Sentinel lymph node biopsy detects occult metastases in 43.5% of patients with papillary thyroid cancer who have metastases at initial diagnosis. Of these, 20% are located only in the lateral compartments.

**Background:** Papillary thyroid carcinoma (PTC) spreads preferentially to the lymph nodes. It is debated whether prophylactic lymph node (LN) dissection improves prognosis and survival in patients with PTC but without suspicion of lymph node metastases. Appropriate staging of these patients is lacking. Ultrasonography for preoperative evaluation of cervical LN metastasis in thyroid cancer has a wide range of sensitivities (52% to 84%). To stage LNs by neck dissection increases morbidity and may be unnecessary in most cases. Radical central compartment dissection increases the risk of hypocalcemia and injury to the recurrent laryngeal nerve. The presence of LN metastases increases the risk of locoregional recurrence and decreases survival; cervical LN metastases account for most cases of locoregional recurrence.

**Objective:** To determine if sentinel lymph node biopsy (SLNB) detects occult metastases in PTC.

**Design/Methods:** 23 patients with PTC were evaluated prospectively. The injection of radiocolloid labeled with Tc-99m phytate was performed under ultrasonographic guidance. Peritumoral injection of 0.2 mCi in 0.1 mL saline solution was preformed as either a single injection or 2 injections (1 in each lobe in cases of multifocal disease). Patients underwent lymphoscintigraphy 15 minutes after Tc-99m phytate injection and approximately 2 hours prior to thyroidectomy. Lymph nodes detected by SPECT/CT were reported according to level, size, and depth. Hot spots were marked with a dermatography pen on the skin. Intraoperatively, a handheld gamma probe was used to locate the SLNs. After completion of thyroidectomy, radioactive nodes were removed, regardless of counts, as well as nonradioactive nodes in the central compartment. When preoperative lymphatic mapping revealed SLNs in the lateral neck compartment, intraoperative scanning of these compartments was also performed.

**Results:** Metastases were found in the SLN in 7 patients (30.4%), in a nonSLN in 3 patients (13.1%), and in the lateral compartments in 20% of patients. Lymph node (LN) metastases were significantly associated the presence of angiolymphatic invasion \((P = 0.003)\).

**Conclusions:** SLNB can detect occult metastases in 43.5% of patients with PTC who have metastases at initial diagnosis. Of these metastases, 20% are found solely in the lateral compartments. Patients not submitting to SLNB are most likely understaged.

**Reviewer's Comments:** The inaccuracy of staging in thyroid cancer patients who are not undergoing LN dissection has long been a clinical concern. This is the first paper I've seen that clearly describes the procedure and also documents the added value of scintigraphic SLN searching in staging thyroid cancer. Limitations include operator dependence (the procedure appears to have a learning curve) and the need for SPECT/CT, which is not yet a resident in most nuclear medicine labs. (Reviewer-C. Richard Goldfarb, MD).

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**Keywords:** Papillary Thyroid Carcinoma, Occult Metastases, Sentinel Lymph Node Biopsy

Print Tag: Refer to original journal article
Thyroid Stunning by Preablation I-131 Does Not Impact Outcome

No Adverse Affect in Clinical Outcome Using Low Preablation Diagnostic 131I Activity in Differentiated Thyroid Cancer: Refuting Thyroid-Stunning Effect.

Yap BK, Murby B:

J Clin Endocrinol Metab 2014; 99 (July): 2433-2440

Low diagnostic I-131 activity (1.1 mCi) given 6 days prior to thyroid remnant ablation does not adversely affect the long-term clinical outcome in patients with thyroid cancer.

Background: Thyroid stunning by diagnostic I-131 (decreased uptake of subsequent therapeutic I-131) is debated in the literature, either supporting or refuting the phenomenon. Factors that could influence the observed differences include the size of I-131 dose for diagnostic whole-body radioiodine scan (WBS), delay between diagnostic scan and treatment, and magnitude of the therapeutic I-131 dose. The presence of thyroid stunning is usually based on failure of ablation. But even in such cases, thyroid stunning may have no relevance to eventual clinical outcome.

Objective: To compare the clinical outcome in patients with thyroid cancer who did versus those who did not undergo preablation diagnostic WBSs with 1.1 mCi I-131.

Design/Methods: Retrospective study of 305 patients who had a diagnostic WBS with 1.1 mCi of I-131 prior to radioiodine ablation and 237 patients who did not undergo diagnostic I-131 WBS prior to I-131 ablation. Ablation doses were at least 82.4 mCi I-131. The recurrence rate at 3 years, quantitative assessment using diagnostic I-131 WBSs, and TSH-stimulated thyroglobulin levels at 3 to 12 months after ablation were measured.

Results: The 3-year recurrence-free survival rate was 96.4% in total. Recurrences were seen in 4.3% of patients who underwent preablation WBS and in 3.4% of those not having preablation scans (P = 0.91). The ablation success rates measured by diagnostic I-131 WBSs were 97.6% in those with preablation WBSs and 100% in those without preablation WBS. The ablation success rates measured by stimulated thyroglobulin were 85.3% in the group that underwent preablation WBSs and 85.8% in the group that did not undergo preablation WBS (P = 0.62).

Conclusions: Low diagnostic I-131 activity (1.1 mCi) given 6 days before radioiodine ablation does not adversely affect the long-term clinical outcome in patients with thyroid cancer.

