99mTc-MIBI can be used to predict chemotherapy drug resistance.

**Background:** 99mTc-methoxyisobutylisonitrile (99mTc-MIBI) is best known for its use as a myocardial perfusion agent. However, it is also concentrated by many types of solid malignancies. Importantly, it is also transported out of tumors by the same glycoprotein P that is related to chemotherapy drug resistance. Predicting which patients harbor this protein in advance of chemotherapy treatment might have a substantial impact on outcome.

**Objective:** To examine the peer-reviewed literature for evidence supporting the value of 99mTc-MIBI in this role and to determine whether using this agent might prove cost-effective in patients with lung cancer.

**Design:** The authors performed a MEDLINE search through July 2007 and also PubMed using the terms MIBI, lung cancer, and chemotherapy response. A meta-analysis was then performed on the data retrieved in the search. A cost-effective analysis was performed using accuracy results obtained from the meta-analysis in which one scenario included MIBI imaging in all patients, followed by chemotherapy when clinically appropriate, in only those individuals with positive 99mTc-MIBI activity within the lung malignancy.

**Results:** The analysis was performed on 235 patients taken from 8 individual studies that fit all of the search parameters. The sensitivity and specificity for identifying chemotherapy responders in patients with lung cancer using 99mTc-MIBI was 94% and 90%, respectively. The strategy using 99mTc-MIBI to image and preselect patients for chemotherapy was the most cost-effective strategy resulting in only an average life expectancy difference of 7 days. Only when the cost of chemotherapy was reduced by a factor of 3 did it become more cost-effective to simply treat every patient without preselection using 99mTc-MIBI.

**Conclusions:** According to the authors, "The use of 99mTc-MIBI to preselect chemotherapy responders would result in significant cost savings for the health-care system. In our opinion, the cost of treating all patients outweighs the modest gain (7.5 days) in life expectancy achieved."

**Reviewer's Comments:** Morbidity was not evaluated in this study but may well have been reduced in the MIBI scenario. The authors make a compelling case for large prospective trials to confirm this role for 99mTc-MIBI in patients with lung cancer. (Reviewer-David Bushnell, MD).

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Keywords: Lung Cancer

Print Tag: Refer to original journal article
131I Tx More Effective Than ATDs for Hyperthyroidism

Comparison of the Long-Term Efficacy of Low Dose 131I Versus Antithyroid Drugs in the Treatment of Hyperthyroidism.

Chen DY, Jing J, et al:

Nucl Med Commun 2009; 30 (February): 160-168

In a Chinese population, 131I therapy was more effective than ATDs in rapidly and permanently curing hyperthyroidism with an acceptably low long-term hypothyroidism.

Objective: To compare the efficacy and safety of 131I against antithyroid drugs (ATD) in the treatment of thyrotoxicosis.

Design: 9-year prospective, randomized, open-label blinded end point study.

Participants/Methods: 460 hyperthyroid patients were divided into 2 treatment groups. The 131I group received 50 to 150 microcuries 131I/g based on length of diverse course, severity of symptoms, age, and complications multiplied by the estimated thyroid size and percent uptake at 24 hours. Maximum administered activity was 15 microcuries. The ATDs patients received were methimazole or propylthiouracil for at least 18 months. Primary outcomes were euthyroidism, persistent hyperthyroidism, recurrence, and clinical and subclinical hypothyroidism. Ophthalmopathy and complications were also classified.

Results: Euthyroidism was achieved in 70% with 131I, but only 40% using ATDs. Nineteen percent remained hyperthyroid with ATDs, but only 2% with 131I. Hypothyroidism occurred in 22% with 131I and 9% with ATDs. There was recurrence in 30.5% with ATDs, but in only 6% with 131I. Time to cure was faster with 131I. Large goiters predicted failure of ATD treatment. Improvement of ophthalmopathy was more frequent following the 131I than ATD therapy (P=0.010). The incidence of ophthalmopathy in both therapy groups after treatment was not significantly different. Gland weight decreased after 131I treatment (P<0.001), but not in the ATD group.

Conclusions: 131I therapy is more effective than ATDs in rapidly and permanently curing hyperthyroidism with an acceptably low long-term hypothyroidism.

Reviewer’s Comments: I strongly recommend a read of this paper. If its results are transferable to a non-Chinese population, then the author’s rigorous dose calculation method is worth emulating. That method is described in simple, clear terms that make it quite feasible to all. The remarkably successful outcome of 131I, with lower than usually reported hypothyroid and ophthalmology rates, may be due to the detailed dose calculations aiming at the lowest effective dose. Alternatively (and equally likely), the Chinese population is unique. I nevertheless would recommend a study of the methods section of this paper that cookbooks a method that bested ATDs in every response category with the best hypothyroid rate I have seen. (Reviewer-C. Richard Goldfarb, MD).

© 2009, Oakstone Medical Publishing

Keywords: Hyperthyroidism

Print Tag: Refer to original journal article
A 3-mm pulmonary nodule discovered during a cardiac CTA examination in a non-smoker does not require follow-up.

**Background:** Radiologists and nuclear medicine physicians involved in the interpretation of PET/CT examinations or cardiac CT angiography (CTA) are often faced with detection of ≥1 unanticipated pulmonary nodules on CT. It is useful, therefore, to be familiar with features that suggest malignancy and the guidelines for how to proceed when such findings become apparent.

**Objective:** To review pulmonary nodules detected by CT.

**Methods:** The authors describe nodule characteristics typical of malignancy, such as spiculated borders.

**Results:** Calcifications that are usually most suggestive of benignity may nevertheless be present in a stippled or eccentric pattern in malignant nodules. Macroscopic fat is associated with benign lesions such as hamartomas. Subsolid nodules have a higher rate of malignancy than solid opacities of the same size. Subsolid lesions may be a mixed pattern of solid and ground-glass opacity or primarily ground-glass only in appearance. Subsolid malignancies are typically adenocarcinomas and bronchoalveolar carcinomas. Nodule size has an important impact on the likelihood of malignancy, with solid nodules <4 mm carrying a 1% chance of malignancy. On the other hand, in patients with a previously diagnosed solid malignancy elsewhere in the body, nodules <5 mm in diameter may carry up to a 42% chance of being malignant. Solid nodules stable in size for ≥2 years can be considered benign in nature. Many radiologists refer to the Fleischner Society guidelines for management of nodules <8 mm in diameter with no known underlying malignancy. According to these recommendations, nodules in low-risk patients (≤4 mm) need no follow-up.

