70 patients with mild disease on CCTA, 8 had ICA, 3 had PCI, and 2 had late revascularization. Of the 36 patients with an abnormal CCTA (>50% stenosis), 24 had ICA, 15 had PCI, and 2 had a late revascularization. Overall, prior to CCTA, there were 125 patients scheduled to undergo ICA. After CCTA, only 32 underwent ICA.

**Conclusions:** CCTA dramatically reduces the rate of ICA in patients with equivocal stress imaging tests.

**Reviewer’s Comments:** The authors state that a normal CCTA is associated with an excellent intermediate-term prognosis. However, they fail to state this in their study cohort, because an abnormal CCTA was also associated with an excellent intermediate-term prognosis. All of the adverse events were only late revascularizations. Furthermore, there were only 3 patients of the 199 who underwent a late revascularization, one with nonobstructive disease (stenosis ≤50%) on CCTA and 2 with obstructive (>50%) disease by CCTA. It is questionable whether CCTA was helpful in identifying these 3 patients, but CCTA did appear to decrease the number of conventional coronary angiograms. (Reviewer-Thomas F. Heston, MD).

© 2009, Oakstone Medical Publishing

Keywords: Coronary Artery Disease, Inconclusive Stress Imaging Tests, CCTA

Print Tag: Refer to original journal article
Normal FDG Distribution in Kids, Adults May Differ

Pediatric FDG PET/CT: Physiologic Uptake, Normal Variants, and Benign Conditions.

Shammas A, Lim R, Charron M:

Radiographics 2009; 29 (September-October): 1467-1486

Physicians who interpret pediatric PET/CT exams should be aware of normal variations in FDG activity in children.

Background: PET/CT exams in children do not necessarily have the same physiologic distribution of FDG as in adults. An appreciation of normal physiologic variants is essential for optimal interpretation of these exams in children.

Objective: To highlight these normal patterns in children and to discuss other benign causes of FDG accumulation.

Results: In young children especially, uptake in the Waldeyer ring may be particularly intense due to very active lymphoid tissue. The symmetric pattern should alert the interpreter to the normalcy of this pattern. Similar to adults, symmetric salivary gland activity is also present to a greater or lesser degree. Unlike adults, intense uptake may often be seen in the ocular muscles in children. The inverted V appearance of the normal thymus gland in the anterior mediastinum on coronal images is unique to children. In contrast, adults may show some normal thymic uptake after chemotherapy. Like adults, children may demonstrate variable bowel uptake, which is often most intense in the cecum. Testicular activity levels are often fairly high but symmetric, whereas before puberty, uptake is typically not seen in normal ovaries. After puberty, uptake within the ovaries is variable depending on the menstrual cycle. FDG uptake may be seen in the diaphragm and intercostal muscles if the child was crying during injection. Brown adipose tissues are not uncommon, particularly during winter and may, at times, be asymmetric. Well known sites for brown fat uptake include neck, paravertebral, and mediastinum in addition to the perinephric region. Brown fat uptake can be notably reduced by warming the individual before injection of FDG or administering propranolol or diazepam. Some benign bone conditions may cause variable and high FDG uptake. Nonossifying fibromas, osteoid osteomas, or chondroblastomas may all cause high FDG accumulation. As in adults, infectious conditions may also lead to higher concentrations of FDG.

Conclusions: The authors conclude, “Many of the normal variants in children are similar to those in adults. However, the normal distribution of FDG uptake in children is unique and may differ from that in adults, such as the physiologic activity of the lymphatic tissue in the Waldeyer ring, as well as uptake in the ileocecal region, thymus, hematopoietic bone marrow, and skeletal growth centers.”

Reviewer's Comments: In general, normal variants in children and adults are similar, but these authors also point out certain distinctions. The images and illustrations in this presentation are excellent. (Reviewer-David Bushnell, MD).

© 2009, Oakstone Medical Publishing

Keywords: PET/CT, FDG Distribution, Pediatrics

Print Tag: Refer to original journal article
Dosimetry Helps Us Adjust I-131 to Maximize Efficacy, Safety

Utility of the Radioiodine Whole-Body Retention at 48 Hours for Modifying Empiric Activity of 131-Iodine for the Treatment of Metastatic Well-Differentiated Thyroid Carcinoma.

Van Nostrand D, Atkins F, et al:

Thyroid 2009; 19 (October): 1093-1098

For patients undergoing treatment of thyroid carcinoma, the percent whole-body retention of I-131 at 48 hours helps identify patients in whom the empiric prescribed dose if I-131 may be increased or decreased.

Background: I-131 is commonly used in the treatment of metastatic well-differentiated thyroid carcinoma (WDTC), but no firm guidelines for dosimetry have been established. Current clinical practice makes no attempt to assess radiation absorbed either to the cancer or other critical organs. Dosimetry is a lengthy process that requires ≥4 days and several blood samples at various times.

Objective: To assess the utility of the percent whole-body retention of I-131 at 48 hours (%WBR-48hr) to identify patients who may need dose adjustments, and to evaluate the thresholds proposed by Sisson et al in 2003.

Participants: 142 patients with WDTC who underwent a total or near-total thyroidectomy and had I-131 whole-body dosimetry performed between 2000 and 2005.