Reviewer's Comments: This paper is intended to reassure those who are concerned that stunning may affect the success of subsequent ablation, consequently causing them to avoid preablation scanning. Unfortunately, the low 1.1-mCi dose is likely to miss foci of remnant tissue and possible metastases (regional and distant). In our anecdotal experience, a diagnostic dose of 2 mCi misses approximately 50% of the metastases visualized on the scan performed after the therapeutic dose. I would like to see similar lack of effect on clinical outcome with diagnostic WBS doses of 5 to 10 mCi. (Reviewer-C. Richard Goldfarb, MD).

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Keywords: Thyroid Cancer, Thyroid Stunning, Preablation I-131 vs Clinical Outcome

Print Tag: Refer to original journal article
I-124 PET Does Not Predict Negative Post-Thyroidectomy Scan

Do Negative 124I Pretherapy Positron Emission Tomography Scans in Patients With Elevated Serum Thyroglobulin Levels Predict Negative 131I Posttherapy Scans?

Khorjekar GR, Van Nostrand D, et al:

Thyroid 2014; 24 (September): 1394-1399

In patients with thyroid cancer, a negative pretherapy diagnostic I-124 PET scan has a low predictive value for a negative I-131 posttherapy scan after treatment with I-131.

**Background:** Imaging of thyroid cancer with I-124 via a PET scan, as compared to I-131 imaging, is better able to combine the images with those of CT or MRI. I-124 PET images detect more foci of residual thyroid tissue and/or metastases than do I-131 PET images, but the usefulness of negative I-124 PET scans in deciding whether to perform "blind" I-131 therapy is unknown.

**Objective:** To determine whether a negative I-124 pretherapy PET scan in patients with high serum thyroglobulin (Tg) levels, a negative diagnostic I-131 planar scan, and a negative I-124 PET scan predict a negative I-131 posttherapy scan.

**Participants:** 5 women and 7 men who had elevated Tg levels (>2 ng/mL), a negative diagnostic I-131 planar scan, a negative diagnostic I-124 PET scan, therapy with I-131, and an I-131 post-therapy scan.

**Results:** Of the 12 patients, 10 had positive foci on I-131 posttherapy scans and 2 had negative I-131 posttherapy scans.

**Conclusions:** I-131 posttherapy scans are often positive in patients who have high Tg levels, a negative diagnostic I-131 planar scan, and a negative diagnostic I-124 PET scan. A negative pretherapy I-124 PET scan has a low predictive value for a negative posttherapy I-131 scan after treatment with I-131.

**Reviewer’s Comments:** This paper’s relevance exceeds the still investigational world of I-124 PET imaging. The notorious Tg-positive/radioiodine-negative conundrum is most often solved by proceeding with treatment. What does not show up on the initial diagnostic scan frequently appears on the posttherapy I-131 scan. Even if the posttherapy scan is negative, the Tg levels may drop. The absence of visualized tissue in the neck on low-dose I-131 imaging following thyroidectomy does not prove that there is nothing left to ablate. Often, remnant thyroid tissue is seen on the post-ablation scan. (Reviewer-C. Richard Goldfarb, MD).

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Keywords: Thyroid Cancer, Pretherapy I-124 PET, Predictive Value for Posttherapy I-131 PET

Print Tag: Refer to original journal article
The pathological hallmark of dementia with Lewy bodies is the presence of intracellular aggregates of an abnormal protein known as α–synuclein throughout much of the brain.

Lewy body dementia (dementia with Lewy bodies, DLB) is always associated with a cardinal pathologic finding: an aggregate of abnormal protein known as α–synuclein. This feature of the disease is present in neuronal cells throughout much of the brain. DLB is considered the second most common type of dementia overall, and it accounts for approximately 25% of the dementias that are diagnosed. Lewy bodies are also found in Parkinson disease (PD), but they are restricted primarily to the substantia nigra and brainstem in this condition. Many patients with DLB will also have β-amyloid deposits in regions of the brain similar to that seen in Alzheimer dementia (AD).

**Clinical Features:** Often, patients present initially with fluctuating attention, visual hallucinations, and/or parkinsonian symptoms. One of the most distinguishing clinical features of DLB is the visual hallucination, which often occurs at night but is distinctly different than simple dreaming. Another early feature of DLB is a sleep disturbance known as rapid eye movement sleep behavior disorder. Gait disturbances and motor symptoms typical of PD are not uncommon in patients with DLB. Early on, levels of cognition may fluctuate substantially, whereas memory impairment may be limited to later stages of the disease.

**Diagnosis:** The clinical diagnosis of DLB is based primarily on 3 clinical features: fluctuating cognitive impairment, motor symptomatology typical of PD, and recurrent visual hallucinations. When all 3 features are seen together, this triad of clinical findings has a very high diagnostic specificity (95%) but a very low sensitivity (35%). Dementia specialists will make the diagnosis of "probable DLB" if dementia plus 2 of the 3 features are present. If only 1 of the 3 clinical features is present, clinicians will typically classify the disorder as "possible DLB." Consequently, in many patients, diagnostic imaging procedures may be of great value for better establishing the diagnosis of DLB. **Treatment:** The cholinesterase inhibitors sometimes used to treat AD can be quite effective for the treatment of DLB in some patients. Likewise, memantine may be beneficial in the treatment of DLB. In contrast, antipsychotic medications may lead to severe side effects in DLB patients and should be avoided.

**Reviewer's Comments:** FDG-PET imaging often shows a pattern of abnormalities similar to those seen in AD. However, in some cases, reduced FDG uptake in the visual cortex will be seen, which is fairly specific for DLB. Other molecular imaging techniques may be useful as well, including SPECT brain imaging with ioflupane or cardiac imaging with MIBG. (Reviewer-David Bushnell, MD.)