**Conclusions:** According to the authors, in regard to the management of pulmonary nodules, "The clinical context is important in terms of stratifying an individual's risk factors and guiding subsequent management."

**Reviewer's Comments:** Incidentally identified FDG-negative nodules <8 mm in patients with underlying malignancy should be further evaluated. However, a 3-mm nodule discovered during a cardiac CTA examination in a non-smoker does not need follow-up. (Reviewer-David Bushnell, MD).

© 2009, Oakstone Medical Publishing

Keywords: Pulmonary Nodules

Print Tag: Refer to original journal article
18F-FDG PET/CT Predicts Outcome Postchemotherapy for Osteosarcoma

18F-FDG PET/CT as an Indicator of Progression-Free and Overall Survival in Osteosarcoma.
Costelloe CM, Macapinlac HA, et al:


18F-FDG PET/CT is effective for determining prognosis for patients with osteosarcoma.

**Background:** Osteosarcoma often requires a combination of surgery and chemotherapy for optimum management. The degree of tumor necrosis measured following adjuvant chemotherapy is considered an important prognostic indicator.

**Objective:** To determine whether 18F-FDG PET/CT could be used specifically to predict tumor response to adjuvant chemotherapy and more generally predict outcome for patients with osteosarcoma.

**Participants:** 31 subjects were included in this study, and the median follow-up was 2.6 years.

**Methods:** 18F-FDG PET/CT imaging was performed before and following completion of adjuvant chemotherapy and prior to tumor resection. The maximum standard uptake value (SUV$_{\text{max}}$) and the total lesion glycolysis (TLG) were measured for each tumor. TLG is a new measure that represents the average SUV (of pixels above some minimum threshold) divided by the total primary tumor volume. The changes in SUV$_{\text{max}}$ and TLG following completion of chemotherapy were also determined.

**Results:** The mean SUV$_{\text{max}}$ for the group dropped from 10.6 g/mL before chemotherapy to 4.76 g/mL afterwards. The group mean TLG dropped from 254.6 g to 232.0 g after adjuvant therapy. A prechemotherapy SUV$_{\text{max}}$ ≥15 (n=4) and/or a postchemotherapy SUV$_{\text{max}}$ ≥5 (n=7) were associated with significantly reduced progression-free survival (PFS). Five patients died during follow-up. There was no relationship between either pre- or post-therapy TLG and PFS. SUV$_{\text{max}}$ postchemotherapy and TLG before therapy were independent predictors of overall mortality. Greater than 90% tumor necrosis following adjuvant chemotherapy was a good indicator of survival. Changes in SUV$_{\text{max}}$ were significantly related to tumor necrosis >90%. SUV$_{\text{max}}$ after completion of chemotherapy showed a borderline significant relationship to tumor necrosis >90%.

**Conclusions:** The authors concluded, “Our study has shown that 18F-FDG PET/CT is a predictor of PFS, overall survival, and tumor necrosis in osteosarcoma.”

**Reviewer’s Comments:** I was unfamiliar with the TLG measure used by the authors in this study, and it appears that SUV$_{\text{max}}$ performed better in terms of predicting outcome than did TLG. The authors noted that larger prospective trials addressing this issue are ongoing. The ability of 18F-FDG PET/CT to predict outcome following chemotherapy is a theme that is appearing with greater frequency in the literature. (Reviewer-David Bushnell, MD).

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Keywords: Osteosarcoma

Print Tag: Refer to original journal article
Computer-aided diagnostic software appears to improve the sensitivity of bone scan evaluations without diminishing specificity.

**Background:** A previous paper in this issue of *Practical Reviews in Nuclear Medicine* described a computer-aided diagnostic (CAD) approach to reading nuclear medicine bone scans where the method was tested against clinical results. How well this routine aids physicians is addressed in this recent paper. **Objective:** To evaluate the efficacy of a CAD software system for physicians reading nuclear medicine bone scans. **Methods:** A test set of 59 whole-body bone scans from patients was sent to 35 physicians representing 18 of 30 nuclear medicine clinics in Sweden. These studies were read by the physicians in 2 phases. In the first phase, the bone scans were evaluated with no ancillary information. In the second phase, the physicians reviewed the scans along with the results obtained from the CAD software. The gold standard of truth for the bone scans was determined by final clinical assessment, and bone scan interpretations were determined by an experienced nuclear medicine physician. The sensitivity, specificity, and accuracy of each reading phase were computed along with statistics that monitored the extent of reading agreement. This included percent agreement and the kappa coefficient. **Results:** The level of agreement between the 35 physicians was compared at baseline and with the use of the CAD. On average, both the percent agreement (64% to 70%) and the mean kappa (0.48 to 0.52) improved when the CAD was employed. A similar comparison was made that looked at the physician group performance compared with the gold standard interpretation. The percent agreement improved from 66% without CAD to 73% with CAD and kappa values went from 0.49 to 0.58. The sensitivity went from 78% without CAD to 88% with CAD, while the specificity remained essentially constant at 0.94 leading to an improvement in accuracy from 0.89 to 0.92 when CAD was used. The statistics were also evaluated for 3 subsets of the physicians based on experience (inexperienced, moderately experienced, and experienced). No statistically significant difference in the performance parameters was found between the subsets. **Conclusions:** The CAD approach can both improve diagnostic sensitivity and reduce interobserver variation in reading bone scans. **Reviewer's Comments:** Effective CAD programs may improve a physician's diagnostic confidence and on occasion, may help in the recognition of an abnormality that might have been missed. One would expect that the value of CAD would be greater for less experienced readers. It is surprising to me, therefore, that experience seemed to play no role in the sensitivity improvement found with the use of CAD. It is possible that the case mix used in this investigation is responsible for that result. (Reviewer-Mark T. Madsen, PhD).

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Keywords: Radionuclide Imaging

Print Tag: Refer to original journal article
IDIFs Have Wide Applicability

Image-Derived Input Functions for PET Brain Studies.
Mourik JEM, Lubberink M, et al:


When an appropriate artery supplying the tissue under evaluation is in the field of view, the IDIF can be accurately used in determining compartmental components.

