V/Q lung scintigraphy appears to be more reliable than pulmonary CTA for imaging suspected cases of pulmonary embolism in pregnant women.

There has been some suggestion that pregnant patients with suspected pulmonary emboli are not good candidates for pulmonary CT angiography (CTA) due to poor exam quality. This has not been an issue with ventilation perfusion (V/Q) lung scintigraphy.

**Objective:** To determine the frequency of nondiagnostic-quality CTA exams in pregnant patients with suspected pulmonary embolism (PE) with an attempt to gain insight into possible causes for this problem.

**Design:** Retrospective study.

**Methods:** The authors identified 25 pregnant individuals who underwent 28 CTA exams along with 25 other pregnant patients who underwent 25 V/Q exams during a 2-year study interval.

**Results:** 10 of the 28 CTA exams (36%) and only 1 of the 25 V/Q exams (4%) were inadequate for diagnostic purposes ($P<0.01$). Inadequate CTA exams were much more frequent in pregnant (36%) than nonpregnant women (2%) with suspected PE. After careful image analysis, the primary reason for the inadequate exam in pregnant individuals was mixing of the non-contrast blood of the inferior vena cava (IVC) with the contrast bolus coming from the superior vena cava. The known increased pressure and flow from the IVC during pregnancy account for this problem. Nondiagnostic CTA exams in this study showed a mean main pulmonary artery attenuation level of 111 HU compared to 228 HU for diagnostic exams.

**Conclusions:** For the diagnosis or exclusion of PE in pregnant women, the imaging technique of choice is lung scintigraphy because it more frequently produces diagnostic images than does pulmonary CTA. However, pulmonary CTA may be the technique of choice if the image quality can be optimized through adapted breathing maneuvers and contrast administration.

**Reviewer’s Comments:** I would also add that the other important reason to image these young patients with V/Q exams as opposed to CTA is the much lower radiation dose to breast tissue (and perhaps a consideration for the fetus, as well). The authors seem to hedge a little in their concluding statement. Their data certainly supports the initial use of V/Q imaging in this setting. (Reviewer-David Bushnell, MD).

© 2010, Oakstone Medical Publishing

Keywords: Pulmonary Embolism, Pregnancy, CTA vs V/Q Scintigraphy

Print Tag: Refer to original journal article
Background: Dobutamine is an alternative to vasodilator stress in patients with suspected coronary artery disease (CAD) who are unable to undergo exercise stress testing. Although human studies have not shown a difference in the prognostic value of vasodilator versus dobutamine stress, animal studies suggest that perfusion heterogeneity is less pronounced with dobutamine when using Tc-99m sestamibi as the perfusion agent.

Objective: To quantify the difference, if any, between sestamibi uptake induced by dipyridamole versus dobutamine in patients with suspected CAD.

Design: Consecutive prospective cohort.

Participants: 25 patients presenting with suspected CAD. Exclusion criteria were known CAD, other cardiac disease (including rhythm disturbances), valvular heart disease, cardiomyopathy, and contraindications to dipyridamole or dobutamine.

Methods: All patients underwent rest, dipyridamole stress, and dobutamine stress myocardial perfusion imaging. The 3 acquisitions were performed 24 hours apart and in random order. Coronary angiography was performed in all patients within 15 days of scintigraphic imaging. The uptake ratio of Tc-99m sestamibi was calculated for the left anterior descending, circumflex, and right coronary artery territories and was expressed as a percent of baseline uptake.

Results: Of the 25 patients, 20 had significant CAD (1-vessel disease, n=8; 2-vessel disease, n=6; 3-vessel disease, n=6) resulting in 38 vascular territories with CAD. On a per-patient basis, SPECT sensitivity was 85% for dipyridamole versus 70% for dobutamine. On a per-vessel basis, SPECT sensitivity was 66% for dipyridamole versus 42% for dobutamine (P<0.05), and specificity was 92% versus 86%, respectively, for dipyridamole versus dobutamine. The uptake ratio difference between CAD versus no-CAD territories was larger using dipyridamole compared to dobutamine.

Conclusions: Dobutamine stress induces less Tc-99m sestamibi uptake heterogeneity compared to dipyridamole stress in patients with CAD compared to patients with normal coronary arteries.

Reviewer’s Comments: The results of this study suggest that pharmacologic stress utilizing dipyridamole is superior to dobutamine in the identification of normal versus stenotic coronary artery territories when performing Tc-99m sestamibi myocardial perfusion imaging. (Reviewer-Thomas F. Heston, MD).

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Keywords: Myocardial Perfusion Imaging, Stress Induction, Sestamibi Uptake

Print Tag: Refer to original journal article
Recurrence Risk Increased for Multifocal Micropapillary Cancer

Recurrence After Treatment of Micropapillary Thyroid Cancer.
Ross DS, Litofsky D, et al:
Thyroid 2009; 19 (October): 1043-1049

Among patients with micropapillary thyroid cancer (primary <1 cm), those with multifocal disease have a small but definite risk of recurrence.

Background: Micropapillary thyroid cancer (primary papillary cancer <1 cm at its maximal diameter) is common worldwide. In the United States, the prevalence is increasing yearly, and the annual incidence has more than doubled since 1972. Although mortality rates associated with micropapillary thyroid cancers are very low, locoregional recurrence is relatively common, and uncertainty exists regarding the role of surgery and radioiodine. The American Thyroid Association guidelines recommend radioiodine for “selected patients with stage I disease, especially those with multifocal disease, nodal metastases, extrathyroidal or vascular invasion, and/or more aggressive histologies.” The National Thyroid Cancer Treatment Cooperative Study Group established a registry in 1987 to prospectively follow up thyroid cancer patients. Despite the benefits of I-131 for stage II, III, and IV disease, no clear added value for I-131 has been demonstrated for patients with stage I disease.

Objective: To report outcome data from patients with micropapillary thyroid cancer.

