Compared to N-13 ammonia PET, Rb-82 PET is able to accurately measure absolute myocardial blood flow.

**Background:** Rb-82 cardiac PET utilizes a generator system and, therefore, is available to clinics that lack a cyclotron. Quantitation of myocardial blood flow (MBF) and coronary flow reserve (CFR) has been done with O-15 water and N-13 ammonia, but there is only limited experience using Rb-82 PET.

**Objective:** To determine the accuracy and reproducibility of MBF using Rb-82 PET.

**Design:** Observational study.

**Participants:** 22 patients who were at risk for or had known coronary artery disease were included in the study, as were 20 healthy volunteers.

**Methods:** All patients were studied with Rb-82 PET on 2 occasions separated by a 2-week interval. Results from the initial scan were compared with the results from an Rb-82 PET scan (to assess reproducibility, n=22) or an N-13 ammonia scan (to assess accuracy, n=20). The interobserver and intraobserver variability of MBF quantitation was evaluated using 4 repeated estimations by each of 4 observers. MBF was estimated by fitting the blood pool and tissue time-activity curves to a 2-compartment kinetic model for Rb-82 and to a 3-compartment model for N-13 ammonia.

**Results:** The reproducibility of MBF estimates in repeated Rb-82 studies was very good at rest and during stress, as was the reproducibility of the CFR estimates. The intraobserver and interobserver reproducibility for Rb-82 PET was excellent. Using N-13 ammonia as the gold standard, the accuracy of MBF by Rb-82 PET was excellent, with a correlation coefficient of r=0.93. CFR was slightly underestimated by Rb-82 compared to N-13 ammonia.

**Conclusions:** MBF quantitation using Rb-82 PET has excellent reproducibility, accuracy, intraobserver reliability, and interobserver reliability compared to N-13 ammonia PET for MBF of up to 2.5 mL/g per minute.

**Reviewer's Comments:** Quantification of MBF using Rb-82 PET appears to be accurate and reproducible when using the method utilized in this study (generalized factor analysis). (Reviewer-Thomas F. Heston, MD).

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Keywords: Myocardial Blood Flow, PET Flow Tracers

Print Tag: Refer to original journal article
With SPECT imaging, lung perfusion-ventilation scans are nondiagnostic in only 1% of patients suspected of having a pulmonary embolism.

**Background:** Lung scans have been largely replaced by CT pulmonary angiograms (CTPA) for diagnosis of acute pulmonary embolism (PE). This is largely due to probabilistic interpretation criteria used for reading lung scans, which results in a substantial number of scans considered nondiagnostic by referring physicians. Lung scans are generally obtained in a planar fashion. SPECT imaging improves the resolution of perfusion and ventilation abnormalities and may improve the accuracy of lung scans.

**Objective:** To evaluate the utility of lung perfusion-ventilation SPECT (V/P SPECT) in the diagnosis of PE.

**Design:** Retrospective analysis.

**Participants:** 2328 consecutive patients imaged with V/P SPECT because of clinical suspicion of PE.

**Methods:** Lung ventilation SPECT studies were obtained with Tc-99m DTPA or Tc-99m Technegas® (not available in the United States). Perfusion images were obtained with Tc-99m MAA. Both SPECT studies were done with 128 projections over 360°, requiring 10 seconds per projection for the ventilation scan and 5 seconds per projection for the perfusion scan. A segmental reduction or a subsegmental total deficiency of uptake was assigned a value of 1 point. Segmental total deficiency corresponded to 2 points. PE was diagnosed if there was a mismatch of at least 2 points. Matched defects and a maximum of 1 mismatched point were considered to be negative for PE. The final diagnosis of PE was based on V/P SPECT and clinical and laboratory findings. In 152 patients, CTPA was also obtained. A negative V/P SPECT was considered a true negative if the patient did not develop PE in the 6-month follow-up.

**Results:** V/P SPECT was feasible in 99% of patients and could not be obtained in 1% of patients due to obesity or discomfort in supine position. A nondiagnostic V/P SPECT interpretation was provided in only 1% of patients. Overall, 1785 patients were available for the full analysis. V/P SPECT was negative in 1159 patients, and only 6 of these patients had PE (negative predictive value, 99%). V/P SPECT was positive in 607 patients. Except for 6, all of these patients were anticoagulated by the referring physicians.

**Conclusions:** V/P SPECT yields a high negative and positive predictive value, with only 1% of scans being nondiagnostic.

**Reviewer’s Comments:** The limitation of this paper is that V/P SPECT false-positive rates cannot be determined within this study design. The major point of this study is the very low percentage of nondiagnostic studies with V/P SPECT. This should be a sufficient reason to consider SPECT imaging for lung perfusion and ventilation scans. (Reviewer-Yusuf Menda, MD).

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Keywords: Pulmonary Embolism, SPECT Lung Scan

Print Tag: Refer to original journal article
Agreement Good Between Low-Pitch and Time-Averaged CT

Comparison of Low-Pitch and Respiratory-Averaged CT Protocols for Attenuation Correction of Cardiac PET Studies.

Nye JA, Hamill J, et al:

Med Phys 2009; 36 (May): 1618-1623

When used for attenuation correction of cardiac PET data, time-averaged CT and low-pitch helical CT protocols show good agreement and negligible bias.

**Background:** Respiratory motion can cause problems with CT scans used for attenuation correction in myocardial perfusion PET/CT scans.

**Objective:** To evaluate 2 approaches for matching CT image studies with PET: low-pitch helical CT (HCT) at a pitch of 0.45 was compared with multi-bed position CT averaged over a breathing cycle.