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Keywords: Lewy Body Diseases, Dementia With Lewy Bodies, Clinical Features, Diagnosis

Print Tag: Refer to original journal article
Two Imaging Techniques Accurate for Lewy Body Dementia

Iodine-123 Metaiodobenzylguanidine Scintigraphy and Iodine-123 Ioflupane Single Photon Emission Computed Tomography in Lewy Body Diseases: Complementary or Alternative Techniques?

Treglia G, Cason E, et al:
J Neuroimaging 2014; 24 (March/April): 149-154

MIBG cardiac imaging and brain SPECT with ioflupane are both similarly accurate for diagnosing dementia with Lewy bodies in patients presenting with parkinsonian features and dementia.

**Background:** Parkinson disease (PD) can be difficult to differentiate from other parkinsonian conditions, such as multisystem atrophy. Dementia with Lewy bodies (DLB) can be difficult to distinguish from other causes of dementia. SPECT brain imaging with I-123 ioflupane demonstrates an abnormal pattern in patients with PD. I-123 MIBG cardiac imaging is also known to show abnormally low cardiac uptake of this agent in patients with PD. Both imaging procedures demonstrate abnormalities in patients with DLB, as well.

**Objective:** To compare the sensitivities and specificities of these 2 molecular imaging procedures in diagnosing patients with parkinsonian symptoms with and without dementia.

**Participants:** 68 subjects with parkinsonian features without dementia and 31 patients with both parkinsonian features and dementia.

**Methods:** All subjects in this study were imaged with I-123 MIBG and I-123 ioflupane. Semiquantitative image analysis was performed for both imaging procedures, and normal cutoff values were obtained using 2 separate normal control groups. The final diagnosis for all 99 subjects was based on clinical categorization. The imaging results were then compared to this final diagnosis as the gold standard.

**Results:** For the 31 individuals with both parkinsonian features and dementia, the final clinical diagnosis was DLB in 20. For the 68 individuals with parkinsonian symptoms without dementia, the final clinical diagnosis was PD in 40. For distinguishing between PD and other parkinsonian disorders, cardiac MIBG uptake had a sensitivity of 80% and a specificity of 75%. In the same group of patients, SPECT ioflupane brain imaging had a 95% sensitivity but only a 21% specificity for differentiating PD and other parkinsonian disorders. Among the patients with DLB, the authors report a sensitivity of approximately 90% and a specificity of approximately 90% for both cardiac MIBG imaging and ioflupane brain imaging.

**Reviewer's Comments:** A couple of points stand out in this study. These 2 imaging procedures appear to be relatively accurate for the diagnosis of DLB. In addition, cardiac imaging with MIBG appears to be notably more specific for distinguishing PD from other parkinsonian conditions, such as multisystem atrophy, than is ioflupane brain imaging. Finally, these 2 imaging studies may be even more accurate than the authors report because the gold standard used in this study was the clinical diagnosis, which we know has definite limitations for DLB and PD. (Reviewer-David Bushnell, MD).

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Keywords: Lewy Body Diseases, Parkinson Disease, Dementia With Lewy Bodies, Imaging

Print Tag: Refer to original journal article
Vizamyl Sensitive for Detecting Brain Amyloid

Hatashita S, Yamasaki H, et al:


F-18 flutemetamol (Vizamyl) shows abnormal cortical uptake in nearly all patients with Alzheimer disease.

Background: F-18 flutemetamol is a radiopharmaceutical used for the identification of β-amyloid plaques in the brain, similar to the better-known agent florbetapir (Amyvid™). F-18 flutemetamol will be marketed by GE Healthcare under the trade name Vizamyl™. C-11-labeled PIB (Pittsburgh compound B) has been the standard for amyloid brain imaging to which other agents have been compared.

Objective: To compare flutemetamol to C-11 PIB in patients with a range of cognitive impairments.

Participants: The study included patients with Alzheimer disease (AD) and mild cognitive impairment (MCI). Cognitively normal older control subjects were also included.

Methods: All patients underwent PET/CT brain imaging with both C-11 PIB and F-18 flutemetamol. Images were compared visually by blinded reviewers and quantitatively using SUV ratios.

Results: The authors found a very high correlation between cortical uptake of C-11 PIB and F-18 flutemetamol. For distinguishing patients with AD from older control patients, the sensitivity and specificity of PET/CT with F-18 flutemetamol was 97% and 85%, respectively. These results were the same for PET PIB. The authors also found very high inter-reader agreement for interpretation of the F-18 flutemetamol images. C-11 PIB consistently showed higher cortical activity in patients with AD than did flutemetamol, even though the activity levels in the cortex were highly correlated.

Reviewer's Comments: The findings in this PET/CT study with F-18 flutemetamol (Vizamyl) are virtually identical to findings from other studies using F-18 florbetapir (Amyvid). Vizamyl is FDA-approved but not yet available on the market. In contrast, F-18 florbetaben (NeuraCeq™), a third FDA-approved amyloid targeting agent marketed by IBA Molecular, is currently available twice a month. The Centers for Medicare and Medicaid Services has not yet approved reimbursement, but private insurance may reimburse with pre-authorization. A 20-minute PET image should be acquired starting 90 minutes after IV injection. Unlike FDG brain imaging following injection, patients do not need to be in a restricted environment prior to imaging with amyloid-targeting agents. (Reviewer-David Bushnell, MD).

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Keywords: Cognitive Impairment, Beta-Amyloid Plaque, Imaging, Alzheimer Disease

Print Tag: Refer to original journal article
Major depressive disorder and mild traumatic brain injury both show hypoperfusion in the frontal lobe on brain SPECT but are difficult to distinguish by visual analysis alone.