Design: The registry was analyzed for recurrences in unifocal versus multifocal micropapillary cancer, with versus without nodal disease, less-than-near-total thyroidectomy versus total near-thyroidectomy, and no adjuvant I-131 versus postoperative adjuvant I-131. Of 698 patients with micropapillary cancer, 27 had gross extrathyroidal invasion, 9 had distant metastases, and 1 had both gross extrathyroidal invasion and distant metastases. The remaining 661 patients had intrathyroidal tumors. The mean time to recurrence was approximately 3 years.

Results: 30 patients (6%) had recurrences, and there was 1 distant metastasis. In patients who did not receive I-131 therapy, recurrence was more common with multifocal disease versus unifocal disease (7% vs 2%). But I-131 did not reduce recurrences in patients with multifocal disease or patients with positive nodes. Patients with positive nodes had more recurrences than node-negative patients, regardless of I-131 use.

Conclusions: Patients with micropapillary multifocal disease have a small but definite risk of recurrence, which is reduced by total or near-total thyroidectomy compared with less surgery. It is not certain whether I-131 ablation of thyroid remnants is advantageous in patients with micropapillary cancer.

Reviewer’s Comments: This paper leaves some important questions unanswered, but it eliminates at least 1 important misconception — multifocal cancers <1 cm do not recur after thyroidectomy. An important unanswered question that remains is, “What is the role, if any, for radioiodine ablation in these patients?” For now, I will go with the American Thyroid Association guidelines, which recommend ablation for stage I patients with multifocal disease or risk factors such as nodal metastases, aggressive histologies, or vascular invasion. (Reviewer-C. Richard Goldfarb, MD).

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Keywords: Thyroid Cancer, Prognosis

Print Tag: Refer to original journal article
In thyroid cancer, prophylactic lymph node dissection detects low-risk patients benefitting most from I-131 ablation and helps determine the best dose in all patients.

The recently published 2009 American Thyroid Association Guidelines for Management of Thyroid Nodules and Differentiated Thyroid Cancer includes several noteworthy revisions in regard to surgical and consequent ablative treatment of thyroid cancer. A 2007 study of >50,000 patients demonstrated significantly improved outcomes, less recurrence, and higher survival rates after thyroidectomy versus lobectomy for tumors >1 cm. This large study should end the debate about total thyroidectomy versus lobectomy. The new guidelines distinguish between prophylactic neck dissection (for clinically and radiologically node-negative patients) and therapeutic neck dissection (for patients with evidence of local node involvement). Central and lateral neck dissection should be performed for patients with clinically involved central or lateral neck nodes. This is based on evidence that therapeutic neck dissection enhances the efficacy and reduces the need for repeated I-131 treatment. However, prophylactic neck dissection is of uncertain benefit. Prophylactic central compartment neck dissection has never been shown to definitely increase the proportion of patients documented with unmeasurable thyroglobulin levels postoperatively, but logically, there seem to be benefits to the dissection. The new guidelines state that operative inspection without dissection of the central compartment is not sensitive for detecting metastatic nodes. Ultrasound detection of nodes in the central compartment is also poor. Therefore, prophylactic lymph node dissection appears to be the best method of nodal staging. The advantage of precise staging of low-risk patients is that I-131 use can be modified by the presence or absence of lymph node metastases. In 82 patients with small primary tumors, central neck dissection revealed more aggressive tumors than suspected in 15% and provided evidence in favor of radiiodine therapy. Radioiodine was avoided for another 15% of cases. Also, >25% of tumors will show no radioiodine uptake, so surgery is necessary for these cases. Local lymph node metastasis is an independent risk factor for decreased survival for patients aged >45 years.

Conclusions: The evidence favoring central compartment neck dissection is growing, assuming the surgeon is skilled and experienced. More accurate staging would detect low-risk patients who would benefit from I-131 ablation and help determine the best dose of I-131 in all patients undergoing ablation.

Reviewer’s Comments: The updated guidelines devote much attention to precise surgical staging to tailor I-131 treatment to each patient. The sharpest surgical debate involves central and lateral compartment neck node dissection. The same trend toward enhanced staging accuracy is reflected in the new American Thyroid Association recommendation for pre-ablation whole-body radioiodine scanning to refine the ablative I-131 dose. (Reviewer-C. Richard Goldfarb, MD).

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Keywords: Thyroid Nodules, Differentiated Thyroid Cancer, Management

Print Tag: Refer to original journal article
Hybrid SPECT/CT is now available, and evidence for added benefit in imaging bone metastases is beginning to be reported. Utsunomiya and colleagues demonstrated that SPECT/CT allowed fewer equivocal interpretations, less interobserver disagreement, and greater accuracy in differentiating benign from malignant bone lesions when compared to separate SPECT and CT images or planar and SPECT images. SPECT/CT permitted classification of benign versus malignant in 17 of 82 lesions for 1 observer and in 8 of 82 for another observer. Romer and colleagues studied 52 indeterminate skeletal lesions on SPECT and found it possible to classify them as benign or malignant with SPECT/CT in all but 4 patients. But PET/CT may compete. Available PET tracers include 18F-fluoride and 18FDG. 18F-fluoride is bone-specific, while 18FDG is tumor-specific. Comparisons of 18F-fluoride PET and planar or SPECT 99mTc-MDP show better diagnostic accuracy for 18F. In a 1999 study of 34 patients with breast cancer, 18F detected 64 metastases in 17 patients, while 99mTc-MDP detected 29 metastases in 11 patients. The greatest benefit of PET is in the spine and pelvis, but this was compared to planar rather than SPECT for MDP. Schirrmieister and colleagues then reported on 53 patients with lung cancer. Of the 12 patients with bone metastases, there were 6 false-negatives for SPECT and no false-negatives for 18F-fluoride PET. The difference between PET and SPECT was not significant, suggesting that the differences between MDP and 18F-fluoride PET were only differences in the tracers. Looking at 103 patients with lung cancer, the same group found a statistically significant increase in accuracy with 18F-fluoride PET compared to SPECT but at higher costs. It has also been reported that when 18F is combined with CT as hybrid PET/CT, accuracy is improved compared to SPECT alone. A prospective study of 500 patients with breast, prostate, and lung cancers comparing 99mTc-MDP planar with 18F-fluoride PET/CT is currently in progress in the United States.