Methods: A retrospective study was performed to determine %WBR-48hr. Sisson’s proposed criteria, based on the %WBR-48hr, are as follows. If %WBR-48hr is ≤9%, then increase the activity of I-131. If %WBR-48hr is <5%, then increase the activity of I-131 by 50% to 100%. If >24.8%, then decrease the activity of I-131. If >40%, then substantially decrease the activity of I-131. Evaluation of Sisson and colleagues’ 4 thresholds was done relative to an empiric activity of 200 mCi of I-131.

Results: Of patients with a %WBR-48hr of ≤9%, 100% could have had their dose increased without exceeding a radiation absorbed dose of 200 rads to the blood. Of the patients with %WBR-48hr <5%, 100% could have had their dose increased by at least 500 mCi. Of the patients with a %WBR-48hr of >24.8%, 50% would have exceeded a 200-rad dose to the blood. Of the patients with a %WBR-48hr >40%, 83% would have exceeded a 200-rad dose to the blood.

Conclusions: %WBR-48hr of I-131 helps identify patients in whom the empiric prescribed dose may be increased or should be decreased so as not to exceed the maximum tolerated activity (MTA). Sisson and colleagues’ thresholds are applicable and provide a template for dosimetry.

Reviewer’s Comments: Since Sisson and colleagues published their recommendations 6 years ago, many centers including ours have incorporated the 48-hour whole-body measurements into their protocol. This article not only confirms the value of the 48-hour whole-body measurement, but it also offers specific quantitative guidelines for determining when and how much I-131 to add or subtract from an empirical dose. (Reviewer-C. Richard Goldfarb, MD).

© 2009, Oakstone Medical Publishing

Keywords: Thyroid Carcinoma, I-131 Dosimetry, Retention

Print Tag: Refer to original journal article
I-131 Significant Risk Factor for TAO Development

Thyroid-Associated Ophthalmopathy After Treatment for Graves’ Hyperthyroidism With Antithyroid Drugs or Iodine-131.

Traisk F, Tallstedt L, et al:

J Clin Endocrinol Metab 2009; 94 (October): 3700-3707

Compared to antithyroid drugs for treating hyperthyroidism, I-131 significantly increases the incidence of the development of Graves ophthalmopathy but not the incidence of the worsening of ophthalmopathy.

Background: I-131 therapy for hyperthyroidism has been linked to progression of the course for thyroid-associated ophthalmopathy (TAO). Recent searches of the literature reported that radioiodine treatment increases the risk of TAO development or progression compared with medical therapy. But, because randomized trials are very few and definitions of TAO vary from study to study, it is not firmly established that I-131 causes or worsens TAO.

Objective: To compare I-131 with medical therapy for TAO worsening or development.

Design: A 4-year prospective multicenter trial.

Participants: Inclusion criteria were age 35 to 69 years; symptomatic Graves hyperthyroidism; elevated uptake of I-131; and scans compatible with Graves disease (even distribution of radionuclide).

Methods: Patients were randomly assigned to either I-131 (n=163) or medical treatment (n=150). The primary end point was the difference in worsening or development of TAO between the 2 groups.

Results: The incidence of TAO development was significantly higher in patients receiving I-131 treatment (n=53) compared to those receiving antithyroid drugs (n=23). However, incidence of TAO worsening did not differ significantly between I-131 patients (n=10) versus medically treated patients (n=9). Of the 41 patients with preexisting TAO, 10 in each group improved. Smoking increased the risk of TAO worsening or development, but in smokers, the choice of treatment did not have a significant impact on TAO. In nonsmokers, I-131 treatment increased the risk of TAO worsening or development. Corticosteroid treatment of TAO was required in more patients in the I-131 treatment group (n=15, 9.2%) than in the medically treated group (n=4, 2.7%). Eye changes requiring steroids included soft tissue changes only in 3 patients, increased proptosis (≥3 mm) in 2 patients, impairment of eye motility in 2 patients, and both increased proptosis and impairment of eye motility in 12 patients. No patient suffered optic nerve compression.

Conclusions: The study confirms an association between I-131 treatment and TAO and between smoking and TAO. A watchful follow-up for development of TAO is important.

Reviewer’s Comments: The effect of I-131 therapy on Graves ophthalmopathy is a matter that has remained blurry since I-131 was first used to treat Graves disease >70 years ago. This paper deserves attention as the most current, carefully conducted study on the topic. It is novel and most welcome news that I-131 in Graves disease doses does not worsen already existing ophthalmopathy. Although eye signs may appear after I-131 treatment, all cases can be monitored or treated with steroids before they become severe. (Reviewer-C. Richard Goldfarb, MD).

© 2009, Oakstone Medical Publishing

Keywords: Graves Disease, Thyroid-Associated Ophthalmopathy, I-131

Print Tag: Refer to original journal article
FDG-PET/CT is an important imaging technique for patients with Ewing sarcoma. For example, FDG signal can help establish tumor borders (particularly when combined with MRI), which aids in surgical planning.

**Background:** Ewing sarcoma is the second most common bone malignancy in children. Although survival for patients with localized disease has improved notably, those with distant metastases remain difficult to successfully treat. FDG-PET/CT can be useful for staging and for evaluating response to therapy in many types of malignancy.

