In adapting the iPad to their daily routine, physicians face 2 main concerns: bandwidth when downloading images and device security. As technology improves, the iPad will be used more frequently as an image viewer.

According to a recent survey, approximately 80% of health care providers use the iPad® (Apple, Inc) professionally. But, whether the iPad’s use is beneficial to the imaging community is being debated. Many radiology-related iPad applications assist members of the radiology community by providing after-hours and remote access to cases/images by allowing review of cases/images with referring physicians and by providing the ability to share educational materials and images to patients. The iPad offers a platform to access current literature and online journals, many of which offer iPad applications (apps) containing full content. Using the iPad for image sharing increases transmission of information from the referring physician to the radiologist, and ultimately to the patient. Although the iPad has many relevant and beneficial uses, the Food and Drug Administration (FDA) has approved only 1 app that enables radiologists to interpret MRI, CT, and nuclear medicine images directly on the device. However, despite FDA approval, many radiologists prefer to view images on workstations where they know the quality is sufficient to make diagnoses. The 2 main concerns physicians face in adapting the iPad as part of their daily routine are (1) bandwidth when downloading images and (2) device security. As a result of these concerns, the iPad most likely will not replace workstations anytime soon, but instead, it will likely supplement daily practice. The American College of Radiology is currently working with vendors to address these concerns while stimulating research and development focused on the needs of imaging physicians. As technology continues to improve and people become more comfortable with it, the iPad will be used more frequently as an image viewer. Areas expected to use the iPad the most are telemedicine and in foreign countries with limited resources.

**Reviewer’s Comments:** I find it difficult to believe that 4 of 5 health care providers actually own an iPad, but it is very likely that they use some wireless device professionally. The younger generation (the digital generation) is so comfortable and accustomed to getting their information online that it is simply a matter of time—and probably not much more time—before scan reading goes exclusively digital and increasingly mobile. Nonetheless, for nuclear medicine, mobile is not a plus. Scintigraphic studies frequently benefit from physician-patient interaction and careful correlation with images from other studies. Both are enhanced by workstations located in the imaging suite. Additionally—and I believe this is easily quantifiable—patient satisfaction is enhanced substantially by interaction with the physician interpreting the study. (Reviewer-C. Richard Goldfarb, MD).

**Keywords:** Mobile Devices for Image Interpretation, iPad

**Print Tag:** Refer to original journal article
Dosimetry-based I-131 therapy may improve outcomes in patients with advanced well-differentiated thyroid cancer.

**Background:** For many years, there have been 2 competing approaches to the treatment of advanced stage well-differentiated thyroid cancer (WDTC). Using a fixed level of administered activity, sometimes referred to as “empiric-based therapy,” is simpler and less costly. The alternative patient-specific dosimetric method allows patients to be safely treated with higher levels of administered activity but requires more time and expense to complete properly. Although there are reasons to believe the dosimetric method would be more efficacious, few data are available to confirm this.

**Objective:** To compare the effectiveness of individualized dosimetry-based radioiodine treatment with the fixed-dose empiric approach.

**Design:** Retrospective study.

**Participants:** 87 patients with WDTC who had locally advanced disease or distant metastases.

**Methods:** Records were reviewed from 2 institutions from 1996 to 2009. At 1 institution, patients had been routinely treated with an empiric dosage of I-131, and at the second institution, the treatment dosage was always determined using a dosimetric approach. The dosimetric approach involved determining administered activity levels that would deliver ≤200 cGy to the patient’s blood. Response was determined using Response Evaluation Criteria in Solid Tumors (RECIST), and therefore, all subjects had to have had at least 1 follow-up CT/MRI exam to evaluate treatment response. Time to disease progression was also determined.

**Results:** Of the 87 patients enrolled, 73% had papillary thyroid cancer, 6% had follicular histology, 7% had Hürthle cell histology, 8% had insular histology, and 6% had tall cell histology. The distribution of histologies was not significantly different between the dosimetry group versus the empiric treatment group. Logistic regression analysis controlling for age, gender, and presence of metastases indicated that the dosimetry group was 70% less likely to show disease progression than was the empiric treatment group. However, the difference in actual progression-free survival (PFS) rate was not statistically significant in the subgroup of patients with distant metastases. Nonetheless, dosimetric therapy demonstrated a trend toward significantly improved PFS within the subgroup of subjects with locally advanced disease.

**Conclusions:** The authors concluded that their study provided evidence for the advantage of using dosimetrically-based therapy with I-131 therapy for the treatment of WDTC.

**Reviewer’s Comments:** The study’s follow-up was limited (mean, 38 months) for patients with metastases who were treated dosimetrically. This may account for the fact that significance in PFS between the 2 therapy approaches was not seen in this group. In fact, looking at the Kaplan-Meier curves, the surviving fraction drops substantially at approximately 7 years for patients with distant metastases treated empirically, but data for the group treated dosimetrically is not available at this time. (Reviewer-David Bushnell, MD).

**Keywords:** Differentiated Thyroid Cancer, Radioiodine Therapy, Empiric vs Dosimetric Approaches, Predicting Survival

Print Tag: Refer to original journal article
Because PET has a high sensitivity for detecting mesothelioma, PET/CT should be considered for differentiating benign pleural disease versus mesothelioma in patients with evidence of plural disease on chest x-ray.

**Background:** In patients with a history of asbestos exposure, determining the presence of malignant pleural mesothelioma (MPM) may be very difficult without an invasive biopsy procedure.

**Objective:** To determine if PET/CT is accurate in differentiating benign plural disease from MPM.

**Participants:** Patients with evidence of plural disease on chest x-ray during a 3-year study interval, either with or without a history of asbestos exposure.

**Methods:** PET/CT was obtained in all subjects. Pleural biopsy or clinical follow-up for a minimum of 3 years was used to establish the final disease diagnosis. Patients with evidence of thoracic infectious disease were excluded. Ultimately, patients were placed into 1 of 3 categories after a final diagnosis was established: (1) MPM, (2) benign asbestos-related lung disease, or (3) benign pleural thickening.