**Participants:** 54 consecutive patients undergoing Rb-82 myocardial perfusion PET.

**Methods:** All patients had both a helical CT study with a pitch of 0.45 (120 kVp; 76 mA; total scan time, 14 seconds) and a 6-second-per-bed-position time-averaged cine CT of the heart region (80 kVp; 13 mA; 5 bed positions; total scan time, 40 seconds). Acquisition parameters were set so that each procedure had a CT dose index (CTDI) of approximately 5 to 6 mSv and were performed during free breathing. HCT is available on all CT systems, while the generation of the time-averaged CT requires additional software that is not widely available. The registration between the reconstructed Rb-82 and the corresponding CT scans was determined from the volume of myocardial overlap. The stress and rest Rb-82 studies were reconstructed twice using each of the CT procedures for attenuation correction. Polar maps of the Rb-82 images were generated, and comparisons of the 2 attenuation correction methods were made among the standard 17 segments.

**Results:** There were no significant differences in the overlap volume found in either the stress or rest studies between the 2 CT techniques. However, inspection of the CT images showed visual respiratory artifacts in 68% of the low-pitch CT studies and in 32% of the time-averaged CT images. The time-averaged CT artifacts were primarily due to photon starvation associated with the low kVp and mA. The polar map segmental comparison showed overall good agreement between the 2 attenuation correction methods, with essentially no bias.

**Conclusions:** Overall, both methods have similar accuracy for myocardial perfusion imaging. The low-pitch helical CT is available on all systems, but it is more prone to breathing artifacts. The time-averaged CT in this study had half the artifacts but was susceptible to photon starvation artifacts on large patients.

**Reviewer’s Comments:** The time-averaged approach had greater flexibility and provided the best attenuation map when sufficient x-rays were available. Problems were encountered with larger patients only because the selected CT parameters were too low because of radiation dose concerns. However, in a patient study that is clinically indicated, this should not occur. The diagnostic information from an indicated, well-performed study justifies using an appropriate level of radiation. (Reviewer-Mark T. Madsen, MD).

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Keywords: Cardiac PET/CT, Attenuation Correction

Print Tag: Refer to original journal article
PET/CT Detects High Number of Synchronous HN Cancers

Head and Neck Squamous Cell Carcinoma (HNSCC) - Detection of Synchronous Primaries With 18F-FDG-PET/CT.


In selected patients with head and neck cancers, PET detects a high proportion of synchronous primary malignancies during initial staging and should be utilized for this purpose.

Background: Second primary tumors are not uncommon in patients with head and neck (HN) malignancies. PET imaging with FDG has the potential to detect these additional primary tumors. The primary locations of these additional malignancies are HN, lung, and esophagus, and the tumors are typically squamous cell in origin.

Objective: To evaluate FDG-PET/CT imaging for detecting synchronous second primary malignancies at initial screening in patients with known HN tumors.

Design/Methods: PET/CT exams obtained for initial staging in 589 subjects were retrospectively evaluated for evidence of synchronous primary tumors. The presence of the second primary malignancy was established via clinical, imaging, and endoscopy follow-up, along with histology.

Results: The oral cavity and oropharynx were the most common sites of the known malignancies for which the patients were undergoing evaluation. The diagnosis of 56 synchronous tumors was eventually established in 44 of the 589 subjects (7%). PET/CT imaging correctly detected 47 of these tumors in 41 of the patients. The 9 false-negative PET tumors were small and generally located in the lungs or HN region. Of the 56 second malignancies, 46 were located in the aerodigestive tract. Six individuals had 3 synchronous malignancies each. Most patients who had synchronous malignancies were eligible for curative intent therapy. There were 22 instances of false-positive PET findings for second malignancies. Five of these were determined to be physiologic activity in the HN, and 8 were colonic polyps.

Conclusions: PET detects a high proportion of synchronous primary malignancies and should be utilized for this purpose in selected patients with HN cancers.

Reviewer’s Comments: The results from this study are compelling and support the use of PET/CT for this purpose. At first, I was mildly concerned about the number of false-positive findings. However, detection of colonic polyps is not necessarily a bad thing because many of these may represent pre-cancerous lesions. In addition, the rate of 22 false-positive results out of 589 PET/CT exams is actually pretty darn good. (Reviewer-David Bushnell, MD).

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Keywords: Synchronous Second Primary Tumors, PET/CT

Print Tag: Refer to original journal article
During cardiac SPECT studies, conventional motion correction cannot correct for the motion that occurs during the acquisition of a projection, while a visual-tracking system can detect respiratory motion.

**Background:** The duration of SPECT and PET studies make patient motion inevitable, and this motion is associated with image artifacts that can mimic coronary artery disease (CAD). While there are data-driven methods for detecting and correcting motion, these have limitations.

**Objective:** To investigate the use of a commercial visual-tracking system (VTS) applied to motion correction in SPECT myocardial perfusion studies.

**Methods:** The VTS was the Vicon MX system which detects reflective markers located on a band stretched around the patient's chest and abdomen using infrared video cameras. Heart motion is monitored by the chest markers, while the abdomen markers monitor respiratory motion. Multiple infrared cameras provide stereoscopic tracking of the markers with submillimeter accuracy. List-mode acquisition of the SPECT and marker information allows for in-frame as well as between-frame motion. The precision and accuracy of the marker location was verified by adding Tc-99m to the markers to compare the reconstructed SPECT locating with the tracking system. Motion correction using the tracking was first performed on an anthropomorphic phantom and later on 77 patients referred for myocardial perfusion studies. The tracking source correction method was validated on 10 patients who had repeat resting studies in which they moved on purpose.

**Results:** Reconstructed phantom images with no motion correction exhibited artifacts that were substantially reduced when the motion-tracking information was included. The chest and abdomen markers on the 77 SPECT patients were reliably tracked 94% and 92% of the time, respectively. For the repeat studies, the marker-corrected motion studies best matched the original resting studies with no motion. Differences in the segmental summed scores between the repeat resting studies were significantly better when the marker motion correction was employed.

**Conclusions:** The visual-tracking approach produced better diagnostic results than either foregoing motion correction or using the data-driven motion correction method supplied by the vendor.