**Background:** Functional neuroimaging with functional MRI (fMRI) or SPECT shows decreased blood flow in the frontal lobe in patients with mild traumatic brain injury (mTBI) and in patients with major depressive disorder (MDD). About 26% of patients with mTBI meet criteria for MDD, and an additional 20% report minor depressive symptoms 1 year after injury. 

**Objective:** To investigate the relative contribution of depression to cerebral hypoperfusion in patients with mTBI.

**Participants:** 52 patients with mTBI and 15 patients with MDD.

**Methods:** Patients underwent SPECT imaging of the head using 20 mCi of Tc-99m ethyl cysteinate dimer. Investigators compared SPECT brain images of patients with mTBI with depressive symptoms, patients with mTBI without depressive symptoms, and patients with MDD who did not have mTBI. SPECT images were analyzed quantitatively and visually.

**Results:** 13 patients with mTBI also had depressive symptoms, and 39 patients with mTBI had no depressive symptoms. Visual analysis resulted in no significant differences between the groups. Quantitative analysis revealed decreased perfusion in patients with MDD relative to patients with mTBI with or without depressive symptoms. Major differences were observed in the bilateral orbitofrontal gyri, right inferior frontal gyrus, bilateral middle frontal gyri, left superior frontal gyrus, right anterior cingulate cortex, right superior temporal gyrus, and bilateral posterior cingulate cortices. Among patients with mTBI, no significant differences were seen between those with versus those without depressive symptoms. No significant correlations were seen between right orbitofrontal gyrus perfusion and performance on a standardized cognitive test.

**Conclusions:** Using quantitative analysis but not visual analysis, SPECT perfusion can differentiate between patients with MDD and those with mTBI. SPECT cannot differentiate between patients with both mTBI and depressive symptoms versus patients with only mTBI (no depressive symptoms).

**Reviewer’s Comments:** I found this paper interesting for showing that visual analysis alone is inadequate for using brain SPECT to differentiate MDD from mTBI. The algorithm used for quantitative analysis is a black box to me, so I cannot really comment on its reliability, but some healthy skepticism is warranted when it comes to using brain SPECT to diagnose psychiatric conditions. (Reviewer-Shayne Squires, MD).

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Keywords: Traumatic Brain Injury vs Major Depressive Disorder, Cerebral Perfusion, SPECT

Print Tag: Refer to original journal article
Need PET-CT, Biopsy to Detect Bone Marrow Mets in DLBCL

Combined PET and Biopsy Evidence of Marrow Involvement Improves Prognostic Prediction in Diffuse Large B-Cell Lymphoma.

Cerci JJ, Györke T, et al:


PET/CT and bone marrow biopsy together are significantly better than either one alone for establishing bone marrow involvement in diffuse large B-cell lymphoma.

**Background:** Prognosis in diffuse large B-cell lymphoma (DLBCL) is strongly affected by the presence of bone marrow metastases. Because bone marrow metastases can be focal and heterogeneous, it is possible for biopsy of the iliac crest to miss their presence. F-18 FDG-PET/CT can detect bone marrow metastases even when biopsy is negative.

**Objective:** To determine whether bone marrow biopsy is necessary in DLBCL when PET/CT is used for staging.

**Participants:** 327 consecutive patients from 8 centers were included.

**Methods:** Each patient underwent PET/CT after 2 to 3 cycles of chemotherapy and 4 to 8 weeks after all chemotherapy.

**Results:** 25% of patients were considered to have marrow involvement at diagnosis. Of these cases, 57% were identified by PET alone, 12% were identified by bone marrow biopsy alone, and 30% were identified by both. Of 18 who demonstrated diffuse marrow activity on PET imaging, 4 also had positive bone marrow biopsy. Patients with diffuse marrow uptake on PET were considered to have marrow involvement only if bone marrow biopsy was positive. Median follow-up for the entire cohort was 35 months. By multivariate analysis, detection of marrow involvement by both PET/CT and bone marrow biopsy had a significant impact on survival, but detection by biopsy alone did not. The 2-year event-free survival rate for patients with marrow involvement by both PET and biopsy was 45%, and the overall survival rate was 55%. Among patients with no marrow involvement by PET/CT or biopsy, 2-year event-free and overall survival rates were 81% and 88%, respectively. Patients with marrow involvement by either PET/CT or biopsy alone did not have a significantly worse prognosis compared with patients who had no marrow involvement.

**Conclusions:** Neither PET/CT nor bone marrow biopsy alone is adequate for evaluating marrow involvement in patients with DLBCL. Both should be included to accurately assess prognosis in these patients.

**Reviewer's Comments:** I think the authors make a good case for including both PET/CT and bone marrow biopsy for detecting marrow involvement in DLBCL. One of the other useful findings in this study was that most patients with diffuse FDG uptake in the marrow on interim PET did not have marrow involvement by iliac crest biopsy, but >20% did, suggesting that diffuse marrow uptake on interim PET cannot be dogmatically interpreted as marrow rebound. (Reviewer-Shayne Squires, MD).

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Keywords: Diffuse Large B-Cell Lymphoma, Bone Marrow Metastases, PET

Print Tag: Refer to original journal article
PET-CT Helps Stage Resectable Colorectal Liver Metastases

The Influence of FDG PET-CT on the Detection of Extrahepatic Disease in Patients Being Considered for Resection of Colorectal Liver Metastasis.

Lake ES, Wadhwani S, et al:


FDG-PET/CT has significant incremental value over contrast enhanced CT only in the preoperative evaluation of patients with potentially resectable colorectal liver metastases.

**Background:** Resection of colorectal cancer liver metastasis (CLM) offers patients a chance of disease-free survival. Five-year survival rates following resection are approximately 30%. The liver and lung are the most common sites of recurrence after liver resection.