**Objective:** To discuss the value and limitations of PET for patients with Ewing sarcoma.

**Results:** The most common site of a primary Ewing sarcoma is the pelvis, followed by femur and tibia. Metastatic disease may be seen in the bone marrow and/or lungs. Mean standard uptake values (SUVs) for this tumor are reported to be approximately 5.0. However, there is notable overlap with the SUV levels from benign bone tumors. Examples of benign bone lesions with notable FDG uptake include chondroblastoma, histiocytosis, fibrous dysplasia, and sarcoidosis. Many of these lesions have characteristic CT findings which make PET/CT imaging all the more valuable in this setting. It has been found that FDG signal from PET can aid in the establishment of tumor borders, particularly when combined with MRI, and, in this way, it can improve surgical planning. Some studies have also found that the SUV level of the primary tumor can predict outcome following adjuvant chemotherapy prior to definitive surgery. SUV levels <2 to 2.5 appear to predict excellent outcome in this regard. PET has been found to be superior to other imaging techniques for detecting bone and nodal metastases. However, it appears to be less accurate than CT for detecting pulmonary metastases from Ewing sarcoma. PET also seems to be superior to CT and MRI for detecting local tumor recurrence following initial surgical or radiation therapy.

**Conclusions:** The authors conclude that, “…optimal evaluation of Ewing sarcoma consists of FDG PET combined with correlative anatomic imaging modalities such as radiography, CT, and MR imaging.”

**Reviewer's Comments:** If you find yourself evaluating a PET/CT exam in a patient with Ewing sarcoma, this is a nice article to reference. (Reviewer-David Bushnell, MD).

© 2009, Oakstone Medical Publishing

Keywords: Ewing Sarcoma, Assessment, PET/CT

Print Tag: Refer to original journal article
I-131 ablation using 100 mCi results in minor decreases in platelet and white blood cell counts for a year after thyroid remnant ablation. These findings support our continued efforts to tailor doses to individual patients.

**Background:** Bone marrow suppression, leukemia, and pulmonary fibrosis are uncommon but concerning complications following repeated high-dose I-131 therapy. I-131 is cleared from the blood more rapidly after Thyrogen (rhTSH) preparation as compared to thyroid hormone withdrawal (THW). Toxic adverse side effects of I-131 may be fewer after remnant ablation with rhTSH than with THW. Thrombocytopenia in the first 2 months after 100 mCi I-131 for ablation occurred in 21% of patients prepared with THW versus 7% with rhTSH. The mean decrease in neutrophils (nadir) was twice as high in the THW group compared with the rhTSH group. Six months after ablation, platelet and neutrophil counts had returned to normal in 10 of 12 patients. Longer follow-up was not done. The risk of persistent anemia, leukopenia, and thrombocytopenia after an initial ablative treatment of I-131 is not well-defined.

**Objective:** To evaluate the complete blood count (CBC) obtained 1 year after I-131 treatment.

**Design:** Retrospective review.

**Participants:** 206 thyroid cancer patients undergoing initial I-131 remnant ablation. Most patients were prepared with rhTSH (78%). Administered activities were similar in the rhTSH cohort (median dose, 108 mCi) and the THW group (102 mCi).

**Results:** At the 1-year reevaluation point, no patient had clinical complications from lower blood counts, none had severe thrombocytopenia, and none had significant leukopenia. Low white blood cell (WBC) counts were found in 10% of patients at 1 year versus 4% of patients at baseline. Platelet counts showed a similar outcome (5.8% at 1 year versus 1.5% at baseline). At 1 year, 30 patients had an abnormal CBC, 20 patients had WBC levels below the normal range, 12 had abnormal platelet counts, and 1 had a hemoglobin abnormality.

**Conclusions:** I-131 ablation using 100 mCi results in minor decreases in platelet and WBC counts for a year after ablation. These changes have little clinical significance, and the risks do not outweigh the benefits of I-131 ablation.

**Reviewer's Comments:** Since the 30-mCi maximum rule for outpatients was abolished, we have been routinely administering 100 mCi of I-131 for ablation. In the past 2 years, we have been scaling back to 50 or 75 mCi in some patients by paying attention to risk stratification. Although there were no clinically significant adverse events in this series, the finding that 100 mCi causes long-term marrow suppression supports continued effort to tailor doses to individual patients. (Reviewer-C. Richard Goldfarb, MD).

© 2009, Oakstone Medical Publishing

Keywords: Hyperthyroidism, I-131 Remnant Ablation, Marrow Suppression

Print Tag: Refer to original journal article
Resolution recovery algorithms have been shown to improve quality of SPECT studies, and that improvement can be used to reduce the administered activity, imaging time, or some combination of both.

Background: Myocardial perfusion SPECT procedures require 2 to 3 hours per patient. Can this time be reduced with resolution recovery software? 

Objective: To evaluate the Philips’ Astonish processing software on stress myocardial perfusion studies (MPS) corrected for attenuation by comparing the results against conventional rest and stress myocardial perfusion SPECT.

Methods: 110 patients from 3 different medical centers had gated rest and stress MPS with radionuclide attenuation correction. Eighteen patients had <5% likelihood of coronary artery disease, while 92 received catheterization studies of the coronary arteries. Each acquisition had 64 projections, so the half-time (that is, 32 projections) and full-time acquisitions could be directly compared. The full-time stress and rest studies were not corrected for attenuation and were reconstructed with filtered back projection. The half-time studies were processed with the Astonish reconstruction software that provides resolution recovery and scatter correction. The half-time studies were also corrected for attenuation. The full- and half-time data sets were randomized and interpreted by 2 readers who were blinded to the clinical information.