**Reviewer's Comments:** Many centers are using FDG PET/CT for staging and eliminating bone-specific scintigraphy. The data tend to support such an approach initially for staging most cancers, but there is the frequent indication for evaluating pain that is suspected to be skeletal. For this, a bone-specific agent may be better than FDG, even combined with CT. In fact, a paper presented at the 2009 Radiological Society of North America annual meeting by Rau and colleagues found 18F superior to FDG for both detecting and predicting painful thoracolumbar metastases. (Reviewer-C. Richard Goldfarb, MD).

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Keywords: Skeletal Metastases, SPECT/CT

Print Tag: Refer to original journal article
Background: Brown fat uptake of FDG is now a well-known phenomenon, yet it still may be a source of potential interpretation error especially when seen in only 1 or a few unusual sites on PET. Brown fat represents a heat-regulating mechanism for the body, which explains the increase in visualization of this substance during colder months of the year.

Objective: To review the issue of brown fat uptake with PET-FDG and to provide the reader with some excellent examples of different patterns of this finding.

Results: In most instances, careful correlation with co-registered CT can distinguish between FDG signal emanating from fat as opposed to lymph nodes or other soft tissues that could represent tumor. CT densities for fat range from -50 to -150 HU. The typical locations for brown adipose include supraclavicular, mediastinal, neck, paravertebral, and perinephric regions. Other more atypical locations include posterior neck, retrocrural area, and axillary sites. The authors point out that perhaps the most important method of reducing brown fat activity is to ensure that patients are kept warm on arrival and during and following injection of FDG. They recommend room temperatures of 75 degrees.

Conclusions: PET and CT findings must be correlated to prevent misinterpretation of brown fat uptake of FDG, especially when seen in atypical locations.

Reviewer's Comments: Brown fat is known to be regulated by sympathetic innervation, and a number of studies have demonstrated that the beta-blocker propranolol given 1 to 2 hours before FDG injection can effectively suppress brown fat uptake. Benzodiazepines also reduce brown fat FDG activity levels. Like most centers, we routinely give patients Xanax prior to injection but still occasionally see uptake in brown fat. (Reviewer-David Bushnell, MD).

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Keywords: PET-FDG, Brown Fat, Locations

Print Tag: Refer to original journal article
Gated SPECT estimates of left ventricular ejection fraction and end diastolic volume are highly reproducible in patients with atrial fibrillation.

**Objective:** To determine the reproducibility of myocardial perfusion gated-SPECT for calculation of end-diastolic volume (EDV), end-systolic volume (ESV), and left ventricular ejection fraction (LVEF) in patients with atrial fibrillation (AF).

**Methods:** 115 consecutive patients with AF (mean age, 69 years) from 3 participating hospitals were included in the study. All patients underwent 2 separate gated SPECT acquisitions at rest with at least a 30-minute interval between them. Quantitative data were obtained using both the Cedars-Sinai QGS program and Emory Cardiac Toolbox (ECT) software algorithms. Average resting dose given before the first rest study was 24 mCi of either Tc-99m sestamibi (n=101) or Tc-99m tetrofosmin (n=14). R-R interval tolerance was set at 90%.

**Results:** Heart rate was similar in both studies: 75 ± 15 beats/minute versus 73 ± 16 beats/minute. QGS yielded an LVEF of 54.4%/53.8%, an EDV of 100 mL/101.5 mL, and an ESV of 51 mL/52.3 mL. Using ECT, the LVEF was 63.6%/62.9%, EDV was 125.8 mL/127.4 mL, and ESV was 54.1 mL/56.3 mL. Correlation between the 2 acquisitions was high (r >0.948) for both methods for LVEF, EDV, and ESV. Interassay correlation coefficients for each method (QGS vs ECT) were 5.3% versus 4.8% for LVEF, 4.9% versus 5.2% for EDV, and 9.9% versus 12.8% for ESV. When the ESV was <20 mL, the coefficient of variation was >20% for both QGS and ECT.

**Conclusions:** In patients with atrial fibrillation, the reproducibility of LVEF and EDV with gated-SPECT in patients with AF is excellent. The reproducibility of ESV measurements is suboptimal, particularly when ESV is <20 mL.

**Reviewer’s Comments:** With current technology, gated imaging gives highly reproducible estimates of a patient’s LVEF, EDV, and ESV, even in patients in atrial fibrillation. The greatest variation (worst reproducibility) was seen in the ESV measurements, especially when the ESV was <20 mL. Compared to echocardiography and MR, the researchers hypothesize that gated SPECT may possibly be the best tool to estimate LVEF and ventricular volumes in patients with atrial fibrillation. (Reviewer-Thomas F. Heston, MD).

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Keywords: Atrial Fibrillation, Myocardial Perfusion Gated-SPECT

Print Tag: Refer to original journal article
Prototype Scanner Significantly Improves Localization

The Imaging Performance of a LaBr₃-Based PET Scanner.

Daube-Witherspoon ME, Surti S, et al:

Phys Med Biol 2010; 55 (January 7): 45-64

Time-of-flight PET improves image quality by decreasing the noise level in the reconstructed image and also by decreasing the number of required iterations.

Background: Current PET systems are limited by the physical properties of the detector materials. New scintillators are being incorporated that will improve both timing and energy resolution capabilities.

Objective: To describe the performance of a prototype time-of-flight PET scanner that uses lanthanum bromide (LaBr₃) detectors.

Methods: The PET scanner uses a total of 38,880 4x4x30-mm LaBr₃ detectors arranged in 24 modules, yielding an axial field of view of 25 cm, although for this investigation, that was limited to 19 cm. The ring diameter is 93 cm and the detectors are sampled by 432 photomultiplier tubes. The system was calibrated so that detector-related timing differences were compiled in a lookup table. The count rate dependence of these values was evaluated. Detector-related energy shifts were also measured and compensated, yielding an overall energy resolution of 7%. Coincidence events were acquired in list mode and were reconstructed using an iterative ordered subset algorithm that included the time-of-flight modeling and compensation for spatial resolution losses. Standard corrections are made for random coincidences and first-order scattered radiation. Performance tests were based on the NEMA NU2-2001 standard and included spatial resolution, count sensitivity, scatter fraction, and phantom contrast measurements. Simulation studies were also performed to help separate performance issues resulting from limitations of the electronics used in the prototype device.