**Reviewer's Comments:** The results of this study demonstrate the superiority of the VTS for correcting motion during SPECT imaging. The ability to detect and correct for respiratory motion of the heart is a new and needed improvement. However, the VTS approach described in this paper requires list-mode acquisition which is not routinely available on all SPECT systems. Hopefully, the vendors will take note of the advantages offered by this method and will make list-mode acquisition a standard option. (Reviewer-Mark T. Madsen, MD).
The Bosniak classification system is helpful for applying CT results to decisions about managing cystic renal masses.

**Background:** Incidental or unexpected CT findings on PET/CT or SPECT/CT are fairly common. One of the more likely and more important potential incidental finding is a renal mass, particularly one that is cystic in nature. Approximately 10% of all renal cell carcinomas present as a cystic mass.

**Objective:** This excellent article was published several years ago and provides a superlative review of features and appearances of benign and malignant cystic renal masses detected by CT.

**Results:** A simple cyst in the kidney is essentially always benign. What distinguishes a simple cystic mass from a cystic mass which may be malignant? A complicated cyst typically appears as a result of hemorrhage or infection involving a simple cyst, and CT features may be quite similar to those of a malignant cystic renal mass. Any combination of septations, wall thickening, loculations, nodularity, calcifications, attenuation >20 HU, or contrast enhancement indicates either a cystic renal mass, which may be the result of renal cell carcinoma, or a complex renal cyst and will then likely require further evaluation or surgery. The presence of a soft tissue component that reveals contrast enhancement dramatically raises the likelihood that the lesion is malignant. However, in some instances, benign cystic lesions will show enhancement. Enhancement is generally considered to be present when there is an increase of ≥15 HU. This article is based primarily on the Bosniak classification schema for cystic lesions in the kidney. In this system, a Bosniak category I lesion is a simple renal cyst, and a category II lesion may have a few fine septa or fine peripheral calcification and probably does not require follow-up. However, Bosniak IIF lesions have minimally thickened septa or walls (1 mm) with more than just fine peripheral calcification, and IIF lesions carry a 5% risk of malignancy. Bosniak III lesions have thickened septa and/or clearly thickened walls which typically show some contrast enhancement, and class III lesions carry a 50% risk of malignancy. Bosniak III lesions are considered surgical, whereas Bosniak IIF lesions can be followed up with repeat CT imaging. Bosniak IV cystic renal masses are very likely to be malignant and must be treated as such. Inter-observer variability is greatest for distinction between Bosniak II versus III lesions. Trying to obtain useful information with a needle biopsy for cystic lesions of the kidneys is futile.

**Reviewer's Comments:** For those physicians who read CT images as part of SPECT/CT or PET/CT exams, this is a very useful article to review and keep for reference. (Reviewer-David Bushnell, MD).

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Keywords: Renal Cystic Mass, CT Features

Print Tag: Refer to original journal article
Age and I-131 Avidity Strong Survival Predictors in DTC

The Importance of Age Over Radioiodine Avidity as a Prognostic Factor in Differentiated Thyroid Carcinoma With Distant Metastases.

Mihailovic J, Stefanovic L, et al:

Thyroid 2009; 19 (March): 227-232

Age and the degree of radioiodine uptake in distant metastases are strong predictors of disease-specific survival in thyroid cancer.

**Objective:** To evaluate the effect of I-131 uptake in distant metastasis of differentiated thyroid carcinoma (DTC) on disease-specific survival.

**Design/Participants:** Retrospective review of 77 patients with metastatic DTC treated with I-131 therapy at the authors' institute from 1977 to 2000.

**Methods:** All patients underwent thyroidectomy. In 76 patients, a diagnostic whole-body scan was performed with 3 mCi I-131 several months after thyroid surgery. All patients were adequately prepared as confirmed by a serum TSH level >30 mU/L 4 to 6 weeks after T4 was withdrawn. To ablate residual thyroid, the dose was 100 mCi. Patients with residual postoperative tumor or metastases in regional cervical lymph nodes, mediastinal lymph nodes, and lungs received 150 mCi of I-131. For bone metastases, 200 mCi of I-131 was given.

**Results:** The most frequent site of distant metastases (in two thirds of patients) was the lung. Bone metastases were present in 9 patients (11.7%). Follicular carcinoma usually metastasized to bones, and papillary carcinoma metastasized most frequently to the lung. Information regarding outcome was available in 74 patients with DTC who had distant metastases. During follow-up, 33 patients were alive (43%) and 44 patients (57%) died, including 7 patients with non-iodine-avid distant metastases. After the appearance of metastasis, 58% of patients survived an additional 5 years, 48% survived 10 years, and 38% survived 20 years. Whole-body imaging, which was done 72 hours after I-131 therapy, showed no iodine uptake in distant metastases in 12 patients (16%). In this group, 9 had papillary and 3 had follicular cancer. Only 2 of the 12 patients with non-iodine-avid distant metastases were younger than 45 years of age. Patients with non-iodine-avid lesions had a 5-year disease-specific survival of <20%. The relationship between I-131 uptake in distant metastases and survival was significant ($P = 0.0006$). When matched for age, iodine non-avidity significantly shortened the survival in patients younger than 45 years of age.

**Conclusions:** Age and the degree of radioiodine uptake in distant metastases are strong predictors of disease-specific survival in thyroid cancer.

**Reviewer's Comments:** The benefit of I-131 therapy in patients with distant metastases in DTC is suggested by the significantly better survival rates in those who received I-131 compared with those who did not. As for staging, the tumor-node-metastasis (TNM) classification does not take into account patient age, which turns out to be a powerful factor. The results of this paper give support to those who favor the MACIS staging system (metastasis, age, completeness of surgery, invasion beyond the thyroid capsule, size of primary tumor) over or, at least, in addition to TNM staging for thyroid cancer. In fact, age in this series had an even greater influence on survival than did radioiodine avidity. (Reviewer-C. Richard Goldfarb, MD).

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Keywords: Thyroid Cancer, Prognostic Factors

Print Tag: Refer to original journal article
RAI Therapy Increases Risk of Leukemia, Not Other Cancers

Second Primary Malignancy Risk After Radioactive Iodine Treatment for Thyroid Cancer: A Systematic Review and Meta-Analysis.
Sawka AM, Thabane L, et al:
Thyroid 2009; 19 (May): 451-457

A large meta-analysis found that, after I-131 treatment for thyroid cancer, patients have a significantly increased risk only for leukemia and not for other forms of cancer.