**Objective:** To determine the incremental diagnostic value of F-18 FDG-PET/CT versus contrast-enhanced CT only in detecting extrahepatic metastases in patients with potentially resectable CLM.

**Design:** Retrospective study.

**Participants:** 133 consecutive patients being considered for resection of CLM.

**Methods:** All patients underwent presurgical FDG-PET/CT and presurgical contrast-enhanced CT of the chest, abdomen, and pelvis. These 2 studies were done within 90 days of each other.

**Results:** Of the 133 patients, 18 (14%) had new significant findings on PET/CT that were not detected by CT alone. Eight of these patients (6%) were upstaged to inoperable. Four patients (3%) had premalignant colonic lesions, which were found to be tubulovillous adenomas on biopsy. Six patients (5%) were upstaged as a result of finding regional or isolated retroperitoneal lymph node disease but were still classified as operable. Eight patients (6%) had indeterminate or suspicious lesions by contrast enhanced CT that were downgraded as likely nonmalignant on PET/CT. There were three (2%) false positives on PET/CT that were each due to uptake in the colon or rectum and were found to be benign by biopsy. Eight patients (6%) had indeterminate findings on PET/CT that were all classified as benign on biopsy and were not seen on CT alone. There were false negatives by PET/CT in three patients (2%) that were detected and interpreted as indeterminate on CT only. These were in the abdominal wall, iliac node, and spleen. PET/CT had no impact in 93 patients (70%).

**Conclusions:** PET/CT has value in staging patients with potentially resectable CLM.

**Reviewer's Comments:** In this study, all lesions that were indeterminate by PET/CT and negative by contrast enhanced CT only were found to be benign on biopsy. These occurred in parotids, tonsils, thyroid gland, skin, breast, and colon. There probably weren't enough such findings in this study to conclude that a negative contrast CT excludes malignancy when PET/CT is indeterminate, but it is suggestive. (Reviewer-Shayne Squires, MD).

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Keywords: Colorectal Liver Metastasis, Extrahepatic Metastases, Diagnosis, PET/CT vs CT

Print Tag: Refer to original journal article
PET Liver SUVs Underestimated in Obese Patients

Optimum Lean Body Formulation for Correction of Standardized Uptake Value in PET Imaging.

Tahari AK, Chien D, et al:


Although the underestimation of lean body mass liver SUV is seen only in women with a BMI ≥35, the effect is also likely to be present for morbidly obese men.

Background: PET standardized uptake values (SUVs) normalized for lean body mass (LBM) appear to be lower in very obese patients. Is there a more appropriate way to determine LBM?

Objective: To evaluate the error associated with the method used to determine the LBM SUV and to determine if there is a better way of estimating LBM for this application.

Methods: 1033 F-18 FDG-PET scans were reviewed, and the LBM SUV for a region in the right lobe of the liver was determined by 2 methods. The first method was the conventional James approach, which is the standard technique used on most PET scanners. The James LBM correction depends on the square of the ratio for body weight to height. The other correction method used the Janmahasatian approach, which includes body mass index (BMI) as a parameter.

Results: The LBM liver SUV derived from the James correction was associated with a significant decrease in women with a BMI ≥35 (1.14) compared to women with a BMI <35 (1.46). There was no apparent BMI effect seen with men. When the Janmahasatian correction was applied, the dependence on BMI was largely eliminated (1.25 for BMI ≥35 vs 1.30 for BMI <35).

Conclusions: The Janmahasatian LBM correction is more appropriate for determining LBM SUV in PET scans, especially in light of the increased incidence of obesity.

Reviewer's Comments: The conventional SUV is a ratio between the concentration of F-18 FDG in a region of interest and the average concentration of F-18 FDG in the body. Since F-18 FDG is not accumulated in fat, SUVs tend to be artificially high in obese patients and the use of LBM corrections is an attempt to account for that issue. From the results of this study, it appears that the James formulation for determining LBM becomes inaccurate for very obese individuals, particularly women. Because obesity is becoming increasingly more common, the authors make a strong case that the James correction should be replaced by the Janmasahatian correction or some other approach that retains its accuracy at the highest BMIs. (Reviewer-Mark T. Madsen, PhD, FAAPM, FACR).

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Keywords: PET, FDG, SUV, SUL, LBM, Gender-Specific

Print Tag: Refer to original journal article
Y-90 PET-CT Accurate for Concentrated Labeled Microspheres

The Impact of Image Reconstruction Bias on PET/CT 90Y Dosimetry After Radioembolization.

Tapp KN, Lea WB, et al:


Using algorithms designed for F-18 to reconstruct Y-90 data overestimates radioactivity because corrections for random coincidences lead to negative values that, when truncated to 0, artificially increase the activity.

**Background:** Although Y-90 is usually thought of as a pure β emitter, it has a pair production path that results in positron emission for about 3 of every 100,000 decays. Thus, PET can be used to image the distribution of Y-90-labeled microspheres injected intra-arterially to treat liver cancer. Are there problems with the accurate quantification of the radioactivity concentration due to the relatively high random coincident rate associated with the bremsstrahlung radiation at such low true coincident event rates?

**Objective:** To evaluate the quantitative accuracy of Y-90 PET/CT and its usefulness in estimating the radiation dose to tumors and liver tissue in the treatment of liver cancer with labeled microspheres.

**Methods:** 5 syringes filled with different activities of Y-90 (range, 30 MBq to 380 MBq) were positioned inside a water-filled cylindrical SPECT phantom. PET studies were acquired of the phantom daily for 5 days and again at 13 days using a standard patient protocol. The image bias was assessed by comparing the known syringe activity with the activity estimated in the reconstructed images. In addition, the PET/CT studies of 59 patients who had TheraSphere® administration were retrospectively analyzed by comparing the estimated total activity with the intra-arterial administered activity after correcting for any lung shunting. The estimates were based on the standard iterative reconstruction as well as with a direct filtered backprojection algorithm. An estimate of the minimal detectable activity was also generated.