Results: The in-plane spatial resolution at the center of the field was 5.8 mm, with an axial resolution of 6.3 mm. The count sensitivity was about 2 cps/kBq, which is lower than current PET systems that use lutetium-based detectors that have better absorption properties. The scatter fraction for a 35-cm cylinder was only 38% when the energy threshold was set to 470 keV. The timing resolution was 375 picoseconds, which is a substantial reduction over current time-of-flight systems. This lead to somewhat improved contrast and faster reconstruction convergence with less image noise. The improved energy resolution (7% vs 12%) also resulted in improved contrast.

Conclusions: The LaBr₃ prototype delivers good overall PET performance with excellent time-of-flight and energy resolution. Further studies are needed to optimize the performance through improved electronics, reconstruction software, and energy level selections.

Reviewer's Comments: The excellent energy resolution and timing afforded by LaBr₃ are offset somewhat by its lower detection efficiency when compared to LSO/LYSO. However, this prototype may well result in a commercial PET scanner in the near future and will certainly stimulate the development of other new approaches. We can expect future PET imaging systems to continue providing new levels of image quality. (Reviewer-Mark T. Madsen, MD).

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Keywords: Time-of-Flight PET, Detectors, LaBr₃

Print Tag: Refer to original journal article
Sarco-Osteopenia to Help Predict Fracture Risk

Beyond FRAX: It’s Time to Consider “Sarco-Osteopenia”.

Binkley N, Buehring B:

J Clin Densitom 2009; 12 (October-December): 413-416

Sarcopenia (loss of skeletal muscle mass) plays a key role in fracture risk and can be diagnosed by measuring muscle mass by dual-energy X-ray absorptiometry.

Recognizing that muscle and bone weakness along with overall frailty contribute to high fracture risk, the World Health Organization (WHO) crafted the so-called FRAX® system which predicts 10-year fracture probability. Fracture risk increases markedly with age, even at the same bone mineral density (BMD), and can be quantified using FRAX. In particular, muscle weakness contributes to age-related fracture risk. Muscle mass loss (recently coined “sarcopenia”) plays a key role in fracture risk. Sarcopenia, which describes the age-related decline in amount and function of skeletal muscle, can be diagnosed by measuring muscle mass by dual-energy X-ray absorptiometry (DXA). Sarcopenia would be defined as ≥2 standard deviations below young normal, similar to the approach used in the classification of osteopenia and osteoporosis. The advantages of DXA for evaluation of sarcopenia are that it is quantitative, available, imparts minimal radiation, and is inexpensive. Patients with both low bone mass and low muscle mass and/or performance could be diagnosed with sarco-osteopenia or “sarco-osteoporosis.” This combination classification would better identify those at higher fracture risk. Combining loss of bone and muscle strength into a single diagnosis of “sarco-osteopenia” is not only logical, but it is already documented in the literature. Lang and colleagues recently demonstrated that combining muscle size with age, height, body mass index, and BMD maximized the true-positive rate of identifying those with hip fracture. To bring the sarco-osteopenia concept to clinical care, DXA may well be an excellent technology to identify sarco-osteopenia. Appendicular lean mass could be determined by total body measurement at the time of routine DXA. Even hip DXA can estimate lean muscle mass.

Reviewer’s Comments: FRAX attempts to reduce over-reliance on bone densitometry measurements for predicting fracture risk and optimizing pharmacologic intervention. Measuring sarco-osteopenia is a clever BMD method of further enhancing and objectifying fracture risk. Drs Binkley and Buehring merit recognition for getting the BMD measurement of sarco-osteopenia out of the research closet and priming it for clinical trials. At the same time, they are reinforcing the premier role of densitometry in fracture prevention. (Reviewer-C. Richard Goldfarb, MD).

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Keywords: Fracture Risk, FRAX, Muscle Mass, Sarco-Osteopenia

Print Tag: Refer to original journal article
Physiologic FDG Uptake Common in Tonsils, Extraocular Muscles

[18F]Fluorodeoxyglucose-PET/CT Differentiation Between Physiological and Pathological Accumulations in Head and Neck.
Nakamura S, Okochi K, et al:
Nucl Med Commun 2009; 30 (July): 498-503

In the head and neck region of the body, increased FDG activity is almost always seen in normal tonsils and submandibular glands.

**Background:** Evaluation of PET images in the head and neck may be quite difficult for a variety of reasons, including the variable physiologic FDG activity noted in normal structures.

**Objective:** To assess and present the normal physiologic patterns of FDG uptake in the head and neck region of the body.

**Methods:** The authors evaluated 112 PET/CT exams during a 1-year study interval in patients referred with head/neck cancer without any prior treatment. PET/CT was performed 1 hour after injection of FDG. Activity on images was considered physiologic if it was symmetric. In addition, sites of increased uptake were confirmed to be physiologic based on clinical follow-up.

**Results:** The mean patient age was 61 years. The tongue and oropharynx accounted for the primary tumor location in 67 subjects. In 7 of 112 patients, FDG uptake was not visible in the primary tumor site. The mean primary tumor SUV\textsubscript{max} in the remaining cases was 12 with a standard deviation of 7. Increased FDG activity was seen in normal tonsils, extraocular muscles, and submandibular glands in all subjects. The authors noted the highest physiologic FDG activity was found in the extraocular muscles (mean SUV\textsubscript{max}, 6.2) and tonsils (mean SUV\textsubscript{max}, 5.4). ROC analysis indicated optimal SUV\textsubscript{max} cutoff to distinguish tumor from physiologic activity to be 4.0 for the parotid gland, 4.5 for the submandibular gland, 5.5 for the sublingual gland, 8.0 for the tonsil, and 4.5 for the vocal cord. No physiologic uptake showed right-to-left (R/L) asymmetry greater than 1.5. Normal submandibular glands showed the greatest R/L levels of asymmetric uptake (mean value, 1.24).