**Background:** The possibility of inducing a cancer due to radioiodine (RAI) therapy is of concern in thyroid cancer patients.

**Objective:** To assess whether the risk of inducing a secondary malignancy is increased in patients who have received RAI therapy compared to those not treated with RAI.

**Design:** Review of the medical literature for studies reporting the risk of a second primary malignancy (SPM) in thyroid cancer treated with RAI.

**Results:** Of 1607 reviewed publications, only 2 studies were included in the review after considering the inclusion and exclusion criteria. The median age at diagnosis was in the early 40s, and the overall median follow-up periods were 8.6 years in one study and 13 years in the other. In the first study, a third of patients had I-131 therapy with external beam radiotherapy. In the second study, 62% of individuals received RAI, 17% received external beam radiotherapy, and 9% received both. The cumulative activity of I-131 received was not reported in the first study but averaged 6.0 GBq (range, 0.2-55.5 GBq) in the second study. **Results:** The relative risk of SPM in those with I-131 therapy was significantly increased to 1.19 relative to thyroid cancer survivors not treated with I-131, using a minimum latency period of 2 to 3 years after thyroid cancer diagnosis. The relative risk of leukemia was significantly increased to 2.5, but there was no increased risk of bladder, breast, central nervous system, colon and rectum, digestive tract, stomach, pancreas, kidney (and renal pelvis), lung, or skin melanoma associated with I-131 therapy.

**Conclusions:** The overall risk of a second primary malignancy in thyroid cancer survivors treated with I-131 is slightly increased compared to thyroid cancer survivors not treated with RAI, accounted for largely by leukemia in patients receiving high doses. There was no increased risk of bladder, breast, central nervous system, colon and rectum, digestive tract, stomach, pancreas, kidney (and renal pelvis), lung, or skin melanoma associated with I-131 therapy.

**Reviewer’s Comments:** This study is actually reassuring in that the only SPM to show significantly increased risk was leukemia. Such patients were likely treated with very high activities of I-131 and were at substantial risk of death from thyroid cancer. There is no evidence to date that ablative doses routinely given for thyroid cancer induce any cancer of any sort. (Reviewer-C. Richard Goldfarb, MD).

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Keywords: Thyroid Cancer, Radioiodine-Induced Cancers

Print Tag: Refer to original journal article
Coughing Improves Sensitivity of GER Scintigraphy

The Role of Coughing as a Gastroesophageal-Reflux Provoking Maneuver: The Scintigraphical Evaluation.
Yapici O, Basoglu T, et al:

Nucl Med Commun 2009; 30 (June): 440-444

Coughing as a straining maneuver during gastroesophageal reflux scintigraphy substantially improves the sensitivity of the study. It is noninvasive, readily available, and easy to perform.

Background: In the radionuclide method, gastroesophageal reflux (GER) can be quantified using regions of interest over the esophagus and the stomach. Reflux >4% is considered abnormal. This coincides with visible refluxed radioactivity on the gamma camera screen. To enhance the sensitivity of gastroesophageal scintigraphy, a higher temporal acquisition rate (5-15 seconds) improves sensitivity for the detection of reflux compared with the older method of 30-second to 60-second acquisition. Maneuvers such as gastric acid loading and abdominal compression have been suggested to enhance sensitivity but are uncomfortable. It has been suggested that deep inspiration or coughing may overcome lower esophageal pressure and thereby demonstrate reflux.

Objective: To evaluate coughing as a means of demonstrating GER in children.

Participants: 71 girls and 54 boys (mean age, 9.2 years) having the clinical probability of GER and able to cooperate for coughing on command were included.

Methods: Orange juice (20 mL/kg) containing 0.5 to 1 mCi Tc-99m tin colloid was given orally. Sequential images were obtained for 60 minutes in supine position. The total 60 minutes was divided into 10-minute intervals. Patients were asked to cough gently 4 to 6 times per minute during the second, fourth, and sixth of these intervals. Any visible esophageal activity was interpreted as reflux.

Results: 64 patients (51%) with a mean age of 8.4 years showed GER. Of the positive 64 patients, GER was seen only during the coughing intervals in 25 (39%), during both coughing and noncoughing intervals in 33 (52%), and only during noncoughing intervals in 6 (9.4%). The symptom severity score was significantly lower in the group of 25 patients presenting with GER episodes exclusively during the coughing intervals. Straining by means of coughing increased the number of reflux episodes from 36% to 64%. No correlation was found between the number of reflux episodes and symptom severity. Conclusion: Coughing as a straining maneuver during GER scintigraphy substantially improves the sensitivity of the study. It is noninvasive, readily available, and easy to perform.

Reviewer's Comments: GER and lung aspiration studies in infants comprise the major business of GER studies in many labs, including ours. It is unfortunate that this clever maneuver, which I intend to use for our adults, cannot be applied to the very young pediatric population in whom our yield of positive studies is disappointingly low. Need for cooperation is unfortunately a current limitation for other scintigraphic studies as well in this population. (Reviewer-C. Richard Goldfarb, MD).

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Keywords: Gastroesophageal Reflux, Imaging Maneuvers

Print Tag: Refer to original journal article
**Background:** The clinical course for patients with metastatic neuroendocrine tumors (NETs) varies. **Objective:** To assess the ability of FDG-PET imaging and somatostatin receptor scintigraphy (SRS) to predict the prognosis in patients with metastatic NETs.  

**Design/Participants:** Prospective study of 38 patients with known metastatic disease from NETs.  

**Methods:** Patients underwent PET, OctreoScan, and CT. In addition, Ki-67 staining of the original tumor biopsy samples was performed. Follow-up included both clinical and CT evaluations at regular intervals.  