Background: Quantitative PET studies often require the concentration of the radiotracer in the arterial blood as a function time. Direct blood sampling is possible, but is invasive and requires additional technology.

Objective: To test a previously developed image-derived method for obtaining arterial input functions on a variety of different PET brain radiotracers.

Methods: The imaged-derived input functions (IDIFs) method was previously tested on [11C]flumazenil. That same method was tested on [11C]PIB (detects amyloid-β accumulation in Alzheimer patients), [11C]verapamil (measures P-glycoprotein function), and [11C]PK11195 (inflammation marker in neurological disorders). Dynamic scans of these agents were acquired on a 3-dimensional dedicated PET scanner. Blood samples were acquired with a continuous automatic blood sampling device. The PET scans were repeated twice over a 4-hour period. The acquired PET data were reconstructed using an ordered subset expectation maximization (OSEM) iterative algorithm that provided compensation for partial volume averaging. The IDIF was obtained from time activity curves generated from regions located over the arteries feeding the circle of Willis. Compartmental analysis was performed using both the sampled blood and the IDIFs to derive estimates of exchange rate (K1), tissue volume (VT), and blood volume (VB).

Results: Comparisons between the IDIF and blood sample input functions (BSIFs) showed that the IDIFs were always sharper with a higher maximum value. In addition, there was significantly more dispersion of the BSIF for [11C]PIB than with the other tracers, likely from blood sticking in the sampling tube due to the lipophilicity of the tracer. For all 3 of the tracers, the correlation between VT found using the 2 input functions was very high, with Pearson's correlation coefficient (R2) ranging from 0.92 to 1.0. The slope and intercept of the regression lines were close to 1 and 0, respectively, for all of the tracers except for the uncalibrated [11C]PIB results where the slope was 1.6. This also appeared to be a manifestation of the sticky blood. The variability on test-retest studies was evaluated for [11C]PIB and [11C]verapamil and was found to be relatively uniform with a mean value of approximately 0.10.

Conclusions: Using IDIF for the PET brain tracers is not only feasible, but may also be more reliable because of potential problems with blood sticking in the sampling tubes.

Reviewer's Comments: This paper points out the need for evaluating methods in the specific applications in which they will be used. The authors provide convincing evidence that IDIFs have wide applicability, and this approach avoids some of the mechanical problems of the so-called gold standard blood sampling. (Reviewer-Mark T. Madsen, PhD).

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Keywords: PET Brain Studies

Print Tag: Refer to original journal article
Methodology to Reduce Brown Fat Uptake Simple Without Risk

Constant Ambient Temperature of 24°C Significantly Reduces FDG Uptake by Brown Adipose Tissue in Children Scanned During the Winter.
Zukotynski KA, Fahey FH, et al:


For most patients, brown fat uptake of FDG can be significantly reduced if the patient is kept at a room temperature of 75°F for 30 minutes before FDG injection and during the uptake period.

**Background:** Physiologic FDG uptake in the brown fat in the neck, mediastinum, paravertebral, and retroperitoneal regions may confound the interpretation of PET scans. The brown fat tissue has a role in thermogenesis, and FDG uptake in the brown fat appears to reflect sympathetic stimulation in response to cold stimuli.

**Objective:** To determine if warming the room immediately prior and during the uptake phase to a constant temperature of 75°F reduces the brown fat uptake.

**Participants/Methods:** 40 patients, ≤21 years of age, were imaged with FDG PET between December 2007 and March 2008. None of these 40 patients received sedation or other premedication known to reduce brown fat uptake. Patients were taken to the temperature controlled uptake room 30 minutes prior to injection of FDG and kept in the same room for the 60-minute uptake period. The temperature in the uptake room was maintained at a constant 75°F using a thermostatic controller. PET images were obtained on a dedicated PET scanner in general from the skull base to proximal thighs. Another group of 45 patients imaged with FDG PET between December 2006 and December 2007 served as the control group. The temperature of the uptake room in the control group was 70°F to 72°F. The outside temperatures on the days of the studies were similar in the study and control groups. The presence or absence of brown fat uptake was compared in the study and control group. PET images were considered positive for brown adipose tissue uptake if they showed uptake greater than background in characteristic distribution of brown adipose tissue.

**Results:** Brown fat uptake of FDG was observed in 5% of patients in the study group who were kept in the warmed uptake room. This was significantly lower than the control group, who showed brown fat uptake in 31% of patients ($P <0.002$). Among the 40 patients in the study group kept in the warmed uptake room, 26 had previous PET studies available for comparison. In this subset of 26 patients, only 1 had brown fat uptake following preparation in the warmed room compared to 12 patients with routine preparation.

**Conclusions:** Brown fat uptake of FDG can be significantly reduced in most patients if they are kept at a room temperature of 75°F for 30 minutes prior to injection of FDG and during the uptake period.

**Reviewer's Comments:** I believe that with the use of integrated PET-CT, physiologic brown fat uptake can be correctly identified in most patients. There is, however, the potential case when lymph nodes are in very close proximity to metabolically active brown fat, which may complicate the interpretation of the PET scan. The methodology described in this paper to reduce brown fat uptake is simple to implement and without risk.

(Reviewer-Yusuf Menda, MD).

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Keywords: Brown Adipose Tissue

Print Tag: Refer to original journal article
Increased ESV and Decreased LVEF Post-Stress Equals Higher CAD Risk

Diagnostic Value of Left Ventricular Function After Adenosine Triphosphate Loading and at Rest in the Detection of Multi-Vessel Coronary Artery Disease Using Myocardial Perfusion Imaging.

Hida S, Chikamori T, et al:

J Nucl Cardiol 2009 Jan-Feb; 16 (): 20-7

Gating both rest and post-adenosine stress images helps better identify patients with multi-vessel CAD.

**Background:** There are few data on the potential role of measuring the left ventricular (LV) function and size post-adenosine triphosphate (ATP) stress compared to rest in the identification of extensive coronary artery disease (CAD).

**Objective:** To determine the predictive power of stressed versus resting LV function and size data in the prediction of extensive CAD.

**Design:** Retrospective review.

**Participants:** 569 consecutive patients were referred for clinical reasons to a Japanese academic center to undergo post-stress and resting gated single photon-emission computed tomography (SPECT). Of these patients, 119 subsequently underwent coronary angiography and were analyzed.