**Conclusions:** This data would be useful for distinguishing primary tumor FDG accumulation from that due to normal physiology.

**Reviewer's Comments:** In this study, using the 8.0-SUV\textsubscript{max} cutoff recommended by the authors for the tonsils resulted in a suboptimal sensitivity for malignancy of 68%. Using a combination of asymmetry plus level of SUV should improve overall accuracy for distinguishing malignancy from normal tissue. However, the authors did not attempt to specifically assess this in their article. (Reviewer-David Bushnell, MD).
**Tau Levels, SPECT Reflect Intensity of AD Process**

*Brain Perfusion SPECT Correlates With CSF Biomarkers in Alzheimer’s Disease.*

Habert MO, de Souza LC, et al:

*Eur J Nucl Med Mol Imaging 2009; October 10 ():* epahead of print

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**Background:** It is well known that beta-amyloid and tau proteins in senile plaques and neurofibrillary tangles are histopathological hallmarks of Alzheimer disease (AD). These markers can be measured from samples of the cerebrospinal fluids (CSF) and have been shown to be of diagnostic and prognostic value in patients with AD. Brain SPECT imaging in these patients, which shows decreased perfusion in the associative posterior cortex, has also been shown to correlate with the degree of cognitive decline.

**Objectives:** To determine if correlation exist between CSF biochemical markers of Alzheimer disease (AD) and brain SPECT imaging.

**Methods:** 31 patients (25 with AD and 6 with mild cognitive impairment) were evaluated retrospectively. Each patient underwent lumbar puncture for the quantification of beta-amyloid and tau proteins (total and phosphorylated). Each patient also underwent brain SPECT imaging within 10 days of lumbar puncture. Voxel-based technology was used to quantitate blood flow on the scans.

**Results:** All patients demonstrated mild to severe perfusion deficits characteristic of AD. Beta-amyloid protein levels were characteristically decreased in 28 of 31 patients. No significant correlation was found between these levels and imaging. The total tau protein levels were characteristically increased in the 18 of 31 patients and the phosphorylated tau protein levels were increased in 28 of 31 patients, with these levels showing a significant correlation with imaging findings.

**Conclusions:** These results suggest that tau protein levels correlate with brain perfusion deficits on SPECT, reflecting the degree of disease progression in patients with AD.

**Reviewer's Comments:** This interesting study suggests that brain SPECT imaging correlates with the well-established CSF markers of AD in reflecting the degree of cognitive decline. It is interesting that the beta-amyloid biomarker did not correlate with imaging parameters. The authors purport that this may be due to the well-known phenomenon of early plateauing of beta-amyloid protein in the course of AD. However, this could likely be fleshed out if more patients were studied. (Reviewer-Damita Thomas, MD).

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Keywords: Alzheimer Disease, Biochemical Markers, SPECT

Print Tag: Refer to original journal article
18F-fluoride PET reflects the decreased bone turnover rate following alendronate therapy in patients with glucocorticoid-induced osteoporosis.

**Background:** Patients undergoing therapy with glucocorticoids are at a significant risk of osteoporosis. Significant risks can occur with therapy doses as little as 6 mg/day for 6 months. As such, alendronate has been advocated for these patients. Prior studies have shown a correlation between fluoride imaging and bone metabolism. However, limited data exist on how regional bone metabolism (spine and hip) is affected by alendronate therapy.

**Objective:** To examine the effect of alendronate on bone metabolism as measured by conventional bone metabolism parameters and by 18F-fluoride PET in patients with glucocorticoid-induced osteoporosis.

**Methods:** 24 postmenopausal women all previously treated with glucocorticoids for various conditions were included. All underwent 18F-fluoride PET scans at baseline and following initiation of alendronate therapy at 3 and 12 months. Serum alkaline phosphate and urinary N-telopeptide levels (markers of bone formation and resorption, respectively) were measured at baseline, and again at 3, 6, 9, and 12 months. Bone mineral density (BMD) was also measured at the left femoral neck and lumbar spine at baseline, 6, and 12 months.

**Results:** At 12 months of alendronate therapy, alkaline phosphate, N-telopeptide, lumbar and femoral neck 18F SUV showed a significant decrease compared to baseline, with a concomitant and significant increase in spine and femoral neck BMD compared to baseline.

**Conclusions:** 18F-fluoride PET reflects the decreased bone turnover that occurs following alendronate therapy in postmenopausal women with glucocorticoid-induced osteoporosis.

**Reviewer's Comments:** The results of this interesting study suggest a correlative relationship between biochemical markers and imaging characteristics of bone metabolism following alendronate therapy in glucocorticoid-induced osteoporotic patients. The correlations are interesting, in that the expected increase in BMD and decrease in alkaline phosphate/N-telopeptide levels (reflecting increased mineralization and decreasing bone turnover, respectively) are accompanied by a decrease in 18F-fluoride SUV. Although the aim of this investigation was not to determine if 18F-fluoride can be used as a tool to measure the efficacy of alendronate therapy, that would be a clinically relevant issue to address in that it would elucidate whether 18F-fluoride PET could be useful in the management of this patient population. (Reviewer-Damita Thomas, MD).

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Keywords: Glucocorticoid-Induced Osteoporosis, Alendronate, Measuring Effect

Print Tag: Refer to original journal article
Gated SPECT phase indices depict significant mechanical dyssynchrony (MD) in patients with mild-to-moderate left ventricular dysfunction. A third of patients with normal QRS durations show evidence of MD by SPECT.

**Background:** Cardiac resynchronization therapy (CRT) has been shown to improve the outcome of patients with heart failure (HF). However, the use of QRS prolongation as a selection criteria has come into question because other studies have shown that significant mechanical dyssynchrony (MD) can exist despite normal QRS duration. The use of gated myocardial SPECT has been examined as a method to identify the degree of MD. The additional information regarding myocardial perfusion obtained from the study can also be beneficial in the selection process.