**Results:** Of the 38 patients, 4 had high-grade histology and 34 had low-grade histology. The primary site was most commonly the small intestine, followed by the pancreas. Twelve patients had unknown primary locations. The liver was the most common site of metastasis. At the 6-month follow-up, 22 subjects had stable disease, and 16 had progressive disease. Overall survival at 1 and 2 years was 86% and 73%, respectively. FDG results were positive in 15 subjects and negative in the remainder. Likewise, OctreoScan images were positive in 27 and negative in the remainder. Early progressive disease was seen in 14 of the 15 FDG-positive subjects and in 9 of the 11 patients with negative OctreoScan results. A World Health Organization high-grade classification and the percentage of Ki-67-positive cells >15% were both highly predictive of progressive disease, but each carried a negative predictive value of <80%. In contrast, FDG-PET carried a 93% positive predictive value and a 91% negative predictive value for progressive disease. OctreoScan imaging was less accurate than PET, particularly with regard to the negative predictive value for disease progression. FDG-negative patients had significantly better overall survival rates compared to FDG-positive individuals. Among the 34 low-grade subjects, this was also true. In addition, in this low-grade group, the 25 with positive OctreoScan uptake had better survival than the 9 with negative findings. In multivariate analysis, only FDG status was independently predictive of survival, and this was for progression-free survival. No measures were found to be independently predictive of overall survival.  

**Conclusions:** PET may be the best available method for predicating outcome in low-grade NETs that have metastasized.  

**Reviewer's Comments:** As far as I could tell, the authors did not assess SUV level in their multivariate analysis, which may have been revealing. Although NETs represent a small fraction of our work, the ability to predict outcome carries great importance, which is why I decided to include this review. (Reviewer-David Bushnell, MD).
Quarter-Time WBR Decreases SPECT Acquisition Times

The wide beam reconstruction method allows gated SPECT myocardial perfusion imaging to be performed in one-fourth the time of conventional imaging using iterative reconstruction, without loss of image quality.

Background: The traditional method of reconstructing SPECT data is filtered back projection. Iterative reconstruction with ordered subset expectation maximum (OSEM) has also become a common reconstruction method. Newer reconstruction methods have the potential to greatly decrease imaging times. One new approach is an iterative algorithm for scatter compensation, noise suppression, and depth-dependent collimator resolution. Another approach is wide beam reconstruction (WBR), which is an iterative reconstruction method simultaneously addressing resolution recovery and noise reduction. These software methods have the potential to decrease imaging time and/or decrease radiation dosage to the patient.

Objective: To determine whether WBR is able to perform quarter-time imaging with image quality similar to OSEM full-time imaging.

Design: Prospective trial.

Participants: The pilot study used to optimize the WBR algorithm included 48 patients referred for clinical reasons. The study group consisted of 209 patients referred for clinical reasons to nuclear myocardial perfusion imaging and were prospectively enrolled.

Methods: Same-day single isotope sestamibi rest followed by stress gated SPECT imaging was performed. Patients initially underwent standard full-time rest imaging (25 seconds/stop) which was immediately followed by quarter-time imaging (6 seconds/stop). After standard stress testing, patients underwent full-time stress imaging (20 seconds/stop) followed by quarter-time imaging (4 seconds/stop). Image sets were presented in random order to 2 expert observers who graded the images for quality.

Results: Quarter-time WBR stress images were found to be significantly better in quality compared to full-time OSEM. There was no significant difference found in the rest images when comparing WBR versus OSEM. There was an excellent correlation between OSEM and WBR for ventricular volumes and ejection fraction. However, the ventricular ejection fraction was about 5 percentage points lower using WBR (based on the analysis by three separate software packages). Artifacts were infrequent (2.8% overall) but were more common in the quarter-time WBR acquisitions. Diagnostic quality of the images was equivalent.

Conclusions: Quarter-time acquisition gated SPECT using WBR is feasible, with an image quality equivalent to full-time imaging using OSEM reconstruction methods.

Reviewer's Comments: WBR and similar reconstruction programs represent a significant advance in nuclear cardiology, allowing reduced scan times and/or a reduced radiation dose. (Reviewer-Thomas F. Heston, MD).

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Keywords: Myocardial Perfusion Imaging, SPECT Data Reconstruction

Print Tag: Refer to original journal article
I-131 Lipiodol Preferred for Advanced HCC

Transarterial Injection of 131I-Lipiodol, Compared With Chemoembolization, in the Treatment of Unresectable Hepatocellular Cancer.

Marelli L, Shusang V, et al:


Among patients with hepatocellular carcinoma, I-131 lipiodol is likely the preferred therapy in patients with portal vein thrombosis or more advanced disease.

Background: Hepatocellular carcinoma (HCC) is the fifth most common neoplasm and third most common cause of cancer-related death. It is noncurative in about 60% of patients, with the most palliative treatment being transarterial chemoembolization (TACE), although there are no standardized regimens. TACE offers improved survival but at the cost of increased morbidity. An alternative in I-131 lipiodol has been sought. Some studies have also shown that the chemotherapy component does not add to the survival benefit — that transarterial embolization (TAE) is just as efficacious as TACE.

Objective: To evaluate differences in survival among patients with unresectable HCC treated with I-131 lipiodol versus TACE or TAE.

Methods: This cohort study evaluated 124 patients, 50 who underwent treatment with I-131 lipiodol and 74 with either TACE or TAE. All patients had baseline CT/MRI to evaluate extent of disease and to evaluate presence of portal vein thrombosis (PVT), which is associated with a more advanced stage of disease. CT was also done 1 month after treatment to evaluate response. All patients had disease graded by several widely used staging systems: Child-Pugh, Model for End-Stage Liver Disease (MELD), Okuda, Cancer Liver Italian Program (CLIP), and Barcelona Clinic Liver Cancer (BCLC).

Results: There were no significant differences in survival among the 2 treatment groups. However, patients with more advanced disease and those with PVT did have a significantly longer survival, though these patient numbers were small. The investigators also found no significant difference among patients treated with TACE versus TAE. independent of the type of treatment used, univariate analysis showed the prognostic factors associated with adverse survival were increasing number of nodules and increasing size of the largest nodule.