Results: The readers found the image quality of the stress studies to be similar, with excellent to good rankings for 82% of the full-time studies and 89% in the half-time studies. Although the differences in normalcy, sensitivity, specificity, and accuracy did not reach statistical significance, the attenuation-corrected half-time images were superior in each category: sensitivity, 83% (full-time, 77%); specificity, 71% (full-time, 61%); and normalcy 100% (full-time, 94%). The summed stress scores (SSS) were also similar, but again the half-time images had the edge. In patients with coronary artery disease, the SSS was 7.4 for full-time versus 7.8 for half-time images. For patients with low likelihood of cardiac disease, the SSS was 0.7 for full-time and 0 for half-time images. The left ventricular ejection fraction determined from both approaches averaged 60%.

Conclusions: The interpretations resulting from the stress-only half-time studies processed with Astonish and corrected for attenuation provided equivalent results when compared with the conventionally processed rest and stress studies.

Reviewer’s Comments: Resolution recovery algorithms have been commercially available for several years, and an increasing number of papers indicate that these products allow either the reduction of acquisition time or administered activity. This paper promises to deliver both through (1) elimination of the rest study and (2) half-time imaging for the stress study. Larger trials will probably be required before this approach is widely applied, but the application of resolution recovery algorithms in myocardial SPECT studies can be expected to expand. (Reviewer-Mark T. Madsen, MD).

© 2009, Oakstone Medical Publishing

Keywords: Myocardial Perfusion SPECT, Resolution Recovery Software

Print Tag: Refer to original journal article
FDG PET Helps Avoid Other Traumatic Diagnostics for FUO

Diagnostic Value of [18F]-FDG PET/CT in Children With Fever of Unknown Origin or Unexplained Signs of Inflammation.

Jasper N, Dabritz J, et al:


F-18 FDG PET/CT may be a useful diagnostic tool in the workup for fever of unknown origin. In a study of children, FDG PET/CT was helpful for establishing a diagnosis in 45% of patients.

**Background:** Fever of unknown origin (FUO) is a diagnostic challenge in adults and children. The multiple lab studies, imaging procedures, and biopsies that are often required to establish a diagnosis represent a considerable morbidity for children (radiation dose from various imaging procedures; multiple, painful blood draws that can lead to hematomas and difficulty establishing subsequent intravenous access; etc). As such, the prospect of using FDG PET/CT earlier in the diagnostic workup for detection of fever-causing disease is being evaluated because it is noninvasive and could negate the need for more studies or, more precisely, direct further diagnostic efforts.

**Objective:** To evaluate F-18 FDG PET/CT as a diagnostic tool in the evaluation of FUO or unexplained signs of inflammation (USI).

**Methods:** 77 FDG PET/CT scans in 69 children were retrospectively reviewed. Scans were either scored as “helpful” or “not helpful” in their ability to help diagnose the cause of FUO/USI. Imaging was also correlated with various laboratory studies commonly drawn in the evaluation of these medical entities.

**Results:** FDG PET/CT was helpful in only 45% of patients. However, among this group, a diagnosis was reached in 77% of patients. FDG PET/CT was more helpful among patients in whom FUO (versus USI) was the reason for the diagnostic workup. Common lab data correlated significantly with scan positivity but not with whether the scans were deemed “helpful” versus “not helpful.”

**Conclusions:** FDG PET/CT can be useful in the diagnosis of FUO/USI in children.

**Reviewer's Comments:** This interesting study seems to highlight the usefulness of FDG PET/CT in the diagnosis of FUO/USI. Although 55% of patients did not benefit from undergoing the scan, 45% did, with most of those having a diagnosis after the scan was performed. Although this may not seem overwhelmingly significant, the fact that a diagnosis was achieved in 45% of patients suffering from one of the most challenging medical entities (made more difficult in the pediatric population) is significant as additional evaluation was either avoided or more precisely targeted to decrease the morbidity associated with the various diagnostic studies. (Reviewer-Damita Thomas, MD).

© 2009, Oakstone Medical Publishing

Keywords: Pediatric Fever of Unknown Origin, Diagnosis, FDG PET/CT

Print Tag: Refer to original journal article
Both fixed and reversible defects seen on Rb-82 PET myocardial perfusion imaging are associated with an increased probability of future cardiac events.

**Objective:** To define the incremental value of Rb-82 PET myocardial perfusion imaging (MPI) and left ventricular ejection fraction (LVEF) assessment over clinical variables for the prediction of survival free of cardiac events and all-cause death.

**Methods:** 1432 patients underwent gated rest and vasodilator-induced stress Rb-82 PET MPI. Of these patients, 985 had rest and peak stress LVEF determined. Patients underwent PET/CT imaging following the IV administration of 40 to 60 mCi of Rb-82. CT was used only for attenuation correction. Images were interpreted by 2 experienced observers who scored the studies semiquantitatively using the standard 17-segment model and a 4-point scoring system to compute summed rest scores (SRS), summed stress scores (SSS), and summed difference scores (SDS). LVEF reserve was calculated as stress LVEF minus rest LVEF. Patients were followed up for a minimum of 1 year. End points were cardiac events, defined as cardiac death or nonfatal myocardial infarction (MI), and all-cause death.