**Methods:** A single-isotope, 1-day protocol, comprised of adenosine triphosphate (ATP) stress myocardial perfusion imaging with 99mTc-sestamibi. Following IV administration of ATP over a 6-minute period, patients waited 3 minutes and were then given IV 99mTc-sestamibi (259 MBq); imaging started 30 minutes after this, and after 4 hours, patients received 99mTc-sestamibi while they were resting. QGS software (developed by Germano et al) was used to calculate left ventricular volumes and ejection fraction (EF). All patients underwent conventional coronary angiography.

**Results:** Univariate comparisons were made between patients with and patients without multi-vessel CAD. Predictors of multi-vessel CAD were the summed stress score (SSS), the summed difference score (SDS), left ventricular EF post-stress, change in end-diastolic volume (EDV), change in end-systolic volume (ESV), change in EF, and the stress-induced volume ratio (SIVR). The change in ESV was more predictive of CAD than just the perfusion variables alone. An increase of >5 mL in ESV or a decrease of >4% in LVEF post-stress compared to rest were associated with multi-vessel disease.

**Conclusions:** An increase in the ESV and a decrease in the LVEF post-stress compared to rest are associated with an increased risk of multi-vessel CAD, and are more predictive than perfusion variables alone.

**Reviewer's Comments:** Having gated both stress and rest images for several years now, my rule of thumb is that if BOTH the ESV goes up AND the LVEF goes down post-stress compared to rest, then there is a greater concern for serious disease. If EITHER the ESV goes up OR the LVEF goes down, then it is a toss-up. If neither happens, then the risk of multi-vessel disease is estimated to be low, based on the LV size and EF data. (Reviewer-Thomas F. Heston, MD).

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Keywords: Multi-Vessel Coronary Artery Disease

Print Tag: Refer to original journal article
SPECT/CT cameras can detect diastolic dysfunction.

**Background:** Gated single photon-emission computed tomography (SPECT) imaging has traditionally used 8-frame gating, which is adequate for systolic function but not diastolic function. The advent of SPECT/CT cameras, affords us the opportunity to more readily perform 16-frame gating allowing the evaluation of both systolic and diastolic left ventricular function. Diastolic dysfunction is frequently a harbinger of subsequent systolic dysfunction.

**Objective:** To evaluate the feasibility of 16-frame gating using a SPECT/CT gamma camera and to define the incidence of diastolic dysfunction.

**Design:** Retrospective review.

**Participants:** 121 patients referred for the primary diagnosis of ischemic heart disease.

**Methods:** Patients underwent 16-frame gated stress and gated rest myocardial perfusion imaging using a SPECT/CT camera. A single-day, stress first, rest second, single-isotope (99mTc-Tetrofosmin) protocol was utilized.

**Results:** 16-frame gating was successful in all patients and allowed the assessment of end-diastolic dysfunction. Approximately 43% of the patients had reversible ischemia on the perfusion images. Isolated diastolic dysfunction was seen in 66%, systolic dysfunction in 11%, and normal function in 23%. Among the patients with normal myocardial perfusion, 48 of 69 showed evidence of isolated diastolic dysfunction and out of the patients with reversible ischemia, 32 of 52 showed isolated diastolic dysfunction ($P = ns$).

**Conclusions:** 16-frame gated SPECT is possible using SPECT/CT and is able to detect diastolic dysfunction.

**Reviewer’s Comments:** The rate of diastolic dysfunction in this study was 66% overall and was not significantly different in those with inducible ischemia versus those without inducible ischemia. The clinical implications are still unclear; however, this paper notes that 16-frame gating is possible using SPECT/CT technology, even on the images using a low-dose of the tracer (10 mCi of 99mTc-Tetrofosmin). (Reviewer-Thomas F. Heston, MD).

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Keywords: Diastolic Dysfunction

Print Tag: Refer to original journal article
Contrast-enhanced CT may be a good initial procedure to use in the setting of GI bleed; then if this test is negative, a 99mTc-labeled RBC examination could subsequently be performed.

**Background:** 99mTc-labeled red blood cells (RBC) imaging has been used successfully for many years for detection and localization of gastrointestinal (GI) bleeding. More recently, contrast-enhanced multi-detector CT (MDCT) has been suggested as an alternative method for detecting GI bleeding.

**Objective:** To compare the 2 imaging techniques in this clinical setting.

**Participants/Methods:** The authors enrolled patients with active GI bleeding who had a creatinine level <1.5. Contrast-enhanced CT was performed immediately following a non-contrast CT. In the majority of subjects, 99mTc-labeled RBC imaging of the abdomen was then performed. Angiograms were performed in select individuals. Fifty-five patients were imaged with CT, from which 41 were subsequently imaged with 99mTc-labeled RBC. Eighteen of these 41 patients eventually went on to angiography. Only patients with positive RBC examination and/or positive CT examination underwent angiography.

**Results:** 20 of the 41 patients had both a negative RBC study and CT exam; 8 were positive on both. There were, however, 11 patients with a positive RBC examination and negative CT, but only 2 with a positive CT and negative RBC study.

**Conclusions:** Contrast-enhanced CT may be a good initial procedure to use in the setting of GI bleed; then if this test is negative, a 99mTc-labeled RBC examination could subsequently be performed. They note that at night, it is often easier to obtain a CT exam than a nuclear study.

**Reviewer's Comments:** This study has some limitations, the most notable of which is probably the absence of confirmation of bleeding sites in the discordant cases. This methodological problem is a difficult one to overcome. Nevertheless, it appears from these data that 99mTc-labeled RBC imaging is more sensitive than the contrast-enhanced CT for detecting GI bleeding. This is of course what we would expect as contrast-enhanced CT would be much more limited in its ability to detect intermittent bleeding compared to 99mTc-labeled RBC imaging. Although the study did not specifically address the issue of accuracy of localization, it seems to me that this may be one area where contrast-enhanced CT might have an advantage over 99mTc-labeled RBC imaging. It may be that SPECT/CT might be useful to improve localization accuracy in some cases when planar images demonstrate RBC pooling at an uncertain location. (Reviewer-David Bushnell, MD).