**Results:** The random coincident rate associated with Y-90 was nearly 3 times larger than that associated with a similar scaled activity of F-18. This appears to be due to bremsstrahlung radiation from the Y-90 β emissions. Both the phantom data and the patient studies had a substantial positive bias: the estimated activity in the images exceeded the administered activity. Positive bias resulted from the areas of very low Y-90 concentration, and the bias was substantially reduced in the filtered backprojection results.

**Conclusions:** The cause of the bias was the truncation of negative numbers in the random corrected projections. The quantitative accuracy was good in areas that concentrated Y-90, and areas of low Y-90 concentration accounted for all the artificial increase in activity.

**Reviewer’s Comments:** The authors of this paper point out the importance of evaluating the quantitative accuracy of new approaches when there are substantial differences in the physical characteristics of the radiotracer. Similar problems have been discovered with other radionuclides, such as Rb-82, which emits a prompt gamma along with the annihilation radiation and has caused problems in scatter correction algorithms that work well for F-18. (Reviewer-Mark T. Madsen, PhD, FAAPM, FACR).

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Keywords: Liver Cancer, Radioembolization, Posttreatment Y-90 Distribution, Reconstruction Bias

Print Tag: Refer to original journal article
F-18 Fluoride Superior for Detecting Sclerotic Skeletal Mets

Usefulness of 18F-Fluoride PET/CT in Breast Cancer Patients With Osteosclerotic Bone Metastases.
Yoon SH, Kim KS:


F-18 fluoride PET/CT is more sensitive than FDG-PET/CT for detecting sclerotic skeletal metastases in patients with breast cancer.

Background: FDG-PET imaging has high sensitivity for detecting metastatic disease in most patients with breast cancer, although it seems to have some limitations for detecting bone metastases in some individuals. F-18 fluoride bone imaging is a sensitive technique for detecting metastatic bone disease.

Objective: To compare FDG-PET/CT to F-18 fluoride PET/CT for detecting sclerotic skeletal metastatic disease in patients with breast cancer.

Participants: 9 individuals who had known or suspected skeletal metastatic disease from breast cancer.

Methods: Each individual underwent FDG-PET/CT, F-18 fluoride PET/CT, and whole-body bone scintigraphy (WBBS) with MDP. Truth data for determining the presence or absence of skeletal metastatic disease were primarily based on clinical and imaging follow-up at 12 months and, in some cases, histologic assessment. Image analysis was performed by 2 experienced reviewers through consensus.

Results: 52 true skeletal metastatic lesions were identified among the 9 patients. Most lesions appeared to be sclerotic on the companion CT scans. Of the 52 skeletal metastatic lesions, F-18 fluoride identified 49 (sensitivity, 94%), FDG detected 20, and WBBS MDP detected 25. The authors reported poor specificity for all 3 imaging methodologies. One patient in this series demonstrated metastatic lesions on F-18 fluorine imaging that were FDG-negative, but on reimaging with 3 months later, the lesions had become positive with FDG as well.

Conclusions: For detecting sclerotic skeletal metastatic disease in patients with breast cancer, F-18 fluoride PET/CT is superior to WBBS MDP and FDG-PET/CT.

Reviewer’s Comments: I believe the results of this 2013 study carry particular importance to our specialty. Although I certainly do not want to claim that this study represents great science, I think it reminds us that F-18 fluoride PET/CT is a more sensitive than WBBS MDP and FDG-PET, at least in this setting. The one thing about the authors’ findings that is notably puzzling, I think, is the low specificity they report for both FDG and F-18 fluoride PET/CT. Other studies with F-18 fluoride PET/CT, at least in patients with prostate cancer, demonstrate a much higher specificity. One possible explanation for this discrepancy in the current study may be related to the fact that these authors performed the companion CT with a low-dose acquisition protocol.
(Reviewer-David Bushnell, MD).

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Keywords: Breast Cancer, Sclerotic Bone Metastases, Imaging

Print Tag: Refer to original journal article
PET-CT Restaging of Breast Cancer Helpful in Younger Women

Retrospective Analysis of 18F-FDG PET/CT for Staging Asymptomatic Breast Cancer Patients Younger Than 40 Years.

Riedl CC, Slobod E, et al:

Patients aged <40 years who have clinical stage I to III breast cancer may benefit from restaging with FDG-PET/CT imaging. In this study, PET/CT demonstrated stage IV disease in 15% of these younger women.

Background: The role of F-18 FDG PET/CT in staging breast cancer is a subject of ongoing debate. Breast cancer in women aged <40 years is associated with more unfavorable biologic factors and a higher likelihood of death compared to breast cancer in older women. This motivates the idea that PET/CT staging may have a bigger clinical impact in women aged <40 years who have breast cancer.

Objective: To evaluate the clinical impact of PET/CT staging in clinical stage I-III breast cancer patients aged <40 years.

Design: Retrospective study.

Participants: 134 patients (median age, 36 years) with clinical stage I-III breast cancer.

Methods: All women underwent PET/CT prior to beginning treatment for breast cancer.

Results: PET/CT detected unexpected extraaxillary regional nodal metastases or distant metastases in 21% of patients. Fifteen patients had extraaxillary regional lymph node metastases (11%), 20 patients had distant metastases (15%), and 7 patients had both. All distant metastases were verified by biopsy as true positives. Patient race, tumor grade, and receptor phenotype were not significantly related to the probability of extraaxillary lymph node metastases or distant metastases. Likewise, the probability of upstaging by PET/CT was also not related to race, tumor grade, or receptor phenotype.