Conclusions: Although there is no difference among TACE, TAE, or I-131 lipiodol therapy, the latter may be the preferred treatment in patients with advanced disease or those with PVT.

Reviewer’s Comments: This study supports the results of other studies regarding the similarities of survival among the treatment with TACE and TAE. The authors mention that TACE is associated with morbidity that can be quite significant in patients with more advanced disease. As such, the clinically applicable conclusion is that I-131 lipiodol offers a similar survival rate with a lower morbidity, and that it may even be preferable in patients with PVT or more advanced disease. (Reviewer-Damita Thomas, MD).

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Keywords: Hepatocellular Carcinoma, Transarterial Embolization

Print Tag: Refer to original journal article
Increasing PET-CT Scan Times Improve Image Quality in Obese

Comparison of Imaging Protocols for 18F-FDG PET/CT in Overweight Patients: Optimizing Scan Duration Versus Administered Dose.

Masuda Y, Kondo C, et al:

J Nucl Med 2009; 50 (June): 844-848

Increasing imaging time improves image quality in FDG-PET/CT for obese patients.

**Background:** Although FDG-PET/CT is an invaluable diagnostic tool, the usefulness of the study is only as good as the information it provides. When images are noisy, as in obese patients, the full potential of this modality is not fully realized because image quality is key in providing accurate diagnostic information. Several studies have shown that either increasing dose or increasing scan time, or both, can improve image quality. However, these have been retrospective studies in which it is difficult to tease out which factor contributes to improved image quality.

**Objective:** To determine whether increasing administered dose or increasing acquisition times will improve PET/CT image quality in obese patients.

**Methods:** This prospective study looked at 120 patients, with 40 patients each grouped into 3 weight tertiles from 60 kg to 85 kg. Weight-corrected administered doses and imaging times were derived from calculated ratios. These ratios were calculated from liver signal-to-noise ratios (SNRs) derived from a matched retrospective subset of 80 patients who had previously undergone PET/CT. These 80 patients served as the control group for comparison to the conventional weight-based imaging protocol used at that institution. Then 20 patients in each weight tertile were imaged using both the dose and imaging time corrected scanning protocols.

**Results:** When compared to the matched control group for each weight tertile, image quality improved when imaging time was increased but not when the administered dose was increased. The SNRs decreased with increasing body weight, which was not overcome by increasing dose, likely secondary to an increasing fraction of random and scatter events with an increase in weight.

**Conclusions:** To maintain image quality in obese patients, you should scan for a longer period of time.

**Reviewer’s Comments:** The results of this quite clinically relevant study show that increasing imaging time, and not administered dose, improves PET/CT image quality in obese patients. The data would be more convincing if each patient had undergone a baseline scan (using the institution’s currently used protocol for larger patients) in addition to the dose and imaging time-corrected scans for direct comparison in the same patient. However, the authors pointed out that the additional scanning could pose an ethical issue as they were not medically necessary. As such, the corrected scans were compared to a weight-matched group of patients who had previously undergone imaging using that institution’s currently used protocol for heavier patients. Despite this limitation, the results do warrant a further look into whether increasing imaging time will consistently improve image quality in obese patients. (Reviewer-Damita Thomas, MD).

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Keywords: FDG-PET/CT, Obesity

Print Tag: Refer to original journal article
Thymic FDG Uptake Seen in Adults, Not Just Pediatric Patients

Physiologic Thymic Uptake of 18F-FDG in Children and Young Adults: A PET/CT Evaluation of Incidence, Patterns, and Relationship to Treatment.

Jerushalmi J, Frenkel A, et al:


Thymic FDG activity is usually greater prior to chemotherapy and during follow-up, and it can be seen in both children and adults.

**Background:** Thymic activity on FDG-PET/CT can represent benign or malignant etiologies, the distinction of which is critical to avoid false-positive interpretations in cancer patients undergoing diagnosis, treatment, and follow-up. Thymic activity is thought to typically occur in prepubescent children (approximate age, 13 years), decreasing gradually over time as the fatty infiltration of the gland reaches its peak by age 49 years. Thymic activity is also known to increase after chemotherapy in adults and children, the so-called "rebound" phenomenon.

**Objective:** To identify patterns of thymic FDG avidity in patients of various ages and treatment stages.

**Design/Participants:** Retrospective study of 559 PET/CT scans from 160 patients of varying ages (ages ≤40 years), with varying cancers, and in varying stages of treatment.

**Methods:** Thymic uptake was visually scored as either T+ or T-. The more objective SUVmax was also measured. The relationship between frequency/intensity of thymic activity and stage of treatment (before, during, or after) was then recorded. Patients were followed up for about 85 months with serial CT studies to confirm that uptake seen on PET/CT was not actually disease.

**Results:** At 85 months, all patients except one were shown to have no thymic malignancy. The authors found that thymic activity was seen in about 25% of the total number of scans, mostly among younger patients (80%) but also in adults aged ≥30 years (8%). Thymic activity was seen more frequently during follow-up but also was seen in a not-infrequent-number of patients (25%) even before any therapy. Thymic activity can persist up to 36 months. The SUVmax averaged around 3.0, being more intense before treatment and during follow-up versus during treatment.

**Conclusions:** Benign thymic FDG activity, though more prevalent in younger children, can be seen in adult cancer patients even prior to chemotherapy.

**Reviewer’s Comments:** This interesting study looks at the pattern of FDG activity of the thymus in a patient population with various ages, with various cancers, and at various stages of treatment. However, the study could have been strengthened if the patient group, of various ages, all had the same disease process (lymphoma for example) and scans before, during, and after similar treatment regimens to gauge changing thymic FDG avidity in each patient. Also in this study, patients had various malignancies with different treatment regimens, which could be a potential confounder as the different regimens may possibly affect thymic FDG avidity differently. (Reviewer-Damita Thomas, MD).