**Results:** Mean follow-up was 1.7 years. Mean age was 63 years, and 30.6% of patients had known coronary artery disease. Overall, 46% of patients had a normal MPI. The frequency of cardiac events and all-cause death increased as a function of the percentage of abnormal (stress defect), scarred (rest defect), or ischemic (reversible defect) myocardium. The observed rates of cardiac death, MI, and all-cause death were 2.9%, 2.2%, and 7.8%, respectively, in the group with mild ischemia compared to 2.4%, 3.3%, and 6.6%, respectively, in the group with moderate ischemia. Compared with a normal MPI, an abnormal MPI was associated with a higher frequency of cardiac events, both in patients with rest LVEF <40% and in patients with LVEF >40%. The frequency of cardiac events and all-cause death was higher in patients with LVEF reserve <0 than in patients with LVEF reserve ≥0. Clinical and historical variables were predictive of cardiac events and all-cause death, but addition of MPI data consisting of percent myocardium affected, scarred, or ischemic resulted in better prediction. The inclusion of LVEF reserve resulted in incremental prognostic value for all-cause death over PET MPI data alone.

**Conclusions:** Rb-82 PET MPI provides incremental prognostic value over clinical variables and rest LVEF alone. Similarly, LVEF reserve provides independent and incremental predictive value over MPI and clinical data.

**Reviewer's Comments:** The incremental prognostic value of SPECT MPI is well-established, but this study helps confirm the value of PET MPI and is the first to demonstrate the incremental value of LVEF reserve.

(Reviewer-Shayne Squires, MD)

© 2009, Oakstone Medical Publishing

Keywords: Myocardial Perfusion Imaging, PET, Coronary Artery Disease

Print Tag: Refer to original journal article
Maximum left and right ventricular uptake of Rb-82 during stress-rest myocardial perfusion imaging can be useful in predicting 3-vessel and left main disease.

**Background:** Myocardial perfusion imaging has the potential to underestimate the severity of coronary artery disease (CAD), particularly in cases of balanced 3-vessel or left main disease.

**Objective:** To determine if quantification of peak left ventricular (LV) and right ventricular (RV) Rb-82 uptake can identify patients with left main or 3-vessel disease.

**Design:** Retrospective review.

**Participants:** 169 patients referred for clinical reasons to both Rb-82 cardiac PET and coronary angiography.

**Methods:** Coronary angiograms were categorized as having no significant coronary stenosis (n=60), 1- or 2-vessel disease (n=81), or left main disease/3-vessel disease (n=28). Maximal LV and RV myocardial Rb-82 uptake was measured during stress and rest by visually identifying the site of maximal uptake on the short axis images, then creating a small region of interest on the corresponding transaxial image, and finally determining the maximum uptake in Bq/cc.

**Results:** Failure to increase the LV uptake by ≥8500 Bq/cc at stress predicted left main or 3-vessel disease with a sensitivity of 93% and a specificity of 61%, with an area under the curve of 0.83. A ≥10% increase in the RV-to-LV uptake ratios with stress over rest was 93% specific (area under curve, 0.74) for left main or 3-vessel disease. These indices incrementally predicted left main or 3-vessel disease compared to models including age, gender, cardiac risk factors, and summed stress and difference scores.

**Conclusions:** The quantification of maximal rest and stress LV and RV uptake with Rb-82 PET myocardial perfusion imaging may independently and incrementally identify patients with left main or 3-vessel disease.

**Reviewer’s Comments:** Figure 5 in this article nicely displays the major findings of this study. The authors found maximal tracer uptake to be a highly reproducible variable. (Reviewer-Thomas F. Heston, MD).

© 2009, Oakstone Medical Publishing

Keywords: Coronary Artery Disease, Myocardial Perfusion Imaging, PET

Print Tag: Refer to original journal article
Adrenal uptake on 123I-MIBG scans is likely benign if the uptake appears less intense than liver.

**Objective:** To determine whether a scoring system can be used to distinguish pheochromocytomas from benign adrenal tissue on 123I-MIBG scans.

**Design:** Retrospective study.

**Methods:** The authors reviewed medical records from 67 consecutive patients who underwent 123I-MIBG scintigraphy. Patients underwent whole-body planar imaging with a low-energy, high-resolution collimator at 4 and 24 hours after the intravenous administration of 300 to 370 MBq of 123I-MIBG. Two experienced nuclear medicine physicians interpreted the images and scored adrenal uptake as follows: less than liver (1); equal to liver (2); moderately more intense than liver (3); and markedly more intense than liver (4). Scans were considered positive for scores of 3 or 4, extra-adrenal uptake, or adrenal enlargement by conventional imaging with inhomogeneous adrenal radiotracer uptake. All patients underwent abdominal CT and had urinary catecholamine and/or fractionated urinary metanephrine levels. Presence of pheochromocytoma was determined by surgical pathology or long-term clinical follow-up.