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Keywords: Lower GI Bleed

Print Tag: Refer to original journal article
**Can PET-Based Estradiol Challenge Guide Treatment for Breast Cancer?**

*PET-Based Estradiol Challenge as a Predictive Biomarker of Response to Endocrine Therapy in Women With Estrogen-Receptor-Positive Breast Cancer.*

Dehdasht F, Mortimer JE, et al:

Breast Cancer Res Treat 2009; 113 (509-517):

A PET-based estradiol challenge appears to help guide systemic therapy in patients with advanced breast cancer.

**Objective:** To determine if a PET-based estradiol challenge could be used to determine the response to endocrine therapy of breast cancer.

**Design/Participants:** This prospective study included 51 women (median age, 59 years) who were postmenopausal with biopsy-proven advanced estrogen-receptor (ER)-positive breast cancer. None of the patients had received hormonal therapy prior to imaging.

**Methods:** PET imaging for each patient occurred over a 3-day period. Each patient underwent both fluoroestradiol (FES) PET and fluorodeoxyglucose (FDG) PET scans at baseline and a repeat FDG-PET scan after 30 mg of estradiol administration (estradiol challenge of 3 oral 10-mg doses). About 6 mCi (222 MBq) of FES was administered intravenously for each FES-PET study, with imaging at 90 minutes postinjection. For each FDG-PET study, about 15 mCi (555 MBq) of this radiotracer was administered intravenously with imaging at 60 minutes postinjection. Standardized uptake values were calculated as a measure of uptake. An SUV cutoff of ≥2.0 for FES uptake was considered positive for ER expression, while a cutoff of ≥12% increase in SUV for FDG was considered metabolic flare. This cut off was determined by ROC curve analysis. The image findings were correlated to clinical responsiveness to endocrine treatment.

**Results:** Approximately 33% of the patients had a response to endocrine therapy, while the remaining patients did not. On FES-PET, significantly higher SUV values for tumors were noted in the responders (3.5 ± 2.5) compared to nonresponders (2.1 ± 1.8). On FDG-PET, there was a significantly higher mean SUV percentage change in responders compared to nonresponders after the estradiol challenge. A significantly longer overall survival (via the Kaplan-Meier method) was noted in patients who had a metabolic flare compared to those who did not regardless of what type of endocrine therapy had been provided (P =0.0062).

**Conclusions:** The authors found that FES uptake at baseline and a metabolic flare after an estradiol challenge could be used to predict the responsiveness of endocrine therapy for patients with ER-positive breast cancer.

**Reviewer's Comments:** As the authors state, a larger-scale study in this area needs to be performed to confirm and validate these findings as to whether a PET-based estradiol challenge can help guide systemic therapy in this patient population. (Reviewer-Twyla Bartel, DO).

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Keywords: PET-Estradiol

Print Tag: Refer to original journal article
Osteoporosis--Individual Guidelines Are Best

Identification of Factors Influencing the Intervention Thresholds for Treatment of Osteoporosis Based on 10-Year Absolute Fracture Risks.

Moayyeri A:


There is a growing sentiment among clinicians and investigators in osteoporosis that an absolute estimation of fracture risk is preferable to categorization based on bone mineral density alone.

**Background/Objective:** There is a growing sentiment among clinicians and investigators of osteoporosis that an absolute estimation of fracture risk is preferable to categorization based on bone mineral density (BMD) alone. This consideration was the impetus for the World Health Organization to estimate country-specific absolute fracture risks using femoral neck BMD and clinical risk factors. The results of this project, which involves >20 prospective cohort studies named the FRAX, have now been published.

**Results:** The estimated 10-year probabilities of fractures (expressed as percentages) provide more understandable measures for a meaningful physician-patient dialog. Algorithms based on age and clinical risk factors can classify patients into the following categories: (1) needing treatment (high risk); (2) needing BMD evaluation (intermediate risk); and (3) needing no treatment now but needing follow-up in the future (low risk). Merely knowing age and gender (eg, a 65-year-old woman), the patient could be treated without BMD measurement because she has a 20% chance of fracture in the next 10 years. Conversely, women considered low risk would be advised to return for a follow-up in the next 2 to 5 years. Women with intermediate fracture risk of 10% to 20% in the next decade would go for BMD assessment. These estimates, however, ideally require country-specific analyses to be clinically useful. Knowledge about the efficacy of osteoporosis treatments for individual patients is limited, so treatment based on FRAX estimates remains subjective. Efficacy, price, safety, and compliance need to be considered. Extended periods of osteoporosis treatments are required to achieve fracture reduction outcome, so changes in life expectancy and quality of life have to be considered. Other factors include poor compliance due to comorbidities or contraindications to treatment.

**Conclusions:** Ideally, "individualized" guidelines should be the goal. Personal-level factors, however, are difficult to fit into an algorithm. They include patient compliance, preference for treatment, occupation (active patients might dare lower fracture risks), place of living (home dwelling vs institution dwelling), lifestyle (independent elderly vs dependent to family), and comorbidities (rheumatoid arthritis or partial immobility due to stroke).

**Reviewer's Comments:** The editorialist (from a department of public health) seeks to reduce utilization of DEXA studies based on epidemiological data and assessment of highly subjective individual factors. I find DEXA BMD measurements simple, straightforward, objective, and easy to apply. In addition, they provide patients with both an incentive to comply with the treatment plan and reassurance that the chosen course is correct. (Reviewer-C. Richard Goldfarb, MD).

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Keywords: Osteoporosis

Print Tag: Refer to original journal article
A high left ventricular ejection fraction is less predictive of a good outcome in women than in men.

**Background:** Little is known about the gender-specific prognostic value of left ventricular ejection fraction (LVEF) and ventricular volume indices on subsequent hard cardiac events.

**Objective:** To determine gender-specific guidelines for LVEF and volume indices in relationship to risk categories.

**Design:** Retrospective review.

**Participants:** Consecutive patients (n=891) referred for clinical reasons for gated SPECT imaging at a tertiary care academic center in New York.

**Methods:** Patients underwent ungated rest SPECT followed by either exercise or pharmacologic stress, and then gated SPECT imaging. Most patients underwent pharmacologic stress (n=594), with the remaining patients undergoing a Bruce or Modified Bruce protocol treadmill stress (n=297). Eight-frame gating was utilized. Dual isotope imaging was performed in all but 1 patient. End points were hard cardiac events (HCE; cardiac death or non-fatal myocardial infarction) or all-cause mortality or non-fatal myocardial infarction (ACMMI). Mean follow-up was 660 ± 400 days.