**Results:** Of the original 40 patients, 5 were excluded due to a final diagnosis of metastatic pleural disease. Of the 31 patients in the final study cohort, 17 had a final diagnosis of MPM, 9 had benign asbestos-related pleural disease, and 5 had non–asbestos-related pleural thickening. All 9 cases of benign asbestos demonstrated no significant FDG uptake in the pleural lesions. In the group of 5 with benign non–asbestos-related pleural thickening, only 1 case showed an abnormal increase in FDG in the pleura. Fifteen of the 17 cases with MPM showed abnormal pleural FDG activity levels. Based on visual image analysis, the authors calculated a sensitivity of 88% and a specificity of 93% for detecting mesothelioma in the study group. They did not provide confidence intervals for these results. The mean SUV$_{\text{max}}$ for the patients with mesothelioma was $6.5 \pm 3.4$ compared to a mean SUV$_{\text{max}}$ of $0.8 \pm 0.6$ for all subjects with benign pleural disease. Using a cutoff of SUV$_{\text{max}}$ 2.2, the sensitivity increased to 94% and the specificity increased to 100%. The area under the receiver operating characteristic (ROC) curve of SUV$_{\text{max}}$ was very high at 0.98.

**Conclusions:** PET/CT should be considered for imaging patients for whom there is a question of benign pleural disease versus mesothelioma.

**Reviewer's Comments:** I have referred in the past to this and a few other papers that show very similar findings in this clinical setting. I reviewed this one because it happens to be the most recent. When reading PET/CT, it is useful to remember that nodular findings in the pleura on the accompanying CT exam are typically indicative of mesothelioma. Finally, let me point out that there is a useful review article in the January 2004, issue of Radiographics that has some high-quality PET, CT, and MRI images of this disease (Wang ZJ, Reddy GP, et al. Radiographics. 2004; 24 [January-February]: 105-119.). (Reviewer-David Bushnell, MD).

**Keywords:** Mesothelioma, FDG-PET/CT

**Print Tag:** Refer to original journal article
In patients aged ≥80 years with suspected coronary artery disease, myocardial perfusion SPECT adds important risk stratification information.

**Background:** Coronary artery disease (CAD) is the leading cause of morbidity and mortality in the elderly. As the population ages, interest is increasing regarding the optimal risk stratification and clinical management of the very elderly patients aged ≥80 years.

**Objective:** To determine the role of SPECT myocardial perfusion imaging (SPECT MPI) in the management of elderly patients with suspected CAD.

**Design:** Retrospective review.

**Participants:** All patients were referred for clinical reasons to SPECT MPI for suspected CAD.

**Methods:** Patients were classified as being very elderly (age ≥80 years), elderly (age range: 65 to 79 years), or middle-aged (age range, 50 to 64 years). Patients with a left ventricular ejection fraction (LVEF) <45% were excluded. Exercise or pharmacologic stress SPECT MPI was performed in standard fashion, and the results were analyzed using summed scoring.

**Results:** Overall, 1093 patients were classified as very elderly, 3369 were elderly, and 4402 were middle-aged with a follow-up in 96%. The very elderly were less likely than younger patients to undergo early revascularization after an abnormal scan, although they have significantly more cardiac events than did younger patients in each group of summed stress scores (≤4, 4 to 8, >8). Myocardial perfusion SPECT was effective at risk stratifying patients of all age groups. Compared to nondiabetic patients, diabetic patients had a significantly lower cardiac event-free survival rate over 2.5 years.

**Conclusions:** SPECT MPI has significant incremental prognostic value in all age groups, including patients aged ≥80 years. The very elderly are less likely to undergo early revascularization after an abnormal perfusion scan, even though their subsequent risk of myocardial infarction and cardiac death is higher than in younger patients.

**Reviewer's Comments:** SPECT MPI effectively stratifies the risk of patients aged ≥80 years, and it significantly impacted clinical decision making. Like in other age groups, the presence of diabetes markedly increases the rate of adverse clinical outcomes. (Reviewer-Thomas F. Heston, MD).

Keywords: Coronary Artery Disease, Elderly, Risk Stratification, Myocardial Perfusion SPECT

Print Tag: Refer to original journal article
CCK-CS Detects Biliary Dyskinesia, Acalculous Disease

Cholecystokinin-Cholescintigraphy in Adults: Consensus Recommendations of an Interdisciplinary Panel.

Dibaise J, Richmond B, et al:

Clin Gastroenterol Hepatol 2011; 9 (May): 376-384

In patients undergoing CCK-CS, low gallbladder ejection fraction is assumed to be predictive of the need for cholecystectomy. Published data supporting this assumption are largely retrospective or anecdotal.

Background: Cholecystokinin-cholescintigraphy (CCK-CS) evaluates patients with a normal-appearing gallbladder on ultrasound but who have symptoms thought to be biliary in origin. This condition is referred to variously as “functional gallbladder disorder,” “acalculous biliary disease,” “chronic acalculous cholecystitis,” and “biliary dyskinesia.”

Objective: To summarize the consensus recommendations for performing CCK-CS in adults. Summary: The recommended protocol for the study includes the following. Optimally, the patient should fast at least 4 to 6 hours before the study. Opiate and anticholinergic drugs should be discontinued for at least 2 days. Other drugs that should not be taken within 24 hours include nifedipine, indomethacin, octreotide, theophylline, benzodiazepines, phenolamine, isoproterenol, and progesterone. Nicotine and alcohol also should be avoided prior to testing. Following 3 to 5 mCi of Tc-99m mebrofenin or disofenin intravenously, when the gallbladder has filled, place the camera in an oblique projection that ensures minimal overlap of the gallbladder with duodenum and small bowel. Visualization of the small bowel is not necessary prior to sincalide infusion. A 0.02 μg/kg dose of sincalide should be drawn into a 30- to 50-mL syringe and diluted with normal saline to the volume of the syringe. The infusion pump or IV drip should be set so that the infusion is completed at 60 minutes. A gallbladder ejection fraction (GBEF) <38% is considered abnormal. A high GBEF is of no clinical significance. CCK-induced abdominal pain does not have diagnostic value because it does not necessarily reflect the presence of gallbladder disease. A low GBEF is assumed to be predictive of cholecystectomy resulting in pain resolution, but published data supporting this assumption are largely retrospective or anecdotal. Yap and colleagues published the only randomized controlled study of this topic, but it was small (Gastroenterol 1991;101:786-793). In this study, 21 patients with suspected functional biliary pain and GBEF <40% were randomly assigned to cholecystectomy and 10 were assigned to no surgery. After cholecystectomy, 10 patients became asymptomatic, and 1 improved. In the group that did not undergo surgery, symptoms were unchanged; 2 requested cholecystectomy and then subsequently improved.