**Results:** 5 scans were true positives based on extra-adrenal uptake, and 1 was a true positive based on inhomogeneous adrenal enlargement. The remaining scans were designated as positive or negative based on the proposed scoring system. This method resulted in a sensitivity of 91.5% and a specificity of 100%. Mean subject age was 48 years. Postsurgical histology was available in 71.6% of patients. In the remainder, adrenal gland status was determined by clinical follow-up (median, 9.25 years). Patients were referred for imaging due to severe hypertension and adrenal or extra-adrenal mass by CT (n=49); familial syndromes such as multiple endocrine neoplasia type IIA, neurofibromatosis type1, or von Hippel Lindau disease (n=14); or incidentally discovered adrenal mass (n=4).

**Conclusions:** Comparison of adrenal uptake with liver uptake on 123I-MIBG scans can help distinguish benign physiologic uptake from pheochromocytoma.

**Reviewer's Comments:** Although there is a higher incidence of benign adrenal uptake using 123I-MIBG than 131I-MIBG, 123I-MIBG is a more desirable imaging agent due to its compatibility with gamma imaging, shorter half-life, and lack of beta emission. (Reviewer-Shayne Squires, MD).
Fluorocholine uptake in prostate cancer metastases is less likely in dense, sclerotic bone lesions.

**Objective:** To determine the sensitivity and specificity of 18F-fluorocholine for the detection of prostate cancer osseous metastases and to compare PET images with morphologic changes on CT.

**Participants:** 70 men with biopsy proven prostate cancer.

**Methods:** 32 patients without prior therapy who had PSA >10 and Gleason score ≥7 were evaluated preoperatively, and 38 patients who previously underwent surgery plus radiation and/or chemotherapy and who had suspected recurrence were evaluated postoperatively. PET images were acquired in 2D mode beginning 1 minute after the IV administration of 18F-fluoromethylcholine (FCH) and reconstructed using standard iterative OSEM. Images were interpreted by 2 nuclear medicine physicians and 1 radiologist who had access to clinical data and prior imaging studies. Lesions that appeared benign or malignant on both CT and PET were classified as true-negative or true-positive lesions, respectively, with positive lesions confirmed on bone scan or MRI. Discrepant lesions were reevaluated 6 to15 months later with a follow-up study: if they showed increased PET uptake with corresponding CT change and clinical progression, they were classified as positive. Lesions that appeared positive on PET initially but negative on follow-up with normal CT were classified as false-positive lesions, and lesions that appeared negative by PET but positive by CT or bone scan were classified as false-negative.

**Results:** Among the 70 patients, there were 318 bone lesions detected by PET/CT, of which 262 showed increased PET uptake. Forty-five lesions were classified as indeterminate due to inability to confirm diagnosis on follow-up and were excluded from the study, and 7 lesions were determined to be due to degenerative joint disease or inflammation. Sensitivity, specificity, and accuracy of FCH-PET were 79%, 97%, and 84% respectively. Interestingly, there was a negative correlation between FCH uptake and density of sclerotic lesions, with most FCH-negative sclerotic bone lesions (false-negatives) occurring in patients on hormone therapy.

**Conclusions:** FCH-PET/CT is capable of early detection of prostate cancer bone metastases.

**Reviewer's Comments:** FCH appears to be more specific but possibly less sensitive than bone scan. Hopefully, in the future, it can be used to detect nodal metastases at initial staging. (Reviewer-Shayne Squires, MD).

© 2009, Oakstone Medical Publishing

Keywords: Prostate Cancer, Bone Metastases, Fluorocholine, PET

Print Tag: Refer to original journal article
Viability Testing Helps Allocate CAD Patients to Treatment

Radionuclide Viability Testing: Should It Affect Treatment Strategy in Patients With Cardiomyopathy and Significant Coronary Artery Disease.

Bourque JM, Velazquez EJ, et al:

Am Heart J 2003; 145 (May): 758-767

Objective: To determine the effect of nuclear viability imaging on treatment strategy and long-term outcome in patients with impaired left ventricular (LV) function and coronary artery disease (CAD).

Design: Systematic review of the literature.

Methods: The authors performed a MEDLINE search for studies on heart failure, CAD, nuclear viability testing, and long-term outcomes. Studies that did not address long-term survival in patients with LV dysfunction and CAD following imaging with PET or SPECT using FDG-, thallium-, or technetium-based agents were excluded. Studies that looked at transient LV dysfunction following myocardial infarction were also excluded.

Results: 14 studies met inclusion criteria. Sample size in each study ranged from 35 to 137 (median, n=85), with a total sample size of 1192. Follow-up ranged from 12 to 46 months (median, 26months) with a total event number of 256. Mean ejection fraction for each study ranged from 24% to 40%, and the percentage of patients with class III or class IV heart failure ranged from 19% to 100%. Definition of significant coronary artery stenosis ranged from 50% to 100%. Comparison of outcomes was limited by the variability in study protocols. For example, some studies used thallium rather than FDG-PET, and some studies looked at only patients who underwent coronary artery bypass grafting, while others looked at patients who had only viability testing. With these limitations, the studies showed that patients with viable myocardium who underwent revascularization had a lower mortality rate than did patients with viability who received medical therapy. Patients without viability had an intermediate survival rate regardless of the treatment modality.

Conclusions: Radionuclide viability studies may be useful for allocating patients with impaired LV function and CAD to medical therapy or revascularization, but larger studies with uniform protocols and longer follow-up are needed.