**Objective:** To examine MD as determined by gated SPECT, and compare its relationship to QRS duration in patients with mild-moderate left ventricular (LV) dysfunction.

**Methods:** This retrospective cohort study examined patients with normal (>50%), mild-moderate (35%-50%), and severe (<35%) LV function. All patients had SPECT myocardial perfusion imaging (MPI) and ECGs to measure QRS intervals. Phase SD and histogram bandwidth obtained from SPECT MPI studies were used to evaluate the degree of MD. This information was correlated with QRS duration.

**Results:** Patients with mild-moderate LV dysfunction had significantly higher SPECT phase indices of MD than did normals, and patients with severe LV dysfunction had significantly greater indices than those in the mild-moderate cohort. Overall, patients with longer QRS intervals tended to have a greater degree of MD. Significant MD was found in 34 of 93 patients in the mild-moderate cohort and in 21 of 73 patients with normal QRS intervals.

**Conclusions:** Phase data from gated SPECT MPI could be useful in the selection of patients who may benefit from CRT.

**Reviewer's Comments:** The results of this interesting study suggest that the potential of gated myocardial SPECT phase indices in the selection of patients who may benefit from CRT. Currently, selection criteria for CRT include a prolonged QRS duration, in that this measure is used as a surrogate for MD. However, the study showed that up to a third of patients with normal QRS durations showed evidence of MD by SPECT phase indices. This is quite valuable information because it seems to enforce the findings of other studies that QRS prolongation may not be sensitive enough of a measure for MD and that gated SPECT may more accurately do so. Prospective studies demonstrating the ability of gated SPECT indices in the selection criteria are needed to further validate this point. (Reviewer-Damita Thomas, MD).

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Keywords: Heart Failure, Mechanical Dyssynchrony, SPECT vs QRS Interval

Print Tag: Refer to original journal article
CIMT Identifies Severe CAD in Asymptomatic Diabetics

Increased Carotid Intima Media Thickness as a Predictor of the Presence and Extent of Abnormal Myocardial Perfusion in Type 2 Diabetes Mellitus.

Djaberi R, Schuijf JD, et al:

Diabetes Care 2009; November 16 (): epub ahead of print

Increased carotid intima media thickness greatly increases the risk of abnormal myocardial perfusion in patients with type 2 diabetes.

Background: Identifying which asymptomatic patients with type 2 diabetes are at increased risk for coronary artery disease remains challenging.

Objective: To clarify the relationship between carotid intima media thickness (CIMT) and abnormal myocardial perfusion in asymptomatic patients with type 2 diabetes.

Design: Prospective cohort study.

Participants: 98 consecutive asymptomatic patients with type 2 diabetes recruited from an outpatient diabetes clinic, referred for cardiovascular risk stratification.

Methods: Patients underwent adenosine stress-rest gated SPECT myocardial perfusion imaging utilizing Tc-99m sestamibi. CIMT was assessed utilizing high-resolution B-mode ultrasound with a 10-MHz linear transducer. Perfusion images were scored using a 17-segment 5-point scoring system. CIMT was assessed by an experienced sonographer blinded to the clinical information. An increased CIMT was defined as ≥75th percentile of reference values for age and gender category, and a normal CIMT was defined as <75th percentile for age/gender. Abnormal myocardial perfusion was defined as a summed stress score of ≥3 (≥4% of left ventricular myocardium), and severely abnormal myocardial perfusion was defined as a summed stress score of ≥8 (≥12% of left ventricular myocardium).

Results: An increased CIMT was an independent predictor of the extent of abnormal perfusion (P<0.001). Patients with an increased CIMT were 8 times more likely to have abnormal myocardial perfusion compared to patients with a normal CIMT (75% vs 9%, respectively). Severely abnormal perfusion was 9 times more common in patients with an increased CIMT than in those with normal CIMT (28% vs 3%, respectively).

Conclusions: Elevated CIMT is significantly related to the presence and extent of abnormal myocardial perfusion.

Reviewer's Comments: The measurement of carotid intima media thickness is relatively straightforward and potentially has a role for being a standard part of a nuclear cardiology clinic. (Reviewer-Thomas F. Heston, MD).

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Keywords: Diabetes, Carotid Intima Media Thickness, Myocardial Perfusion

Print Tag: Refer to original journal article
Rest Imaging Not Required With Normal Stress Study

Chang SM, Nabi F, et al:

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The mortality rate for patients with a normal stress-only gated SPECT scan is similar to that of patients with a normal stress-rest gated SPECT scan.

Objective: To determine the mortality rate of patients with a normal stress-only gated SPECT myocardial perfusion scan compared to patients with a normal stress-rest gated SPECT.

Design: Retrospective review.

Participants: Consecutive patients referred for nuclear myocardial perfusion imaging for clinical reasons.

Methods: All-cause mortality was determined in the 16,854 patients who had a normal gated stress SPECT. The median follow-up was 4.5 years. A stress-only protocol utilizing Tc-99m sestamibi or tetrofosmin was used in 8034 patients (47.6%), and a stress-rest protocol was used in 8820 patients (52.4%). A stress-only gated SPECT study was determined to be normal only when the myocardial perfusion, left ventricular (LV) size, wall motion, and LV ejection fraction (LVEF) were all normal.

Results: The overall unadjusted annual mortality rate was 2.57% in patients with a normal stress-only SPECT study and was 2.92% in patients with a normal stress-rest SPECT (P=0.02). After adjusting for baseline clinical characteristics, there was no significant difference found in patient mortality between the 2 imaging protocols. Patients in the stress-only group received a 61% lower radiopharmaceutical dosage. The independent predictors of worse survival included age, male gender, diabetes, history of coronary artery disease, and inability to exercise (all P<0.001). The type of SPECT protocol used (stress-only vs stress-rest) was not an independent predictor of survival.