Reviewer's Comments: This review represents the consensus opinion of an interdisciplinary panel for performing CCK-CS, which is an increasingly popular procedure. It potentially fulfills an important clinical need: to aid in the decision to remove or preserve a gallbladder in those with typical biliary symptoms but normal sonograms and promptly filling gallbladders on HIDA scan. The committee's 60-minute infusion recommendation is based on results of a multicenter study by Ziessman and colleagues (J Nucl Med. 2010; 51 [February]: 277-281.) comparing 15-, 30-, and 60-minute infusion times. Standardization of the procedure should enhance its clinical utility and facilitate accumulation of data documenting its efficacy. (Reviewer-C. Richard Goldfarb, MD).

Keywords: Hepatobiliary Disease, Diagnosis, Cholecystokinin-Cholescintigraphy, Consensus Recommendations

Print Tag: Refer to original journal article
Oral NaClO4 Reduces Gastric Uptake of Free Pertechnetate

Significance of Oral Administration of Sodium Perchlorate in Planning Liver-Directed Radioembolization.
Sabet A, Ahmadzadehfar H, et al:

J Nucl Med 2011; 52 (July): 1063-1072

Oral sodium perchlorate administered before a test angiogram with Tc-99m MAA avoids free Tc-99m pertechnetate uptake in the gastroduodenal region, increasing the test's accuracy and reporter confidence.

Background: Scintigraphy mapping using Tc-99m MAA prior to radioembolization of the liver is intended to detect extrahepatic shunting to the lung or gastrointestinal tract. Dissociated Tc-99m pertechnetate will falsely suggest shunting to the stomach and GI tract. To reduce the presence of unlabeled technetium, Tc-99m MAA must be prepared with strict quality control assessment and imaging done within 1 hour of injection. But even with careful routine preventive measures, gastric uptake of free Tc-99m pertechnetate is frequently seen in Tc-99m MAA images. Sodium perchlorate (NaClO4), due to its affinity for the sodium-iodine symporter, is used for prophylaxis of iodine-induced hyperthyroidism due to iodinated contrast agents.

Objective: To assess the value of oral administration of sodium perchlorate before Tc-99m MAA scanning to block free Tc-99m pertechnetate gastric uptake.

Methods: 144 patients with primary and secondary hepatic malignancies had 171 diagnostic hepatic angiograms with Tc-99m MAA. The first 72 patients did not receive NaClO4 before Tc-99m MAA (85 angiograms). In the second subgroup, the next 72 patients (86 angiograms) received NaClO4, and then 185 MBq (5 mCi) of Tc-99m MAA was administered intraarterially. Whole-body anterior and posterior scanning within 1 hour of Tc-99m MAA injection was used to calculate the percentage of liver-to-lung shunting. SPECT of the upper abdomen was acquired to rule out extrahepatic gastrointestinal shunting. Additionally, SPECT/CT was performed in the last 90 studies. Scans showing extrahepatic Tc-99m MAA were reviewed to find aberrant arteries for coil embolization via angiography followed by a repeat Tc-99m MAA scan to rule out shunting.

Results: The nonperchlorate group demonstrated uptake in the gastric region in 25 studies (29%), which was interpreted as free Tc-99m pertechnetate in 21 and as true Tc-99m MAA gastric accumulation in 4. In the subgroup receiving perchlorate, gastric uptake was seen in only 2 SPECT scans, while SPECT/CT revealed a gastric accumulation in another 5. Oral administration of NaClO4 significantly increased the negative predictive value from 68% to 93%.

Conclusions: Oral NaClO4 administered before test angiogram with Tc-99m MAA avoids free Tc-99m pertechnetate uptake in the gastroduodenal region, increasing the accuracy and reporter confidence associated with the test.

Reviewer's Comments: Radioembolization of the liver for colon cancer metastases, hepatocellular carcinoma, or neuroendocrine liver metastases is an increasingly popular and demonstrably effective procedure. Oral administration of sodium perchlorate seems like an easy strategy to "increase accuracy" and "boost confidence" of interpreters of scintigraphic mapping prior to radioembolization. I agree that free Tc-99m can potentially be a technical problem, but it probably depends on the situation. We have been doing these studies for >2 years and have not experienced much problem from "free technetium" in the stomach—certainly not in 29% of the studies. The sodium perchlorate strategy seems sensible, but only if you need it. (Reviewer-C. Richard Goldfarb, MD).

Keywords: Extrahepatic Shunting, Liver-Directed Radioembolization, Blocking Gastric Uptake of Free Pertechnetate, Sodium Perchlorate

Print Tag: Refer to original journal article
To maintain a comparable signal-to-noise level, the radiation dose levels required increase inversely with approximately the cube of the resolution element. This leads to the high doses associated with preclinical imaging.

**Background:** Preclinical studies benefit from the use of small animal CT, but the radiation dose from these studies can be very large and may potentially affect study outcomes.

**Objective:** To determine if sufficient CT image quality can be obtained in small animal studies without significant radiation-induced biologic damage.

**Methods:** This study was conducted on the Bioscan NanoSPECT/CT system. The CT radiation dose was determined from the optical density of GAFCHROMIC® film. Imaging studies were performed on 2 strains of mice: 1 with known radiation resistance (C57BL/6) and the other with known radiation sensitivity (BALB/c severe combined immunodeficient). Ten CT protocols were applied to the 2 groups of mice with the kVp ranging from 35 to 65, tube current ranging from 50 to 177 microamps, and the exposure time ranging from 400 to 2400 milliseconds. Macroscopic features used to assess the effect of radiation on the mice included mobility, weight loss, and coat appearance. After imaging, the animals were sacrificed, and leukocytes along with tissue samples from the liver and jejunum were evaluated for radiation damage by staining for γH2AX. These results were compared to nonirradiated control animals.