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Keywords: Thymus, FDG Uptake

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SPECT/CT Aids in Localizing Sentinel Nodes in Breast Cancer

The Yield of SPECT/CT for Anatomical Lymphatic Mapping in Patients With Breast Cancer.

van der Ploeg IM, Nieweg OE, et al:


SPECT/CT can be of additional value in localizing sentinel lymph nodes in breast cancer patients with unusual drainage patterns on planar scintigrams.

**Background:** Lymphoscintigraphy has been shown to be a valuable tool in identifying lymph nodes in patients with breast cancer, aiding in the accurate staging of the disease. However, planar images can occasionally be nondiagnostic with nonvisualization or can be difficult to interpret when extra-axillary foci are seen. SPECT/CT can potentially provide valuable additional information in these cases because of the better resolution and localization that this technique provides.

**Objective:** To determine if SPECT/CT offers additional information in patients whose planar lymphoscintigrams are difficult to interpret.

**Design/Participants:** Prospective study of 134 patients with breast cancer who underwent SPECT/CT lymphoscintigraphy when planar scans were equivocal or nondiagnostic (extra-axillary uptake or nonvisualization).

**Methods:** Planar scans were done 10 minutes, 2 hours, and 4 hours after intratumoral injection and were followed immediately by SPECT/CT imaging. In the event of nonvisualization on SPECT/CT, re-injection was performed at 4 hours, after which delayed planar and SPECT/CT imaging were repeated. Surgical nodal harvesting was performed with adjunctive use of blue dye and gamma probe the following day, and nodes underwent histopathological analysis. Opinion regarding whether SPECT/CT provided additional information that was helpful intraoperatively was surveyed by the operating surgeons.

**Results:** Of the 134 patients, SPECT/CT provided additional value in 31 of 85 patients with unusual drainage patterns on planar images (extra-axillary foci), in 19 of 27 patients who had planar scans that were difficult to interpret (foci close to injection site), and in 6 of 22 patients who had nonvisualization on the 4-hour delayed planar scans. This additional information provided by SPECT/CT involved an additional incision to harvest additional nodes seen only by SPECT/CT or more precise placement of an incision as SPECT/CT provided more accurate anatomical localization.

**Conclusions:** SPECT/CT can provide additional information in terms of identifying more nodes as well as provide more accurate anatomical localization in patients whose planar lymphoscintigrams are equivocal or nondiagnostic.

**Reviewer's Comments:** The results of this interesting and well-executed study show that the addition of SPECT/CT imaging, particularly in patients with unusual drainage patterns (nonvisualization and extra-axillary nodes [internal mammary and intercostals]) on planar scintigrams, identify more nodes and provide better depth localization information for incision planning. As the authors point out, perhaps reserving SPECT/CT for the more challenging cases is prudent as surgeons often use adjunctive methods (intraoperative gamma probe and blue dye) to facilitate nodal localization. These routinely used methods can as easily identify other nodes that the otherwise positive planar imaging would miss. (Reviewer-Damita Thomas, MD).

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Keywords: Breast Cancer, Lymphatic Mapping, SPECT/CT

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Cardiac PET imaging allows a quantitative measurement of myocardial blood flow, which gives unique diagnostic information regarding microcirculation of the myocardium

**Background:** Although substantial advances have been made, cardiovascular disease remains the main cause of death worldwide. Nearly 70% of these deaths are due to coronary artery disease. Further significant reductions in morbidity and mortality may come through more aggressive prevention strategies that would require a greater diagnostic ability to detect subtle changes in coronary circulation. The measurement of absolute myocardial blood flow (MBF) may allow a better characterization of the heart's response to various therapeutic strategies.

**Objective:** To review of the medical literature to help better understand the possible therapeutic role of measuring MBF.

**Design:** Literature review.

**Results:** In this review, data show that the arterioles are most responsive to changes in the intramyocardial concentration of metabolites and are less responsive to changes in pressure and flow. Arterioles are mainly responsible for metabolic regulation of MBF, and thus their functioning primarily is assessed through measuring a patient's MBF. The coronary flow reserve (CFR) is the ratio of the hyperemic MBF divided by the resting MBF. In the setting of a normal resting MBF and lack of coronary stenoses, a reduced CRF indicates a dysfunction of coronary microcirculation. **Agents:** O-15 water and N-13 ammonia have been used successfully in the measurement of absolute MBF. Use of Rb-82 is limited by its relatively low extraction fraction at higher myocardial flow rates. Preliminary studies, however, have found it to be promising.

**Reviewer's Comments:** Some of the newer gamma cameras also purportedly have the potential to measure absolute MBF. Although this review article is primarily theoretical and focuses almost exclusively on N-13 and O-15 PET agents, it provides a good overview of the physiology and potential applications of the measurement of MBF, from early detection to the assessment of response to metabolic therapies. (Reviewer-Thomas F. Heston, MD).

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Keywords: Coronary Artery Disease, Absolute Myocardial Blood Flow

Print Tag: Refer to original journal article
A new fully automated motion correction software program for cardiac SPECT imaging has been developed that appears to outperform existing software programs in clinical use.

**Background:** Motion artifacts are a major cause of imaging artifacts in myocardial perfusion gated SPECT imaging. Motion artifacts are primarily caused by patient motion, respiration, and upward creep. Non-rigid body motion artifacts are due to cardiac motion (addressed primarily by cardiac gating) and respiratory motion (addressed by respiratory gating). Rigid body motion artifacts are due to patient motion and cardiac upward creeping.

**Objective:** To test and validate a new proprietary motion correction software program (STASYS by Digirad Corporation) that automatically detects and corrects rigid body motion of the heart in the acquired projection data for cardiac SPECT imaging.

**Design:** Retrospective review of a de-identified patient database.

**Methods:** Two different motion correction software programs were compared - STASYS versus a current industrial standard, MoCo (Cedars-Sinai Medical Center). Results were graded independently by 2 separate readers, a nuclear cardiologist and an experienced certified nuclear medicine technologist. Included in the database were studies performed on Digirad cameras (Digirad Corporation; Poway, CA).