Conclusions: In this study, 17% of patients with clinical stage IIB cancer had distant metastases. Therefore, women aged <40 years with clinical stage IIB breast cancer may benefit from routine PET/CT staging. A prospective trial to test the benefit of PET/CT staging in this subgroup is warranted.

Reviewer's Comments: The authors set out to investigate PET/CT staging in stage I through III breast cancer, but the study population actually included many more patients with stage II cancer than patients with other stage I or III breast cancer. Patients with stage II cancer showed the highest rates of upstaging. I still doubt that PET/CT staging will provide much benefit in patients with clinical stage I breast cancer, but prospective studies of its usefulness in stage II breast cancer in women aged <40 years are warranted. (Reviewer-Shayne Squires, MD).

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Keywords: Breast Cancer, PET/CT Staging, Clinical Impact

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Metabolic Tumor Volume Predicts Survival in Stage III NSCLC

Value of Metabolic Tumor Volume on Repeated 18F-FDG PET/CT for Early Prediction of Survival in Locally Advanced Non-Small Cell Lung Cancer Treated With Concurrent Chemoradiotherapy.

Huang W, Fan M, et al:


Metabolic tumor volume (the size of FDG-avid tumor on PET imaging) is a significant predictor of survival in stage III non-small cell lung cancer.

**Background:** 80% to 85% of lung cancers are classified as non-small cell lung cancer (NSCLC). Locally advanced NSCLC, which is surgically unresectable, is treated with platinum-based chemotherapy and radiation.

**Objective:** To determine whether F-18 FDG-PET/CT can be used to predict treatment response in locally advanced NSCLC.

**Participants:** 53 patients with stage IIIA or IIIB NSCLC who underwent chemotherapy and radiation treatment.

**Methods:** Each patient underwent a baseline PET/CT study and an intratreatment study at a mean of 28 days later. The percent change in tumor SUV and metabolic tumor volume (MTV) between the first and second PET/CT studies was calculated for each patient.

**Results:** Median overall survival (OS) was 37.5 months for patients whose SUV\_mean decreased >42%, but OS was only 19.5 months for patients whose mean SUV decreased <42%. The 2-year OS was 75% for patients with >42% decrease in SUV\_mean and only 38% for patients with <42% decrease in SUV\_mean. Median OS was 37 months for patients with a >30% decrease in MTV but only 18 months for patients with a <30% decrease in MTV. Univariate analysis showed that decrease in SUV\_max, intratreatment SUV\_mean, change in SUV\_mean, intratreatment MTV, and change in MTV were all predictors of therapy response. Multivariate analysis showed that only change in MTV was an independent predictor of survival.

**Conclusions:** MTV may be a valuable prognostic indicator in NSCLC, and changes in MTV in response to therapy are predictive of OS.

**Reviewer's Comments:** I provisionally accept that MTV may be more predictive of survival than SUV. This makes some intuitive sense. MTV contains information about active tumor size as well as metabolic activity, while SUV only conveys information about metabolic activity. In small studies such as this, I do not put too much stock in exact numerical cutoff values used to discriminate between patients who will respond well to therapy and those who will not, but I do find the overall conclusions to be plausible. (Reviewer-Shayne Squires, MD).

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Keywords: Non-Small Cell Lung Cancer, Intratherapy PET/CT, Prognostic Value of MTV

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Early Post-Stress Imaging Detects Ventricular Stunning

Detection of Post-Exercise Stunning by Early Gated SPECT Myocardial Perfusion Imaging: Results From the IAEA Multi-Center Study.

Mut F, Giubbini R, et al:

J Nucl Cardiol 2014; (September 12): epub ahead of print

In gated SPECT myocardial perfusion imaging, early (15 minutes) post-stress imaging is more likely to detect ventricular stunning than is late (60 minutes) post-stress imaging.

**Background:** The traditional delay between stress testing and post-stress gated SPECT scan acquisition typically ranges from 30 to 60 minutes. This delay may result in a decreased sensitivity for detecting transient post-stress left ventricular (LV) dysfunction due to myocardial stunning.

**Objective:** To determine whether early post-exercise imaging is more sensitive in the detection of ventricular stunning compared to conventional protocols that use a longer delay, without adversely affecting image quality or perfusion imaging.

**Design:** This cross-sectional study was sponsored by the International Atomic Energy Agency and involved imaging centers from 7 different countries.

**Participants:** 229 patients with known or suspected coronary artery disease (CAD) undergoing stress/rest gated SPECT myocardial perfusion imaging.

**Methods:** Both the rest and post-stress acquisitions were gated. Rest studies (R) were acquired at 60 minutes after radiotracer injection. Post-exercise studies were acquired at 15 minutes after radiotracer injection (Stress15) and were repeated at 60 minutes (Stress60). Stunning was defined as the difference between rest and post-stress LV ejection fraction (dLVEF).

**Results:** Image quality and perfusion information were similar between Stress15 and Stress60 acquisitions. There was a significant correlation between the summed difference score and the dLVEF. This correlation was stronger for the stress15 dLVEF compared to the stress60 dLVEF in patients with ischemia.

**Conclusions:** Early post-exercise images show good perfusion images and can potentially improve the detection of post-ischemic stunning.

**Reviewer's Comments:** To take advantage of early post-stress imaging, both the rest and post-stress acquisitions need to be gated. Although the American Society of Nuclear Cardiology guidelines recommend gating both the rest and post-stress acquisitions, many labs still only gate the post-stress acquisition given the limited research into the clinical value of a change in LVEF post-stress compared to rest. The results of this research study suggest that early post-stress acquisitions are feasible and may be more useful clinically than delayed post-stress acquisitions. (See images for this review at practicalreviews.com.) (Reviewer-Thomas F. Heston, MD).