**Results:** The skin dose from the CT procedures used in the leukocyte evaluation ranged from 13 to 690 mGy, while the central axis dose ranged from 6 to 410 mGy. The relative γH2AX staining indicating DNA damage increased linearly with dose with strain-dependent slopes. However, no significant DNA damage was observed for the lowest radiation scans. Both strains of mice demonstrated significant DNA repair after 24 hours. For the experiments in which the liver and jejunum were evaluated, the average CT dose ranged from 8.3 mGy to 3.4 Gy. Similar results were seen for these tissues, with a linear relationship between dose and DNA damage and with significant repair after 72 hours.

**Conclusions:** The standard protocols used in preclinical micro-CT imaging result in significant DNA damage, which is accentuated for longitudinal studies. The lowest dose procedures used in these experiments avoided DNA damage while maintaining sufficient image quality.

**Reviewer’s Comments:** Because of the need to provide sufficient temporal and spatial sampling, the radiation dose imparted to small animals in preclinical scans is often much larger than that given to humans in clinical scans. As this article shows, the radiation dose can be large enough to cause measurable radiation damage, with the potential to alter the physiology of the animal. It is important to understand (1) that imaging protocols provided by the manufacturer need to be evaluated in terms of the radiation dose they deliver and (2) that reducing the dose while maintaining image quality is often possible. (Reviewer-Mark T. Madsen, PhD, FAAPM, FACR).

**Keywords:** Micro-CT in Preclinical Studies, Radiation Dose vs Biologic Damage

**Print Tag:** Refer to original journal article
Adding additional parameters to a compartmental model may improve how well the model fits experimental data at the expense of parameter reliability.

Background: There are often many ways to obtain quantitative results from the pharmacokinetics of PET imaging agents. Are some approaches significantly better than others in providing definitive results that limit the number of subjects required for statistical significance?

Objective: To evaluate several quantitative approaches to F-18 fluoride PET imaging studies to determine which provides the best statistical significance for power calculations.

Methods: The serial F-18 fluoride dynamic PET studies from 20 postmenopausal women were analyzed by 8 different methods which could be classified in 3 ways: (1) methods that modeled the reverse flow of F-18 from the bone mineral, (2) methods in which F-18 was assumed to be irreversibly bound to bone mineral, and (3) simple standardized uptake values (SUV). The fluoride plasma clearance parameter (Ki) from the compartmental methods was used to evaluate response to bisphosphonate treatment, and the statistical uncertainty associated with each method was compared.

Results: The group 1 methods that modeled the reverse flow of F-18 from the bone mineral had the best agreement for estimates of Ki (r=0.97), but the statistical precision was larger than that for the group 2 methods in which F-18 was assumed to be irreversibly bound to bone mineral (14.5% vs 13%, respectively). However, the magnitude of the Ki estimates was about 25% lower for group 2 methods compared to group 1 methods, and the correlation between the 2 groups was reduced (r=0.9). The precision of the SUV was good (10%), but it was not a sensitive indicator of treatment response and had marginal correlation with the compartmental model methods (r=0.6). Using this information, the minimum number of subjects required to verify a statistically significant treatment response was approximately 10 for group 1, 5 for group 2, and 240 for SUV methods.

Conclusions: Although the precision in measuring SUV was good, it was unsuitable for monitoring treatment response. The methods which assumed that F-18 was irreversibly bound resulted in the fewest number of subjects to demonstrate a significant response to therapy.

Reviewer's Comments: The authors of this paper point out challenges associated with compartmental modeling and the importance of a careful analysis of the methodology in the context of a particular outcome. Increasing the number of parameters to a compartmental model can improve how well the model fits experimental data, but because of the dependent influence among the parameters, the precision can actually be adversely affected. In this example, in which response to therapy is the important outcome, ignoring the reverse flow of F-18 actually makes the Ki estimate a more sensitive indicator. (Reviewer-Mark T. Madsen, PhD, FAAPM, FACR).

Keywords: F-18 Fluoride PET, Quantitative Approaches, Precision Errors, Sensitivity

Print Tag: Refer to original journal article
PET/CT is about 97% sensitive and specific for detecting tumor recurrence or metastasis in patients with a history of high-risk melanoma.

**Background:** S100B is a protein biomarker that is elevated in > 80% of patients with metastatic melanoma. A rising S100B level predicts melanoma relapse earlier than other conventional clinical or radiologic imaging methods. Melanoma inhibitory activity (MIA) is a marker for progression from localized to metastatic disease in advanced melanoma and is more specific than S100B for detecting metastasis. F-18 FDG-PET/CT is sensitive and specific in staging high-risk melanoma, but its role in follow-up requires further investigation.

**Objective:** To compare the prognostic value of PET/CT with tumor markers S100B and MIA in patients with a history of high-risk melanoma.

**Design:** Retrospective cohort analysis.

**Participants:** 125 consecutive patients with suspected melanoma metastases. All patients were stage IIB or higher or had suspicious ultrasound findings. Inclusion criteria were Breslow thickness, elevated S100B or MIA levels, positive sentinel lymph node (SLN), or history of known or resected metastasis.

**Methods:** Patients underwent FDG-PET/CT imaging. Metastases were confirmed by histology, follow-up PET/CT or MRI imaging, clinical follow-up for 18 to 48 months, or tumor-associated death. Serum S100B, MIA, and lactate dehydrogenase (LDH) levels were also determined for each patient. **Results:** Of the 125 patients evaluated, 62 had recurrent or metastatic melanoma. The sensitivity and specificity of FDG-PET/CT were each 96.8% (95% CI, 89.0% to 99.1% and 89.1% to 99.1%, respectively). S100B had a sensitivity and specificity of 45.2% and 85.7%, respectively. For MIA, the sensitivity was 36.1%, and the specificity was 95.2%. Patients with positive PET/CT findings had a 17.2-fold higher mortality risk than did patients with a negative PET/CT. Patients with elevated S100B, MIA, or LDH had a 4.2-fold, 6.5-fold, or 6.1-fold elevated mortality risk, respectively. The median survival was 29.7 months in S100B-positive patients, 16.4 months in MIA-positive patients, 16.4 months in LDH-positive patients, and 43.87 months in PET/CT-positive patients. There was a correlation between mortality rate and number of metastases on PET/CT ($P < 0.001$). There was also a correlation between MIA level and mortality ($P < 0.001$). There was no correlation between mortality and S100B level. **Conclusion:** PET/CT has higher diagnostic and prognostic power than S100B or MIA levels in patients with high-risk melanoma.