**Results:** Follow-up data were obtained in 788 patients (88%). Women were more likely to have a positive family history and hypertension, but were less likely to have a history of coronary artery disease or smoking. For equivalent rates of HCE and ACMMI, women had smaller ventricular volume indices and a higher LVEF (56% vs 47%).

**Conclusions:** The LVEF and ventricular volume cut-off values separating low- from high-risk patients is different in women than in men. The higher LVEF and lower ventricular volume indices in women are not necessarily associated with a lower risk of HCE or ACMMI.

**Reviewer’s Comments:** The authors did not discuss the relationship between end diastolic volume, end systolic volume, and adverse outcomes. Only the volume indices were analyzed (volume divided by body surface area). The limits for HCE found by these authors were: (1) high-risk LVEF was <52% for women and <47% for men; (2) high-risk end systolic volume index was >37 mL/m2 for women and >53 mL/m2 for men; and (2) high-risk end diastolic volume index was >80 mL/m2 for women and >95 mL/m2 for men. For example, using these limits, an ejection fraction of 50% would be in the high-risk category for women but in the low-risk category for men. (Reviewer-Thomas F. Heston, MD).

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Keywords: Risk Stratification

Print Tag: Refer to original journal article
Detection of Gastric Cancer Using 18F-FLT PET: Comparison With 18F-FDG PET.

Kameyama R, Yamamoto Y, et al:


FLT PET is as sensitive as FDG PET in the detection of gastric cancer.

**Objective:** To compare F-18-fluorothymidine (FLT) PET with F-18 fluoro-D-glucose (FDG) PET in the detection of gastric cancer.

**Background:** F-18-FDG PET has been useful in the staging and restaging of various malignancies. Its usefulness in detecting gastric cancer is less certain. The authors report that the sensitivity for FDG PET in gastric cancer detection has been highly variable, ranging from 48% to 94%. It is also known that the high physiologic gastric uptake as well as the lesser avid gastric malignancies (ie, signet ring and mucinous carcinomas) often lead to false-positive/false-negative results, respectively. As such, FLT is being studied to evaluate its efficacy in detecting gastric cancer. FLT PET acts as a measure of tumor proliferation via the salvage pathway of DNA synthesis. The authors show how FLT compares to FDG PET in the detection of gastric cancer, as well as correlate both FDG and FLT uptake with the proliferation index Ki-67.

**Design/Participants:** This prospective study included 21 patients diagnosed with gastric cancer.

**Methods:** Patients underwent FLT and FDG PET imaging within 2 weeks of each other. These served as initial staging studies as patients had received no therapy prior to either imaging study. The gold standard was either biopsy or histopathological surgical specimen. Immunohistochemical staining was performed to measure the Ki-67 proliferative index, using linear regression analysis to compare the SUV_{max} from the 2 PET images to the Ki-67 measure.

**Results:** The sensitivities of FLT and FDG for cancer detection were 95.2% and 95.0%, respectively (difference not significant). The FLT SUV_{max} were significantly lower than the FDG SUV_{max} overall. Both FDG and FLT had higher SUV_{max} in the more poorly differentiated cancers. Linear regression analysis revealed no correlation between Ki-67 and either FDG or FLT SUV.

**Conclusions:** FLT and FDG are equally comparable in detecting gastric cancer, with FLT demonstrating lower uptake. No correlation was seen between proliferative index Ki-67 and FLT or FDG.

**Reviewer's Comments:** Overall, this was a well-executed study comparing FDG and FLT PET in the detection of gastric cancer. It is interesting that both modalities missed disease in the same patient with a 2-cm moderately differentiated cancer. Only 2 patients had the characteristically less-FDG-avid signet-ring carcinoma (one in a patient with a tumor >5 cm), and both modalities detected the carcinoma equally well (FDG SUV_{max}, 4 to 4.5; FLT SUV_{max}, 4 to 5.2). It may be that FLT PET is a more of a reliable tracer in gastric cancers that have been shown to demonstrate variable or less-avid FDG uptake, but more studies focusing on the use of FLT in these specific tumor types are needed. It was also interesting that no correlation was seen between Ki-67 and FLT, as both reflect proliferation. The discrepancy may be due to sampling error, where the specimen used for Ki-67 staining did not adequately reflect overall proliferative activity of the tumor. (Reviewer-Damita Thomas, MD).

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Keywords: Gastric Cancer

Print Tag: Refer to original journal article
Structured reports are preferred by referring clinicians over prose reports.

**Background:** There has been little research into the style and content of radiology reports preferred by clinicians. With the advent of more sophisticated information systems and improved integration with picture archiving and communication systems, structured reporting is not only possible but also can be more efficient than the traditional prose report. However, it is unclear whether these alternative formats are appealing or acceptable to referring clinicians.

**Objective:** To assess referring clinician preference for a tabular ultrasound report compared to a prose report.

**Design:** Cross-sectional survey.

**Participants:** Consultant staff with responsibility for requesting ultrasound examinations in a U.K. hospital.

**Methods:** Clinicians were first asked how satisfied they were with the current ultrasound reports. They were then provided with several reports of the varying format and level of detail of both normal and abnormal ultrasound examinations.

**Results:** Of the 99 questionnaires sent, 49 replies were received. On a scale of 1 to 10, the mean satisfaction rating was 7 for content and 6.7 for clarity. When the ratings were lower, the criticisms included the fact that a measurement or detail was given with no assessment of its significance, and that a specific clinical question had not received a specific answer on the report. Overwhelmingly, the structured tabular format was preferred over a prose format report. For the tabular reports, clinicians tended to prefer a more detailed report compared to a brief report. However, note that the detailed report used in this study was actually not that lengthy. One primary difference between the brief and detailed report was that the detailed report included a specific conclusion, whereas the brief report did not.

**Conclusions:** Structured, tabular reports are preferred over prose reports.

**Reviewer's Comments:** Very few studies have compared referring clinician preference for structured reports versus prose reports; however, the studies to date strongly suggest that a structured, tabular format is preferred by our referring clinicians. Additional advantages of structured reporting include potentially greater efficiency and decreased dictation time. This study looked at ultrasonography only. Applying the results to nuclear medicine in some cases may be straightforward (e.g., myocardial perfusion imaging) and in other cases, quite challenging (e.g., whole body PET/CT). (Reviewer-Thomas F. Heston, MD).