Conclusions: Patients with a normal stress-only gated SPECT scan have a mortality rate similar to that of patients with a normal stress-rest gated SPECT scan. Stress-only gated SPECT exposes patients to less than half the radiation as patients undergoing stress-rest imaging.

Reviewer's Comments: The authors of this study state in the methods section that rest imaging was routinely performed prior to stress imaging if the patient presented in the afternoon or reported caffeine intake within 12 hours and was scheduled for pharmacologic stress. Then later, they state that rest imaging was only performed if the stress images were either abnormal or equivocal. Thus, the patient population is not quite homogeneous, and not all stress images were evaluated in the absence of rest images. Nonetheless, their results provide strong evidence that a normal stress-only gated SPECT carries a similar prognosis in terms of all-cause mortality to studies determined to be normal on the basis of stress-rest gated SPECT imaging. Note that a stress-only gated SPECT scan was determined to be normal only when the LVEF, LV size, wall motion, and perfusion were normal. (Reviewer-Thomas F. Heston, MD).

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Keywords: Coronary Artery Disease, Myocardial Perfusion vs Mortality

Print Tag: Refer to original journal article
**Abnormal Perfusion Linked to Impaired Endothelial Function**

*Endothelial Dysfunction in Diabetic Patients With Abnormal Myocardial Perfusion in the Absence of Epicardial Obstructive Coronary Artery Disease.*


Myocardial perfusion abnormalities in the absence of obstructive coronary artery disease are associated with endothelial dysfunction in asymptomatic patients with diabetes mellitus.

**Background:** In approximately 20%-40% of diabetic patients, myocardial perfusion abnormalities are not associated with obstructive epicardial coronary artery disease (CAD). Endothelial dysfunction is a systemic condition in which arteries and arterioles do not dilate fully in response to vasodilatory substances and is thought to precede the development of atherosclerosis.

**Objective:** To determine whether myocardial perfusion abnormalities in the absence of obstructive epicardial CAD are associated with endothelial dysfunction in asymptomatic patients with diabetes mellitus.

**Methods:** 130 asymptomatic diabetic patients were screened prospectively for cardiovascular disease. In addition to clinical screening that focused on traditional risk factors, all patients underwent SPECT myocardial perfusion imaging and noninvasive coronary angiography with multislice CT. SPECT studies were scored semiquantitatively using the 17-segment model proposed by the American Society of Nuclear Cardiology. Studies were considered abnormal if the summed stress score (SSS) was ≥3. Each patient also was evaluated for endothelial dysfunction by looking at flow-mediated dilation (FMD) of the brachial artery using ultrasound. This was done by comparing the brachial artery lumen diameter following distal flow obstruction with a blood pressure cuff to the diameter at baseline. Patients with obstructive CAD shown on CT (n=35) were excluded from further analysis.

**Results:** Of the 95 patients included in the study, 30 (32%) had abnormal myocardial perfusion. Moderate abnormalities occurred in 25 patients, and severe abnormalities (SSS ≥8) occurred in 5. Perfusion defects were reversible in 14 patients (47%), were partially reversible in 6 (20%), and were fixed in 10 (33%). Mean FMD was lower in patients with myocardial perfusion abnormalities than in patients without (3.6% ±2.4% vs 6.4% ±2.6%; *P* < 0.001). Hemoglobin A1c, hypercholesterolemia, and FMD were each independent predictors of the extent of myocardial perfusion abnormality. There was no association between coronary artery calcium score and myocardial perfusion abnormality.

**Conclusions:** Myocardial perfusion abnormalities are common in asymptomatic diabetic patients without CAD and are associated with endothelial dysfunction.

**Reviewer’s Comments:** This study is an interesting companion to the DIAD study published in the *Journal of the American Medical Association*, April 17, 2009, which showed no difference in cardiac event rates for asymptomatic diabetic patients who underwent myocardial perfusion imaging versus patients who did not. Taken together, they suggest that, although myocardial perfusion abnormalities represent real pathology even in the absence of obstructive CAD, good medical management is adequate in this population regardless of the presence of perfusion abnormalities. (Reviewer-Shayne Squires, MD).

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Keywords: Diabetes, Myocardial Perfusion Imaging, Endothelial Dysfunction

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Hematologic toxicity following high-dose radioiodine therapy for high-risk thyroid cancer appears to resolve if dosimetry limits are followed.

**Background:** The European Association of Nuclear Medicine (EANM) has published a standard operating procedure for determining the maximum tolerable dose of I-131 that can be administered for differentiated thyroid cancer, such that the absorbed blood dose is 2 Gy.

**Objective:** To determine the safety and effectiveness of treating advanced thyroid cancer with the maximum tolerable dose (MTD) of I-131 as determined by pretherapeutic dosimetry in accordance with the recommendations of the EANM.

**Methods:** The medical records of 10 consecutive patients treated for advanced thyroid cancer at a tertiary care center were reviewed. Patients who were expected to benefit from higher-than-standard I-131 activity were selected. Dosimetry was performed during the week prior to therapy by administering 9 to 11 MBq of I-131 orally followed by collecting and counting blood activity at 2, 6, 24, 48, 72, 96, and 144 hours after administration. Whole-body scans were also performed at each time.

**Results:** Among the 10 patients, 13 treatments were administered. Six of 10 patients had received ≥1 prior radioiodine therapies. One patient had only bone metastasis. All other patients had pulmonary metastases. One patient also had brain metastasis, and another had hepatic and sacral metastasis. The median calculated MTD was 17 GBq (range 6.6-31.3 GBq). In 9 of 13 therapies, the dose was reduced below the calculated MTD by an average of 27% (9%-44%). Reasons for dose reductions included staff safety, poor patient condition, or diffuse pulmonary metastases. The median administered dose was 14 GBq (range 7-21.4 GBq). Despite antiemetic treatment, posttherapy side effects included nausea (n=5), vomiting (n=3), and sialadenitis (n=3). In the first month after treatment, leukocyte counts decreased a median of 57%, and platelet counts decreased a median of 44%. Erythrocyte counts decreased a median of 10% by the second month. Blood counts normalized by 3 months. Median follow-up was 24 months (range 1-84 months). One patient died of pulmonary embolism, and 1 was lost to follow-up. The remaining 8 patients are currently alive. CT follow-up was available after 7 of the therapies. Lesion size was reduced following 5 treatments and unchanged following 2.