**Reviewer's Comments:** Although PET-positive patients had a higher mortality risk than did patients with positive serum biomarkers, the survival time was much shorter for patients with serum biomarker positivity than for patients with PET positivity. (Reviewer-Shayne Squires, MD).

Keywords: High-Risk Melanoma, Prognostic Value of FDG-PET/CT, S100B, MIA

Print Tag: Refer to original journal article
Retention of β-amyloid plaque in cortical gray matter is associated with an increased risk of cognitive impairment.

Deposition of β-amyloid (Aβ) plaques in cortical grey matter has been associated with the development of Alzheimer disease (AD) and also distinguishes AD from frontotemporal and vascular dementias. Aβ plaque density in AD patients, as determined by PET imaging with Pittsburgh compound B (11C-PiB), is typically 30% greater in the cortical gray matter than in white matter, which usually shows moderate nonspecific uptake. Such variances are sufficiently detectable by visual inspection and correlate with increased risk of subsequent cognitive decline when found in healthy asymptomatic individuals. Unfortunately, the degree of cortical 11C-PiB retention among AD patients is highly variable and does not correlate with symptom severity. However, Aβ plaque burden is directly proportional to both the degree and progression rate of mild cognitive impairment (MCI), which immediately precedes the onset of dementia. 11C-PiB binding in the cerebral cortex may be quantified as a ratio of standardized uptake values (SUVs) normalized to cerebellar gray matter, which typically exhibits significantly less Aβ plaque density. The pons may also be used as a cortical SUV ratio reference in instances of increased cerebellar Aβ plaque deposition, such as familial AD and late-stage AD with advanced dementia. After uptake periods of 40 to 50 minutes, positive scans will show high 11C-PiB binding in the frontal cortex, cingulate gyrus, precuneus, striatum, parietal cortex, and lateral temporal cortex. Similar cortical binding patterns are also seen in positive scans with 18F-labeled amyloid tracers currently in development (florbetaben, florbetapir, and flutemetamol). However, these agents also exhibit high nonspecific white matter binding, which obscures the clear-cut distinction between positivity and negativity otherwise seen with 11C-PiB. Consequently, 18F-based scan images must be tomographically manipulated to discern whether the fine demarcation between gray and white matter is scintigraphically present (normal) or absent (abnormal). Future studies will show whether associations between 11C-PiB and cognitive decline will also hold true for 18F-labeled brain amyloid radioligands.

**Reviewer's Comments:** It is true that brain PET imaging with radioligand-labeled ligands for β-amyloid directly correlates with AD as well as an increased risk of dementia onset in patients showing abnormal patterns of increased localization in the cortical gray matter. This is typically 30% greater than the normal low level of central white matter uptake seen with 11C-PiB, and produces a characteristic ribbon-like rim of cortical activity on tomographic images. The 18F-based β-amyloid radiotracers currently in development typically show nonspecific white matter localization comparable to the levels of abnormally increased cortical uptake. Thus, abnormal (positive) tomographic images with these radioligands will typically show a paradoxical loss of the normally clear delineation between the relatively radiotracer-avid central white matter and relatively photopenic cortical gray matter. (Reviewer-Parren McNeely, MD).

**Keywords:** Dementia, Alzheimer Disease, Diagnosis, Beta-Amyloid PET

**Print Tag:** Refer to original journal article
Ga-68 DOTATOC has a higher tumor-to-kidney uptake than does Ga-68 DOTATATE, but the overall diagnostic value is similar in neuroendocrine tumor imaging.

**Background:** Ga-68 DOTATOC and Ga-68 DOTATATE are radiopharmaceuticals that bind to somatostatin receptors and are used in PET imaging of neuroendocrine tumors (NETs). Somatostatin receptor subtype 2 (SST2) is overexpressed in most NETs. In vitro studies suggest that Ga-68 DOTATATE has a 10-fold higher binding affinity to SST2 than does Ga-68 DOTATOC.

**Objective:** To compare the diagnostic value and tumor uptake of Ga-68 DOTATATE versus GA-68 DOTATOC in the same patients with NETs using PET/CT imaging.

**Participants:** 40 patients with histologically verified gastroenteropancreatic or bronchopulmonary NETs.

**Methods:** Preliminary to peptide receptor radionuclide therapy, each patient underwent PET/CT imaging with Ga-68 DOTATATE and Ga-68 DOTATOC. Images were evaluated semiquantitatively by 2 nuclear medicine readers. Images were evaluated for radiotracer uptake in 8 anatomic regions: head and neck, mediastinum, lungs, liver, pancreas, abdomen and pelvis, bone, and lymph nodes. The number of lesions detected by PET/CT in each region was tallied. If >5 lesions were seen in a region, the number of lesions for that region was truncated at 5.

**Results:** There was no significant difference in the number of regions detected as positive, the average number of positive regions per patient, or the number of patients with at least 1 lesion using either radiotracer. A total of 254 lesions were detected using Ga-68 DOTATATE versus 262 lesions detected using Ga-68 DOTATOC ($P=0.012$). The maximum standardized uptake value ($SUV_{max}$) was significantly higher for Ga-68 DOTATOC than for Ga-68 DOTATATE (mean 20.4 ± 14.7 vs. 16.0 ± 10.8, $P=0.0005$). The difference remained significant after normalizing $SUV_{max}$ to muscle or liver. There was no significant difference in the $SUV_{max}$ for renal parenchyma (12.7 ± 3.0 for Ga-68 DOTATATE vs 13.2 ± 3.3 for Ga-68 -DOTATOC).

**Conclusions:** Ga-68 DOTATATE and Ga-68 DOTATOC have similar diagnostic values in detecting lesions from NETs. SUV$_{max}$ tends to be higher with Ga-68 DOTATOC than with Ga-68 DOTATATE.