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Keywords: Nuclear Medicine

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Lymphatic Rerouting in Lymph Nodes With Confirmed Disease

Visualization of Tumor Blockage and Rerouting of Lymphatic Drainage in Penile Cancer Patients by Use of SPECT/CT.
Leijte JAP, van der Ploeg IMC, et al:

Nodal disease can result in lymphatic rerouting in which radiotracer on lymphoscintigraphy is blocked from uptake to the actual sentinel node.

Objective: To demonstrate the phenomenon of lymphatic rerouting in lymphoscintigraphy in penile cancer patients with palpable, biopsy-proven metastatic inguinal nodal disease.

Background: Lymphoscintigraphy has been used to assess the nodal status of disease. However, it has been shown to be insensitive, with one postulated reason being the phenomenon of lymphatic rerouting due to the tumor burden. In this situation, the true sentinel node is not identified due to blockage by tumor cells, and lymphatic flow is rerouted to another node that may not harbor disease at the time. As such, the true sentinel node (which may not be palpable) may not be identified. This can result in surgical false-negative results due to removal of the uninvolved "neo-sentinel node."

Participants/Methods: This study looked at 17 patients with known penile cancer and clinically positive inguinal lymph nodes, which were also biopsy proven to contain metastatic disease via fine-needle aspiration. SPECT/CT images were acquired 2 hours after an intradermal injection technique. All patients underwent inguinal nodal dissection of the groin containing the confirmed metastatic disease, as well as sentinel lymph node biopsy (SLNB) of the contralateral groin the following day.

Results: Of the 17 patients, only 4 demonstrated radioactivity in the confirmed metastatic lymph nodes. Ten showed no activity in the confirmed nodes, but did demonstrate a "neo-sentinel node" (in 9 ipsilateral groins and 1 contralateral groin). The remaining 3 patients showed complete absence of uptake in the groin with confirmed disease.

Conclusions: This study demonstrates the phenomenon of lymphatic rerouting in lymph nodes with confirmed disease. Because the true sentinel nodes are not detected by lymphoscintigraphy, the authors believe this phenomenon can lead to a subsequent false-negative SLNB.

Reviewer's Comments: This study illustrates how lymphatic drainage from a tumor basin can be rerouted in the presence of a nodal metastasis, effectively blocking its uptake on lymphoscintigraphy. Therefore, a sentinel node may be missed during subsequent SLNB. As lymphoscintigraphy is most often performed on clinically negative disease, this phenomenon of altered lymphatic flow can lead to subsequent fine-needle SLNB. As the authors point out, it is feasible that a clinically negative node may harbor enough disease to cause lymphatic blockage. As such, the true metastatic node may not be visualized. Instead, a "neo-node" that may not contain disease and to which a radiotracer has been redirected may be selectively biopsied while leaving disease behind. (Reviewer-Damita Thomas, MD).

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Keywords: Penile Cancer

Print Tag: Refer to original journal article
Asymmetric uptake in the larynx will be seen in patients with damage to the RLN.

Background: Injury or damage to the recurrent laryngeal nerve (RLN) leads to problems with phonation and vocal impairment. The most common causes relate to tumor involvement of the nerve or surgical procedures in the neck that injure the nerve. PET/CT typically demonstrates some normal metabolic activity in the region of the vocal cords symmetrically.

Objective: To report on the spectrum of findings on FDG PET/CT in the presence of RLN damage.

Discussion: The authors note that not all individuals with RLN damage are symptomatic due to compensation from the other side. Therefore, in many instances, the PET examiner may not know about the condition before reading the images. Normal resting FDG uptake in the region of the vocal cords is symmetric with an SUV of <2.0; however, if the patient speaks following injection of FDG, this rate may go up symmetrically. In patients with RLN damage and vocal cord paralysis, there will be reduced uptake on the side of involvement so that the normal side may show SUV values of ≥6. The concern is that this will lead to a false diagnosis of laryngeal neoplasm. The authors demonstrate these findings with several high-quality PET and CT images. The spectrum of findings on CT in patients with vocal cord paralysis is also presented.

Conclusions: "The typical metabolic appearance of vocal cord paresis on FDG PET/CT should be recognized to avoid misdiagnosis and reported to clinicians owing to its potential serious consequences, including morbidity and even mortality from aspiration."

Reviewer's Comments: This is a brief but useful article for those involved with oncologic PET/CT. Until reading this, I was unaware of the numerous findings on CT alone that may occur in vocal cord paralysis. We have made an effort at our center to minimize physiologic vocal cord signal by requesting that patients not speak following injection of FDG. However, in doing so, it may make it more difficult to identify vocal cord paralysis. (Reviewer-David Bushnell, MD).
Is Pre-Therapy WB Imaging Valuable in Lung Metastases?

Diagnostic Whole-Body Scanning Before Radioiodine Therapy for Pulmonary Metastases of Differentiated Thyroid Cancer: Predictive Value and Recommendations.

Tachi Y, Iwano S, et al:


In patients with known or suspected lung metastases from WDTC, diagnostic WB images provide valuable prognostic information.

Objective: To determine the value of pre-therapy diagnostic whole-body (WB) imaging in patients with lung metastases from well-differentiated thyroid cancer (WDTC).

Design/Methods: The records of 42 patients with pulmonary metastases from WDTC were reviewed. All patients had been treated at least once with radiiodine for their metastatic lung disease. All subjects had followed a low-iodine diet for 2 weeks, and thyroid-stimulating hormone levels were >30 in all subjects at the time of therapy. Diagnostic WB scans were performed in all patients using 5 mCi of I-131 prior to therapy. The majority of subjects subsequently received treatment with 150 mCi of I-131, whereas a few patients received only 100 mCi. Post-therapy imaging was performed at 3 to 4 days and again 7 to 8 days following therapy. There were a total of 62 treatments in 42 patients. Follow-up chest CT scans and serum thyroglobulin (Tg) levels were used to determine response to therapy.

Results: In patients with positive diagnostic WB scans, the CT-determined response was 72%. In contrast, when the diagnostic WB images were negative, regardless of whether the post-therapy images of the chest were positive or negative, the CT-determined response was only 5% to 7%. Furthermore, individuals with a positive diagnostic scan showed a significant decline in Tg levels, whereas those with negative pre-therapy images showed no change or an actual rise in Tg levels.