Reviewer's Comments: Eight studies reviewed in this paper used thallium rest/redistribution to assess for viability, and 5 used FDG-PET. Although the numbers are too small for adequate statistical analysis, the results appeared similar for either method. (Reviewer-Shayne Squires, MD).

© 2009, Oakstone Medical Publishing

Keywords: Coronary Artery Disease, Nuclear Viability Imaging

Print Tag: Refer to original journal article
Patients with classic symptoms of biliary dyskinesia are more likely to have resolution of symptoms following cholecystectomy than are patients with an atypical presentation.

**Objective:** To determine the success rate of cholecystectomy versus observation in patients with gallbladder dyskinesia using clearly defined symptoms to allocate patients to treatment.

**Methods:** This prospective study included 93 patients referred for biliary dyskinesia, defined as gallbladder ejection fraction (GBEF) <35% after stimulation with cholecystokinin (CCK) and negative ultrasound. All patients underwent hepatobiliary imaging following the intravenous administration of 5 mCi of 99mTc-labeled mebrofenin. GBEF was measured following continuous infusion with 0.02 µg/kg CCK. Patients were grouped according to whether they had classic biliary symptoms (group 1) or atypical symptoms (group 2). Group 1 patients had both right upper quadrant pain and pain after meals, as well as at least 1 of the following: nausea, vomiting, radiation to back, worse pain with fatty foods, weight loss, anorexia, or reproduction of pain with CCK. Group 1 patients were offered laparoscopic cholecystectomy right away.

**Results:** 61 patients were assigned to group 1, and 32 patients were assigned to group 2. GBEF was not significantly different between group 1 (19%) and group 2 (16%; $P=0.12$). Twenty-three patients in group 2 eventually had progression of symptoms and were offered surgery. Of all patients in group 2, 28% had resolution without surgery, 41% had symptoms that resolved after surgery, and 31% had persistent symptoms after surgery. Of the patients in group 1, 1 did not undergo surgery but had resolution of symptoms. Of the 60 patients in group 1 who had surgery, 97% had resolution of symptoms. Pathology revealed gallbladder wall inflammatory infiltrate in all patients except 1. The symptoms most predictive of success after surgery were right upper quadrant pain, pain after meals, and reproduction of pain with CCK administration.

**Conclusions:** In patients with established biliary dyskinesia, symptoms are more predictive of success after surgery than GBEF. Patients with classic symptoms are more likely to have resolution following surgery than are patients with an atypical presentation.

**Reviewer’s Comments:** This study was not designed to assess the predictive power of reduced GBEF compared with normal GBEF. All patients in this study had abnormally low GBEFs. Consequently, even though GBEF did not predict success following surgery in this study, it should not be concluded that reduced GBEF (<35%) does not carry a higher probability of symptom resolution with surgery than a normal GBEF. (Reviewer-Shayne Squires, MD).

© 2009, Oakstone Medical Publishing

**Keywords:** Gallbladder Dyskinesia, Treatment, Hepatobiliary Imaging
In patients with renal hydronephrosis, tissue tracer transit is a better predictor renal function than is response to furosemide stimulation or single kidney function <40%.

**Background:** Diuretic renal scintigraphy is used to evaluate the need for intervention in renal hydronephrosis. The currently used parameters only detect a morphological change that alters renal excretion of the tracer, but they do not accurately predict an actual functional decline. However, tissue transit time (TTT) can be potentially used to evaluate functional decline.

**Objective:** To evaluate TTT, response to furosemide stimulation (RFS), and single kidney function <40% (SKF<40%) in predicting renal function and need for surgery in patients with single kidney hydronephrosis.

**Methods:** 50 patients with signs of unilateral hydronephrosis, as identified by a prior imaging study, were included. Of these patients, 37 were pediatric patients. From the images, TTT was scored visually as timely, delayed, or indeterminate. RFS was scored visually from images and renograms as nonobstructive, obstructive, or equivocal. SKF<40% was derived from whole-kidney ROIs with background subtraction. All 3 parameters were separately used to predict whether surgical intervention was needed and were compared with surgical results or subsequent follow-up of renal function in patients who did not undergo surgery.

**Results:** TTT more accurately detected a decline in renal function when compared to RFS and SKF<40%. Decline in function was accurately detected by delayed TTT in 8 of 10 patients, by RFS in 9 of 22 patients, and by SKF<40% in 9 of 21 patients who actually underwent surgery. In those who underwent surgery as predicted by the 3 parameters, only 2 of 10 patients had unchanged function as predicted by TTT, but 11 of 22 and 10 of 22 patients had unchanged function as predicted by RFS and SKF<40%, respectively. These represent patients who underwent surgery unnecessarily.

**Conclusions:** TTT better predicts the need for surgical intervention by more accurately reflecting renal function when compared to RFS and SKF<40%.

**Reviewer's Comments:** The authors of this interesting study question the efficacy of renography parameters that have been in use for so long in predicting renal function. The data are striking in that TTT seems to better select patients who will actually benefit from undergoing surgery, thus avoiding an unnecessary intervention. Although RFS and SKF<40% detect the morphological change that is a sequelae of the renal pathology, a structural change does not necessarily reflect actual or imminent decline in renal function. This study raises the possibility that the different parameters can be used in evaluating different aspects of function, namely the excretion of the pathological kidney and whether that altered excretion significantly reduces its contribution to overall renal function. (Reviewer-Damita Thomas, MD).