**Conclusions:** Treatment with high-dose radioiodine therapy guided by dosimetry was safe and well-tolerated in a small cohort of patients and resulted in radiologic response in most.

**Reviewer's Comments:** The results of this study suggest that permanent hematologic toxicity is less likely following high-dose radioiodine therapy provided the 2-Gy blood-absorbed dose limit is observed. Based on other studies, there remains a significant risk of salivary gland symptoms. (Reviewer-Shayne Squires, MD).

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**Keywords:** Thyroid Cancer, I-131, Dosimetry

**Print Tag:** Refer to original journal article
68Ga-DOTATATE uptake in bronchial carcinoids is higher in lower grade tumors than in higher grade tumors.

**Background:** Bronchial carcinoids comprise 1% to 2% of all lung malignancies. Their malignant potential ranges from low-grade typical carcinoids to more malignant large and small cell neuroendocrine tumors (NETs). They typically carry somatostatin receptors on their surface, which can be targeted with somatostatin analogs such as 111In-pentetreotide. 68Ga-DOTATATE is an analog of somatostatin labeled with a positron-emitting isotope for PET imaging. It has been previously compared with FDG in gastroenteropancreatic NETs.

**Objective:** To compare the uptake of 68Ga-DOTATATE and 18F-FDG in pulmonary NETs and to correlate uptake with tumor grade and histology.

**Methods:** In this retrospective study, findings from 18 consecutive patients with confirmed pulmonary NETs were reviewed. Each patient underwent PET/CT scanning with 68Ga-DOTATATE and 18F-FDG. Scans were performed within 6 weeks of each other with no therapy during the interval between scans. Each patient underwent scanning for staging of primary pulmonary NET or staging of recurrent tumor. Tumors were classified according to World Health Organization guidelines as typical bronchial carcinoid, atypical carcinoid, large cell pulmonary NET, small cell NET of the lung, and non-small cell lung cancer with neuroendocrine differentiation.

**Results:** Typical carcinoids showed more 68Ga-DOTATATE uptake and less 18F-FDG uptake than did higher grade tumors (68Ga-DOTATATE median SUV$_{\text{max}}$, 33 vs 3.5, $P=0.002$; 18F-FDG median SUV$_{\text{max}}$, 4.9 vs 16, $P=0.005$). Four of the 11 patients with typical carcinoid showed little or no 18F-FDG uptake. There were no false positives seen with 68Ga-DOTATATE. With 18F-FDG, there were 3 false-positive hilar nodes ($n=1$) and false-positive uptake in atelectatic lung distal to the tumor ($n=2$).

**Conclusions:** 68Ga-DOTATATE shows high and selective uptake in typical bronchial carcinoids. Higher grade pulmonary NETs show less uptake of 68Ga-DOTATATE but more uptake of 18F-FDG.

**Reviewer’s Comments:** The results of this small study are congruent with those of previous studies comparing 68Ga-DOTATATE and 18F-FDG in gastroenteropancreatic NETs. (Reviewer-Shayne Squires, MD).

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Keywords: Bronchial Carcinoids, Pulmonary NETs, PET

Print Tag: Refer to original journal article
FDG-PET/CT agrees moderately well with colonoscopy in evaluating extent and severity of ulcerative colitis.

**Background:** Ulcerative colitis may extend to the rectum only (proctitis), splenic flexure (left-sided colitis), and further (pancolitis). The extent of disease is used to guide the mode of drug delivery. Colonoscopy is the gold-standard for determining the extent of disease but carries a risk of colonic perforation.

**Objective:** To compare the performance of FDG-PET/CT colonography versus colonoscopy in determining the extent and severity of ulcerative colitis.

**Participants:** 15 adult patients with mild to moderately active ulcerative colitis that extended >15 cm from the anal verge. Ten patients with breast cancer who underwent PET/CT served as controls.

**Methods:** Each patient underwent colonoscopy following colonic lavage. Extent of disease was classified by location: rectum, sigmoid colon, descending colon, transverse colon, ascending colon, cecum, and ileocecal junction. Lesions were scored according to severity: 0 for no lesion; 1 for erythema or mild friability; 2 for moderate friability; and 3 for spontaneous bleeding, severe friability, or ulceration. Each patient underwent PET/CT within 1 week of colonoscopy. A grade was assigned to each region as follows: 0 = activity less than liver; 1 = activity equal to liver; 2 = activity >1 but <3 times that of liver; 3 = activity ≥3 times greater than liver.

**Results:** The total number of segments involved by colonoscopy was 67, and the number of segments detected by PET/CT was 66 (PET/CT detection rate, 98.5%). In 11 patients (73%), there was one-to-one agreement between PET/CT and colonoscopy in determining extent of disease. There was moderate agreement between PET/CT and colonoscopy in determining extent of disease (kappa=0.55, P=0.02). In 6 patients (40%), PET/CT and colonoscopy were in agreement in determining whether grade 2 or 3 disease was present. In 4 patients with grade 2 disease by colonoscopy, grade 3 disease was observed by PET/CT. In 4 patients with grade 3 disease by colonoscopy, grade 2 disease was observed by PET/CT. One patient with pancolitis by colonoscopy had grade 0 disease by PET/CT. In the 10 control patients, no grade 2 or 3 activity was seen in the colon.

**Conclusions:** PET/CT colonography is a novel, noninvasive technique for assessing the extent and severity of ulcerative colitis and agrees moderately well with colonoscopy.

**Reviewer's Comments:** This study is small and must be interpreted cautiously, but these results suggest that larger studies are warranted and the need for invasive colonoscopy to evaluate extent of ulcerative colitis may be reduced. (Reviewer-Shayne Squires, MD).

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Keywords: Ulcerative Colitis, PET/CT Colonography, Colonoscopy

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