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Keywords: Coronary Artery Disease, Post-Stress Gated SPECT, Ventricular Stunning

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Beta-Blocker Withdrawal Not Required Before Stress Test

The Effect of Beta Blocker Withdrawal on Adenosine Myocardial Perfusion Imaging.

Hoffmeister C, Preuss R, et al:

J Nucl Cardiol 2014; (August 15): e pub ahead of print

In patients with coronary artery disease, β-blocker withdrawal prior to adenosine stress testing slightly increases myocardial blood flow, but in most cases, the difference is not clinically significant.

**Background:** Myocardial blood flow (MBF) is increased to comparable levels during pharmacologic stress testing with adenosine, dipyridamole, and regadenoson. Despite maximal vasodilation, however, these agents appear to interact with several cardiac medications, including calcium channel blockers, nitrates, and β-blockers. The effect of β-blockers on MBF in patients undergoing pharmacologic stress testing is not well understood, and research results are conflicting.

**Objective:** To evaluate the effect of β-blocker withdrawal on both quantitative adenosine MBF and myocardial perfusion imaging results.

**Design:** Prospective cohort study.

**Participants:** 20 patients on β-blocker therapy who had a history of coronary artery disease.

**Methods:** Patients underwent quantitative adenosine N-13 ammonia PET. Patients underwent 2 studies -- the first while on β-blockers and the second after β-blocker withdrawal.

**Results:** The global MBF increased from 180 to 194 mL/minute per 100 g after β-blockers withdrawal ($P = 0.02$). Scan interpretation was unchanged in 18 of 20 patients after β-blocker discontinuation.

**Conclusions:** β-blocker withdrawal induces an increase in adenosine MBF. In 90% of cases, however, myocardial perfusion scan interpretation and clinical decision making are independent of β-blocker intake.

**Reviewer’s Comments:** The authors recommend that patient preparation include withdrawal from β-blockers prior to undergoing vasodilator pharmacologic stress testing. However, if this is not possible or if a patient does not comply with withdrawal instructions, the authors recommend going ahead with adenosine stress testing. Of note, the patients in this study underwent adenosine stress testing without supplemental low-level exercise. Although the scan interpretation was changed in 2 of 20 patients after β-blocker withdrawal, this change is not statistically significant, suggesting that either no clinical difference exists or that the study was underpowered. (See images for this review at practicalreviews.com.) (Reviewer-Thomas F. Heston, MD).

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Keywords: Coronary Artery Disease, Pharmacologic Stress Test, Beta-Blocker Withdrawal

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FDG-PET Gaining Popularity for Evaluating NETs

Neuroendocrine Tumor Review.
David Bushnell, MD

Imaging is crucial to optimal care of patients with gastroenteropancreatic neuroendocrine tumors. FDG-PET imaging is gaining popularity for evaluating tumor aggressiveness and patient prognosis.

Gastroenteropancreatic (GEP) neuroendocrine tumors (NETs) arise from precursor cells in the GI tract known collectively as the diffuse neuroendocrine system. The incidence of these tumors has been increasing in the past few decades, with a prevalence of approximately 30 to 40 cases per 100,000 individuals. These tumors are often categorized based on embryologic tissues of origin and are, thus, typically subdivided into foregut, midgut, and hindgut categories. The most common site for midgut tumors is the distal ileum. Some NETs produce bioactive amine and peptide molecules that create distinct and often debilitating clinical syndromes. However nonfunctioning NETs are actually more common. A significant percentage of foregut and midgut NETs are associated with genetic syndromes, such as multiple endocrine neoplasms (MEN) type 1. The most important serum tumor markers are probably serotonin and chromogranin A. Chromogranin A is elevated in most NETs and reflects overall tumor burden in the body. Importantly, a cause of a false-positive chromatogram is an elevation in proton pump inhibitors. Tumor grade and differentiation are important factors for determining the aggressiveness of these types of tumors. The European Neuroendocrine Tumor Society and the World Health Organization classify tumor grade into 3 categories: low-grade tumors (Ki-67 index, <3%), intermediate-grade tumors (Ki-67 index, 3% to 20%), and high-grade tumors (Ki-67 index, >20%). Most NETs fall into the low- or intermediate-grade categories. Small cell carcinoma of the lung is an example of a high-grade NET. The best single diagnostic imaging technique for evaluating NET is somatostatin receptor imaging with PET/CT using a radiolabeled Ga-68 octreotide molecule, which is clearly superior to SPECT/CT imaging with In-111 pentetreotide (OctreoScan™). Unfortunately, Ga-68 PET/CT is only available at a handful of centers in the United States. However, significant efforts are underway in both the academic and industry sectors to obtain approval from the Food and Drug Administration for Ga-68.

Reviewer’s Comments: FDG-PET imaging is gaining popularity for evaluating tumor aggressiveness and patient prognosis in certain individuals with NETs. Some studies have found that FDG levels in metastatic disease are better indicators of survival than are Ki-67 values. A substantial fraction of low-grade NETs will show no FDG uptake, whereas the higher-grade tumors are almost always FDG-positive. Typically, NETs with high FDG uptake have lower expression of somatostatin receptors and, therefore, are less likely to show significant uptake on OctreoScan or PET with Ga-68 DOTATOC/DOTATATE. The reverse is also true. (Reviewer-).

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Keywords: Gastroenteropancreatic Neuroendocrine Malignancies, PET

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