© 2009, Oakstone Medical Publishing
Increased FDG uptake is not only predictive of more aggressive disease in intracranial meningioma, but it can potentially predict patients in whom disease will recur postoperatively.

**Background:** Meningiomas are the most common, benign intracranial tumor. Although they do have a favorable prognosis, the higher-grade tumors tend to have a higher recurrence rate that portends a worse prognosis. The recurrence rate is determined by tumor size, aggressiveness, and grade. FDG uptake correlates with tumor aggressiveness and grade.

**Objective:** To evaluate the ability of FDG-PET in detecting high-grade meningioma as well as in predicting disease recurrence after surgery.

**Methods:** 59 patients previously diagnosed with meningioma by surgery were retrospectively evaluated. All patients had undergone FDG-PET and conventional imaging with CT and/or MRI preoperatively. A tumor-to-gray-matter ratio (TGR) of the lesions was used in lieu of the SUV\textsubscript{max}. FDG-PET images were manually coregistered with CT to precisely derive the ROIs from which the TGRs were derived. Histopathological grade and proliferation index data were obtained from each surgical specimen. Patients were followed up for an average of 34 months.

**Results:** There was no significant difference between the TGRs of low- and high-grade disease, deeming FDG-PET poor at differentiating low- from high-grade disease. However, there was a significant correlation between FDG uptake and the MIB-1 proliferation labeling index as well as the mitotic tumor count, indicating that FDG uptake correlates with tumor proliferation and thus aggressiveness. Increased FDG uptake was also associated with lower recurrence-free survival rates, as shown during follow-up.

**Conclusions:** FDG-PET is not sensitive in the detection of high-grade meningioma, but increased FDG uptake is correlated with disease recurrence and with tumor aggressiveness.

**Reviewer's Comments:** This interesting study shows that FDG-PET is not sensitive in detecting high-grade meningioma. Most of the included patients had low-grade disease, which could potentially skew results in an unfavorable way. However, as this modality is being evaluated as a noninvasive tool to depict tumor grade, the dismally low sensitivity shown here in differentiating low- from high-grade disease suggests that FDG-PET may not be suitable for this purpose. However, it is interesting that increased FDG uptake was correlated with tumor proliferation as well as with poorer recurrence-free survival rates. This suggests that higher FDG uptake is not only predictive of more aggressive disease, but it can potentially predict patients in whom disease will recur postoperatively. This use of PET is important because it has the potential to impact treatment strategies.

(Reviewer-Damita Thomas, MD).

© 2009, Oakstone Medical Publishing

Keywords: Intracranial Meningioma, FDG-PET

Print Tag: Refer to original journal article
The FDG:FES ratio is an informative index regarding the aggressiveness of endometrial cancer. However, the drawbacks of imaging each patient twice may not be offset by the potential diagnostic benefits.

**Background:** Endometrial cancer is a common malignancy among women. Although those with early stage disease have a relatively favorable prognosis, up to 20% of patients with more aggressive disease will relapse. As such, a noninvasive method to accurately stage patients is important for tailoring therapeutic strategies.

**Objective:** To evaluate the uptake of F18-FES and F18-FDG in endometrial cancer and to determine if the uptake correlates with tumor aggressiveness.

**Participants:** 31 patients with suspected endometrial cancer based on cytology, ultrasonography, or MRI were evaluated.

**Methods:** The gold standard was postoperative histopathology (n=25) or whole endometrial curettage (n=6). None had pre-PET biopsy or therapy. ROC was performed to determine the optimal standard uptake value (SUV) cutoff on both FDG-PET and FES-PET in differentiating low-grade from high-grade disease.

**Results:** FDG uptake was significantly higher than FES in high-grade disease, while FES uptake was significantly higher than FDG uptake in endometrial hyperplasia. FDG uptake tended to be higher as disease aggressiveness increased. However, there was no significant difference in FDG uptake between high-and low-grade disease. FES uptake was significantly different between carcinoma and hyperplasia, with the latter demonstrating higher uptake. The FDG:FES ratio was the most sensitive in differentiating carcinoma from hyperplasia. An FDG:FES cutoff of 0.5 adequately differentiated hyperplasia from carcinoma (low- and high-grade disease).

**Conclusion:** FES and FDG show opposing uptake tendencies with increasing disease aggressiveness. The FDG:FES ratio was the most sensitive in differentiating hyperplasia from carcinoma.

**Reviewer's Comments:** The study seems to reiterate known data regarding the uptake characteristics of FES in endometrial cancer. However, it does explore the potential “synergy” of using FES with FDG to more adequately stage this patient population. The authors show that the FDG:FES ratio is better at discriminating hyperplasia from cancer. However, the drawbacks of imaging each patient twice as well as the currently limited availability of FES may not be offset by the potential diagnostic benefits. More studies are needed with larger patient numbers and more variable stages of disease before this dual tracer imaging is routinely used.

(Reviewer-Damita Thomas, MD).

© 2009, Oakstone Medical Publishing

Keywords: Endometrial Carcinoma, Predicting Aggressiveness

Print Tag: Refer to original journal article