**Results:** Both readers found that the STASYS program outperformed MoCo for correcting medium to large axial motion artifacts and for correcting medium to large transaxial motion artifacts. For both software programs, transaxial motion artifacts were harder to correct for than were axial motion artifacts.

**Conclusions:** STASYS was shown to be effective and to correct a larger percent of cardiac SPECT studies than did MoCo.

**Reviewer's Comments:** This was an industry supported and industry conducted research study, which was fully and openly disclosed. Basically, Digirad's motion correction software appears to operate at least as well as Cedar-Sinai's motion correction software, when applied to scans done by a Digirad camera. The authors acknowledge that we do not know how the 2 software programs will compare when used on data collected by other camera systems. (Reviewer-Thomas F. Heston, MD).

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Keywords: Myocardial Perfusion Imaging, SPECT, Motion Correction

Print Tag: Refer to original journal article
WBC imaging using 111In or 99mTc labeling is currently the best scintographic method for diagnosing infections in those with intact immune systems. But it has numerous disadvantages. It is technically demanding and requires skilled personnel; it is labor-intensive and not always available; and it involves direct handling of blood products. Also, it requires sufficient leukocytes to label, which may not be possible in severe leukopenia or in very young patients. For musculoskeletal infection, the need for complementary bone marrow or skeletal imaging adds time and expense to the procedure and is a particular burden for elderly or debilitated patients. Neutrophils constitute the majority of circulating WBCs and, therefore, make up the majority of leukocytes labeled. Therefore, WBC scintigraphy is sensitive for bacterial infections, but it is nonspecific since nonbacterial inflammatory conditions, such as acute rheumatoid and gouty arthritis, also incite a neutrophilic response. WBC scintigraphy is not useful for detecting Pneumocystis carinii pneumonia and tuberculosis, which do not involve a neutrophilic recruitment to the site of inflammation. Efforts to overcome the limitations of in vitro labeling currently focus on labeling antibodies, antibody fragments, peptides, and cytokines that bind to various receptors on WBCs. None of these are available in the United States, even on an investigational basis. PET has the advantage over single-photon gamma camera imaging of higher resolution and more precise location of abnormalities. Semiquantitative analysis, readily available with PET, is less feasible with conventional gamma camera imaging. Quantitation could be useful for differentiating infectious from noninfectious conditions or for monitoring response to therapy. Although exquisitely sensitive for infection, 18F-FDG is not specific. The labeling efficiency of the potentially more specific 18F-FDG leukocytes is significantly lower than that of 111In-oxine leukocytes. Also, the short half-life (110 minutes) of 18F makes the procedure practical only at those institutions that can do labeling on site. Locke et al recently labeled alpha peptide with 64Cu, which has a half-life of 13 hours. In vitro, this labeled peptide had a high binding affinity for human neutrophils. In the May issue of The Journal of Nuclear Medicine, Liberatore et al reported on a 99mTc-labeled antimicrobial peptide. Uptake in a Staphylococcus aureus infection model was significantly higher than uptake in sterile inflammation.

**Reviewer's Comments:** There is still no ideal infection-specific imaging method, but based on current clinical investigations, nuclear medicine may be getting close. Dr. Palestro, editor of this essay, presented the latest news on this front to a packed session at this year's annual Society of Nuclear Medicine meeting in June. The key points are touched on in this teaching editorial, which I recommend reading in the original. (Reviewer-C. Richard Goldfarb, MD).

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Keywords: Infection Imaging

Print Tag: Refer to original journal article
The use of beta-blockers does not diminish the sensitivity of vasodilator stress myocardial perfusion studies.

**Background:** Vasodilator stress myocardial perfusion imaging (vMPI) is an invaluable noninvasive tool in the assessment of coronary artery disease (CAD). Although there have been studies showing that cardiac medications may limit the sensitivity of vMPI, the results have been equivocal, likely due to variation in study design (beta-blocker use does not mimic real clinic situations), studies suffering from small patient numbers, and studies not looking at one cardiac medication in particular.

**Objective:** To determine whether beta-blockers decrease the sensitivity of vMPI in detecting clinically significant CAD.

**Methods:** 555 intermediate- to high-risk patients referred for vMPI because of suspected CAD were evaluated, 52% of whom were on beta-blocker therapy. A second, low-risk group of 329 patients was evaluated, 32% of whom were on beta-blockers. Survival analysis was also performed for a third group of 2646 patients (42% on beta-blockers) who had normal perfusion studies and were not referred for cardiac catheterisation (cath). This analysis was included to overcome cath-referral bias of those with abnormal vMPI studies. A 1-day dual-isotope protocol with adenosine was used in most cases. Global and individual vascular territory scoring using the 17-segment model was performed.

**Results:** There was no significant difference among correlative findings between cath and vMPI among patients on beta-blockers versus those who were not. The same was found for patients in the low-risk group. Although beta-blocked patients had slightly more reversible defects and defects involving the LAD territory, this difference was not statistically significant. Among patients with normal perfusion studies and no cath referral, survival rates were almost identical for those on beta-blockers versus those who were not.

**Conclusions:** Beta-blocker therapy does not diminish the sensitivity of vMPI.

**Reviewer’s Comments:** Although retrospective, this interesting study provides compelling evidence from a large number of patients, both for those at low risk and those at intermediate-high risk for CAD, that beta-blockade does not limit the sensitivity of the test. This study is quite clinically relevant because patients often have beta-blockade therapy on board prior to vMPI for various reasons (were not held by physician; the patient, during daily routine, inadvertently took them), raising the question as to whether the vasodilator stress was adequate. Despite the limitations of the study, particularly one which addresses that patients on beta-blockers tend to be on other medications that could potentially adversely affect the vasodilatory effects of stress agents, still no difference was seen in vMPI studies of these patients who were on other cardiac medications. (Reviewer-Damita Thomas, MD).

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Keywords: Myocardial Perfusion Imaging, Effect of Beta-Blockers

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