**Reviewer’s Comments:** Surprisingly, this study showed better in vivo tumor uptake of Ga-68 DOTATOC than with Ga-68 DOTATATE, despite the higher affinity of Ga-68 DOTATATE for the SST2 receptor. Additionally, the tumor-to-kidney ratio was better for Ga-68 DOTATOC than for Ga-68 DOTATATE. (Reviewer-Shayne Squires, MD).

**Keywords:** Neuroendocrine Tumors, PET, Diagnostic Value of DOTATATE vs DOTATOC

**Print Tag:** Refer to original journal article
PET/CT is more accurate for detecting osseous metastases from Ewing sarcoma family tumors than is either bone scan or MRI.

**Background:** The Ewing sarcoma family of tumors (ESFT) includes Ewing sarcoma of bone, extraskeletal Ewing sarcoma, small cell tumor of the thoracopulmonary region, and soft tissue-based primitive neuroectodermal tumors.

**Objectives:** To systematically review published data on the performance of F-18 FDG-PET and PET/CT in ESFT and to determine the diagnostic accuracy of these imaging studies.

**Design:** Meta-analysis and systematic review of the literature.

**Methods:** The investigators searched PubMed®/MEDLINE®, EMBASE®, and SciVerse Scopus. Studies satisfying all of the following criteria were included: (1) PET or PET/CT performed in patients with ESFT, (2) determination of diagnostic accuracy, and (3) sample size of at least 10 patients. Studies included in the quantitative analysis contained sufficient data to reassess sensitivity and specificity.

**Results:** The systematic review included 13 studies that incorporated a total of 342 patients. Of these 13 studies, 5 included sufficient information to recalculate sensitivity and specificity. These 5 studies included a total of 279 patients. The pooled examination-based sensitivity and specificity were 96% (95% confidence interval [CI], 91% to 99%) and 92% (95% CI, 87% to 96%), respectively. The area under the receiver operating characteristic curve was 0.97. PET performed better than bone scintigraphy and MRI for the detection of osseous metastases. Spiral CT performed better than PET for the detection of pulmonary metastases.

**Conclusions:** PET and PET/CT have high diagnostic accuracy in the evaluation of ESFT. PET/CT is more accurate than PET alone. A combination of PET/CT and conventional imaging is a valuable tool for staging and restaging ESFT.

**Reviewer's Comments:** The authors of this study suggest that PET/CT has a very high accuracy for the detection of ESFT. However, there is 1 caveat: publication bias tends to favor positive studies. Generally, this affects meta-analyses. (Reviewer-Shayne Squires, MD).

Keywords: Ewing Sarcoma, Primitive Neuroectodermal Tumors, FDG-PET

Print Tag: Refer to original journal article
Nomograms Simplify MPS Interpretation, Predict CAD Risk

Nomograms for Estimating Coronary Artery Disease Prognosis With Gated Stress Myocardial Perfusion SPECT.
Shaw LJ, Min JK, et al:
J Nucl Cardiol 2011; November 2 (): epub ahead of print

The nomograms given in this manuscript may help assess cardiac risk in nuclear scintigraphy patients and are based on exercise versus pharmacologic stress, LVEF, and percent ischemic myocardium.

Background: Nomograms can be a useful clinical tool for estimating post-stress-test risk of cardiac disease.

Objective: To create risk-based nomograms for patients undergoing stress myocardial perfusion SPECT (MPS) based on both the percent ischemic myocardium and left ventricular ejection fraction (LVEF).

Design: Retrospective database review.

Participants: 4575 patients with suspected coronary artery disease (CAD) who underwent MPS.

Methods: Patients underwent gated MPS using either exercise or pharmacologic stress testing. Gating was done either at rest or after stress. Follow-up was performed using a scripted telephone interview or during clinical visits. Approximately 1% of patients were lost to follow-up. The cause of death was confirmed by clinical records or review of death certificates. The median follow-up was 1.6 years.

Results: Most patients had an intermediate or high pretest likelihood of CAD, >7% had at least mild ischemia, and nearly 10% had a rest or post-stress LVEF of ≤45%. The overall event-free survival rate was 93%. The best survival was seen in patients with an LVEF >45% and no ischemia who underwent exercise stress testing. In patients with no ischemia who required pharmacologic stress, event-free survival was significantly decreased compared to similar patients able to undergo exercise stress testing. In patients with no ischemia but who required pharmacologic stress testing, the risk was similar to patients with approximately 5% ischemic myocardium but who were able to exercise. Each stage completed on the Bruce protocol treadmill stress test increased the event-free survival rate by approximately 1%. There appeared to be a linear relationship between percent ischemic myocardium and event-free survival.

Conclusions: Nomograms based on percent ischemic myocardium and LVEF may provide a useful clinical tool for physicians managing patients with known or suspected CAD.

Reviewer’s Comments: These easy-to-use nomograms appear readily understandable. The nomograms show that risk increases progressively with percent ischemic myocardium, without any lower threshold. For example, in patients with a post-stress-test LVEF of >45%, the baseline estimated event-free survival rate over 2 years was 96% for those with 0% ischemic myocardium compared to 93% for those with 2.5% ischemic myocardium. For each stage of the Bruce protocol completed, you add an additional 1% to these estimated event-free survival rates. The nomograms given in this manuscript are excellent and highly recommended. (Reviewer-Thomas F. Heston, MD).

Keywords: Coronary Artery Disease, Prognosis, Stress Myocardial Perfusion SPECT, Nomograms

Print Tag: Refer to original journal article
PET-Directed Management in HNSCC Spares Neck Dissection

Results of a Prospective Study of Positron Emission Tomography-Directed Management of Residual Nodal Abnormalities in Node-Positive Head and Neck Cancer After Definitive Radiotherapy With or Without Systemic Therapy.

Porceddu SV, Pryor DI, et al:

Head Neck 2011; 33 (December): 1675-1682

PET has a much higher positive predictive value than CT for residual nodal disease in head and neck cancer (78% vs 14%, respectively).

**Background:** Retrospective evidence indicates that restaging with F-18 FDG-PET has a high negative predictive value in patients with head and neck squamous cell carcinoma (HNSCC) who have previously undergone chemotherapy and radiation.

**Objective:** To prospectively determine the clinical value of PET-directed management of patients with HNSCC who have undergone previous definitive therapy.