Conclusions: In patients with known or suspected lung metastases, diagnostic WB images provide valuable prognostic information.

Reviewer's Comments: I believe these data indicate the utility of pre-therapy radiiodine imaging in this select patient group. However, it may be that the preferred pre-therapy imaging agent is I-123 as opposed to I-131. I might also point out that using higher administered levels of I-131 would likely improve the response rate regardless of the status of pre-therapy imaging findings. For lung metastases, we routinely perform dosimetry measures and deliver 300 to 400 mCi I-31 as long as the blood radiation dose is <200 rad. (Reviewer-David Bushnell, MD).

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Keywords: Thyroid Cancer

Print Tag: Refer to original journal article
SPECT/CT should improve the accuracy of diagnosing osteomyelitis in the midfoot and hindfoot, but, in the forefoot, where the bones are smaller, there is little advantage.

The largest prospective investigation of diabetic foot ulcers evaluated 41 foot ulcers in 35 diabetics. No patient was on antibiotics for >7 days, and biopsies were obtained from all sites. Patients underwent leukocyte imaging. Focally increased activity both on the dorsal and plantar views was the criterion for osteomyelitis. Four-hour leukocyte imaging had both 77% sensitivity and specificity; 24-hour imaging had a sensitivity of 89% and a specificity of 69%. As for Tc 99m labeled WBCs, sensitivities and specificities have an average of 90% for diabetic pedal osteomyelitis. One-third of diabetics develop neuropathy, and 5% eventually develop a Charcot's joint, usually after 40 years of age and involving the tarsal joint in 60%, the metatarsal joint in 30% and the tibiotalar joint in 10%. Differentiating between infection and a neuropathic joint is difficult. Labeled WBCs accumulate in uninfected neuropathic joints due to active marrow. Fractures typically occur in a neuropathic joint, and bone marrow is involved in fracture repair. Performing technetium 99m sulfur colloid marrow scintigraphy differentiates uptake due to active bone marrow from infection. There is doubt, however, regarding the role of the bone scan. Because of its high negative-predictive value, the bone scan is useful to rule out osteomyelitis. However, given the very high likelihood of positive results and low specificity, its value is questionable. Many authors recommend going straight to WBC imaging. Regarding Tc 99m versus 111-In labeled leukocytes: Tc 99m-labeled leukocytes have superior image quality and detect abnormalities within a few hours. Disadvantages include instability of the label. When marrow scintigraphy is necessary, an interval of at least 2 to 3 days is necessary. 111-In labeled WBCs are more steadily labeled, and the half-life of 111-In permits delayed imaging. Disadvantages are poor image quality and a 24-hour interval between injection and scan. The accuracies of the 2 tests are generally similar. SPECT/CT should improve accuracy in the midfoot and hindfoot but, in the forefoot, where the bones are smaller, there is little advantage. FDG PET and PET/CT are currently of little value.

Reviewer's Comments: We continue to have a plenty of requests for evaluation of the diabetic foot. Anatomic imaging modalities—even MRI—find the multitude of problems that occur in the diabetic foot challenging and confusing. Scintigraphy is well suited to sort the problems out, but the interpreter needs to be familiar with what problems are likely to happen, and in which part of the foot they may occur. This abundantly illustrated and clearly written article is the best I've seen on the topic. (Reviewer-C. Richard Goldfarb, MD).
Histologic Grade Strongly Affects FDG PET Polyp Visualization

Effect of Clinicopathologic Factors on Visibility of Colorectal Polyps With FDG PET.
Nakajo M, Jinnouchi S, et al:
AJR 2009; 192 (March): 754-760

Polyp visibility on FDG PET is strongly associated with histologic grade.

Objective: To determine which clinicopathologic factors affect the visibility of colorectal polyps on FDG PET.

Background: FDG PET is used in the detection of primary and metastatic colorectal cancer, and has also been shown to detect adenomatous polyps. However, the authors contend that this study is the first (of their knowledge) to clarify how certain clinicopathologic features affect polyp visibility on FDG PET.

Methods: 50 patients with 87 polyps were included in the study (24 patients having >1 polyp). Patients with known carcinoma, inflammatory disease, or serum glucose >130 mg/dL were excluded. All patients underwent colonoscopy, with histopathological analysis of all 87 specimens. Two nuclear medicine physicians interpreted scans using colonoscopy reports and CT findings. Discrepancies between readers were resolved by consensus. Early (1 hour post-injection) and delayed (2 hours post-injection) imaging was performed in 29 of 50 patients to determine if activity uptake changed during the delayed imaging interval. Statistical analysis was performed to determine if there were significant correlations between polyp visibility and polyp size, histologic grade, polyp type (pedunculated vs sessile), polyp location, and patient age and gender. Analysis also performed to determine if there was a significant difference in SUV\textsubscript{max} of polyps that were malignant versus benign.

Results: Although the overall visibility rate was low at 37% (32 of 87 polyps visualized), the sensitivity, specificity, positive and negative predictive values, and accuracy were 71%, 87%, 78%, and 80%, respectively. A positive correlation was found between FDG PET polyp visibility and increasing polyp size, advancing histologic grade, pedunculated polyp type, and patient age >60 years, with histologic grade showing the strongest correlation. There was no correlation between visibility and gender or the location of the polyp. Although there was a significant difference among the SUV\textsubscript{max} of polyps demonstrating early carcinoma versus those with high-grade dysplasia, no significant difference was noted among polyps with high-grade dysplasia and those with low-grade dysplasia. No significant change in SUV\textsubscript{max} at early versus delayed imaging times was noted.

Conclusions: Histologic grade is the strongest factor affecting FDG PET polyp visualization. With an accuracy of 80%, visualization by FDG PET may be useful in determining which polyps should be removed.

Reviewer’s Comments: The study reiterates results of other trials regarding polyp detection with FDG PET. The use of SUV may not be helpful in determining whether the visualized polyp is malignant (SUV\textsubscript{max} 9.2 vs 7.6 in high-grade vs low-grade polyps; \( P =0.7 \)). Visualization of a polyp should raise concern for malignancy, as this study shows that those seen tend to be of a more advanced grade. (Reviewer-Damita Thomas, MD).

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Keywords: Colorectal Polyps

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