**Participants:** The study included patients with biopsy-proven, node-positive HNSCC without distant metastases. Patients with an unknown primary presumed to have arisen from a head and neck site were also eligible. Patients were included only if they achieved a complete response at the primary site 12 weeks after radiation therapy.

**Methods:** Patients were treated with 3-D conformal radiation therapy for a total of 66 to 70 Gy to known sites of disease and 50 Gy to elective sites. At the discretion of the treating physicians, some patients also received systemic therapy with high-dose cisplatin, carboplatin/5-fluorouracil, or cetuximab. Each patient underwent FDG-PET/CT imaging within 3 weeks before and 12 weeks after radiation therapy. Patients underwent neck dissection if there was significant nodal FDG uptake. If nodal uptake was equivocal, a repeat PET was performed 4 to 6 weeks later. If it remained equivocal, neck dissection was performed.

**Results:** Ultimately, the study included 112 patients. The median follow-up was 28 months. Of 112 patients, 50 had a nodal abnormality by CT at 12 weeks. Of these, 41 were PET-negative and 9 were PET-positive. Of the 62 patients without nodal abnormality by CT, 61 were PET-negative and 1 was equivocal. The follow-up scan was negative for the equivocal case. Among PET-positive patients, there were 2 isolated nodal failures and 1 patient who developed pulmonary metastases who did not go on to neck dissection. Among PET-negative patients, there were no isolated nodal failures. The negative predictive values for nodal response were 98.1% for PET (95% CI: 91% to 99%) and were 96.8% for CT (95% CI: 88.8% to 99.6%). The positive predictive values of PET and CT were 77.8% (95% CI: 40% to 97.2%) and 14% (95% CI: 5.8% to 26.7%), respectively.

**Conclusions:** In patients with initially node-positive HNSCC, PET-directed management of the neck after definitive chemotherapy and radiation spares neck dissection in patients who are PET-negative with residual nodal abnormalities by CT.

**Reviewer's Comments:** To determine whether PET-directed management could spare neck dissections, this study differed from others in that it was limited to the population of patients with complete primary response. Patients without a complete primary response would go on to neck dissection anyway. (Reviewer-Shayne Squires, MD).

Keywords: Head and Neck Squamous Cell Carcinoma, PET, Nodal Metastases

Print Tag: Refer to original journal article
Ga-68 DOTATATE Uptake in NETs Not Impacted by Octreotide

Treatment With Octreotide Does Not Reduce Tumor Uptake of 68Ga-DOTATATE as Measured by PET/CT in Patients With Neuroendocrine Tumors.

Haug AR, Rominger A, et al:


Octreotide therapy may actually help detect primary and metastatic tumors in patients with neuroendocrine tumors undergoing Ga-68 DOTATATE PET/CT imaging.

Background: Studies have shown that Ga-68 DOTATATE PET/CT is more accurate than In-111 octreotide SPECT imaging in detecting disease in patients with neuroendocrine tumors (NETs). However, investigations have not evaluated the impact of octreotide therapy on tracer uptake and how this may affect the sensitivity of disease detection using this tracer. Because some patients are quite symptomatic, it proves challenging to have patients withdrawn from therapy for PET/CT imaging.

Objective: To determine if octreotide therapy affects Ga-68 DOTATATE uptake in NETs.

Design/Participants: 105 patients with NETs (35 previously treated with octreotide and 70 without) were retrospectively evaluated.

Methods: SUV maximum and mean values were measured for the primary and metastatic tumor sites as well as for the normal liver, spleen, adrenal, pituitary, and kidney. Among the patients previously treated with octreotide, differences in uptake were also evaluated between those who underwent imaging either <14 days or >14 days after last treatment.

Results: No significant difference was seen in the SUV of the disease sites between patients previously treated with octreotide and untreated patients. However, SUVs of normal liver and spleen were lower in treated patients than in the nontreated group. Also, among the treated group of patients, the SUVs of disease sites were not significantly different between patients who had at their last dose of therapy <14 days before imaging versus those who had their last dose of therapy >14 days before imaging.

Conclusions: Among patients with NETs, treatment with octreotide does not reduce Ga-68 DOTATATE binding in the target tumor.

Reviewer’s Comments: The findings of this interesting study have potential implications in the management of NET patients undergoing Ga-68 DOTATATE PET/CT imaging. Although the study has a retrospective design and evaluates a relatively small number of patients, data from this study are quite compelling: prior octreotide treatment does not result in lower uptake in primary and metastatic sites, and there may be an enhanced tumor-to-background ratio as normal liver uptake of the tracer is decreased among patients previously treated. Another interesting finding is that uptake did not differ for patients who had stopped Sandostatin therapy within the conventionally recommended 14 days before imaging versus those who had imaging at least 14 days after therapy. This has significant implications in that severely symptomatic patients may be able to continue treatment for longer times prior to imaging without the concern of compromising the ability to detect disease. Although not currently approved in the United States by the Food and Drug Administration, hopefully it will be approved soon, and these are lessons that we can learn from the studies of our European colleagues. (Reviewer-Damita Thomas, MD).

Keywords: Neuroendocrine Tumors, PET With GA-68–Labeled Somatostatin Analogs, Effect of Octreotide on SUV

Print Tag: Refer to original journal article
FDG-PET is very accurate for distinguishing benign from malignant ovarian lesions. In this study, all ovarian lesions with an SUV$_{\text{max}}$ >5 were malignant.

**Objective:** To evaluate the efficacy of FDG-PET/CT to differentiate benign from malignant ovarian lesions.

**Design:** Prospective study.

**Methods:** All women with suspected ovarian cancer underwent FDG-PET/CT imaging to evaluate the ovaries. The CT exams from PET/CT were obtained with contrast enhancement. The clinical suspicion of ovarian cancer was based on CA-125 levels, MRI, and/or ultrasound findings. All patients underwent surgery to remove the suspicious lesion, and histopathology results from the tumor were used as the gold standard for final malignant versus benign determination.

**Results/Conclusions:** 111 ovarian masses were identified in 108 patients whose ages ranged from 32 to 79 years (mean age, 55 years). Using the World Health Organization (WHO) classification, 73 tumors were classified as malignant, 26 were found to be benign, and 12 were classified as borderline. The most common malignancy was papillary serous adenocarcinoma. The mean SUV$_{\text{max}}$ was 7.55 for malignant lesions (range, 1.29 to 22.5), 2.72 for borderline lesions (range, 1.43 to 4.81), and 2.0 for benign lesions (range, 0.88 to 4.22). The differences in SUV$_{\text{max}}$ for these categories were all statistically significant except for the difference between the benign and borderline groups. Combining the borderline cases with the definite malignancies, the authors evaluated sensitivity and specificity for different cutoff values of SUV$_{\text{max}}$. The best overall performance was seen when lesions with an SUV$_{\text{max}}$ of ≤2.5 were considered benign, yielding a sensitivity and specificity of 82% and 77%, respectively. Sensitivity reached 93% for a cutoff value of 2.0, but specificity dropped to 62%. The authors reported the identification of unsuspected malignancies at sites other than the ovaries in 4 of the subjects in this study.

**Reviewer's Comments:** All lesions with an SUV$_{\text{max}}$ >5 were malignant, and this may be of some value in interpreting PET findings in the ovaries. I think it would have been interesting if the authors had looked at the PET findings based on menopausal status. (Reviewer-David Bushnell, MD).

**Keywords:** Ovarian Cancer, Differentiating Benign vs Malignant Lesions, PET/CT

**Print Tag:** Refer to original journal article
Preop FDG Uptake Predicts Postop Myelopathy Outcomes

Prognostic Value of 18F-FDG PET in Monosegmental Stenosis and Myelopathy of the Cervical Spinal Cord.

Floeth FW, Stoffels G, et al:

J Nucl Med 2011; 52 (September): 1385-1391

In patients with monosegmental cervical spine myelopathy, preoperative patterns of FDG uptake at the level of stenosis/cord compression may be predictive of surgical outcome.

**Background:** MRI is the imaging modality of choice when evaluating patients with symptoms of cervical spinal cord stenosis. However, conventional imaging is limited when it comes to predicting clinical outcomes of patients who undergo surgical decompression.

**Objective:** To determine if FDG-PET has prognostic value in patients with monosegmental stenosis and myelopathy of the cervical spinal cord.

**Methods:** 20 patients (10 with myelopathy and 10 normal controls) were evaluated with FDG-PET, and SUV\textsubscript{max} was measured throughout the cervical spine. The 10 myelopathic patients were subdivided into 2 groups: those with distinctly increased uptake at the level of stenosis or compression (group 1) and those with more inconspicuous uptake at the affected level (group 2). Uptake was correlated with postsurgical functional status as assessed by a scoring system used in neurodegenerative disorders.

**Results:** When compared to the control group, FDG uptake below the affected level was significantly lower in both groups of myelopathic patients. Following surgery, there was a significant improvement in functional scores in the group 1 but not among the myelopathic patients in group 2. Also, the uptake pattern of the group 1 patients was associated with more acute phase where symptoms improved with surgery, whereas the more diffuse uptake pattern seen in group 2 patients was associated with more long-term symptoms that did not respond as well to surgery.

**Conclusions:** FDG-PET uptake patterns in myelopathic patients seem to be predictive of surgical outcome.

**Reviewer’s Comments:** This study, although evaluating few patients, yields data that warrants a larger investigation because the findings suggest that the pattern of preoperative FDG uptake is predictive of postoperative functional status. This has important implications: if preoperative uptake patterns accurately correlate with surgical outcomes, patients who would benefit from surgery could be selected, whereas those who would not benefit could be spared surgery and offered other less invasive treatment alternatives. This could be a new application of FDG-PET in the evaluation of this patient population. (Reviewer-Damita Thomas, MD).

**Keywords:** Cervical Myelopathy, Surgical Outcomes, Prognostic Value of FDG-PET

Print Tag: Refer to original journal article
Among patients with primary breast cancer lesions who undergo positron emission mammography, those with triple-negative-receptor tumors have the highest level of FDG uptake.

**Background:** In recent years, some PET machines have been designed and built to specifically image the breast for detection of primary breast cancer lesions. This process is known as positron emission mammography (PEM) and utilizes the radiopharmaceutical FDG. One of the limitations of general PET imaging in patients with breast cancer is the known absence of FDG uptake in a certain small percentage of breast malignancies.

**Objective:** To determine if the primary tumor’s affinity for FDG is associated with the receptor status of the tumor.

**Participants:** Patients with breast cancer referred for PET/CT prior to mastectomy between 2007 and 2009.

**Methods:** All patients underwent PEM following the PET/CT exam so that no additional FDG administration was required. PEM imaging was conducted with a Naviscan® PET system. Resected tumors were evaluated for receptor status, including estrogen receptors (ER) progesterone receptors (PR), and human epidermal growth factor receptor 2 (HER2). Because PEM images are not corrected for attenuation, SUV is not calculated for PEM images. Rather, lesion-to-background ratios are determined.

**Results:** 101 patients referred for PET prior to mastectomy all underwent PEM imaging. Not one of the patients had received neoadjuvant therapy prior to imaging. Three lesions in 3 patients were excluded from analysis because PEM imaging was negative. Therefore, a total of 100 lesions in 98 subjects formed the data analysis group. The correlation between $SUV_{max}$ from the PET/CT and the maximum lesion-to-background ratio from PEM was $r=0.76$. Eleven patients were triple-receptor-negative, and 11 patients were triple-receptor-positive. Sixty-four patients were ER-positive, PR-positive, and HER2-negative. FDG levels were highest in the triple-negative group. However, this only reached significance when compared to the group that was ER/PR-positive and HER2-negative. FDG uptake was also higher in ER-negative patients versus ER-positive patients, and in PR-negative patients versus PR-positive patients. Higher grade tumors also showed greater FDG uptake. None of the 3 excluded subjects had triple-negative tumors.

**Conclusions:** FDG uptake measured during PEM in primary breast cancer lesions is related to the receptor status and grade of the patient's tumor.

**Reviewer's Comments:** I thought the results of this study were interesting, although it seems uncertain as to whether the findings will have practical clinical application. (Reviewer-David Bushnell, MD).

Keywords: Primary Breast Cancer, Positron Emission Mammography, Effect of Tumor Receptor Status on FDG Uptake

Print Tag: Refer to original journal article