# Does Normal Perfusion Scan Mean Low Annual Risk of Hard Cardiac Event?

Patients With Adenosine-Induced ST-Segment Depressions and Normal Myocardial Perfusion Imaging: Cardiac Outcomes at 24 Months.

Sharma J, Roncari C, et al:

J Nucl Cardiol 2010; June 10 (): epub ahead of print

Patients with a normal myocardial perfusion scan have a low risk of adverse cardiac events, even when the adenosine stress electrocardiography test is positive.

**Background:** Patients able to exercise adequately with normal myocardial perfusion imaging (MPI) have an annual hard cardiac event rate of approximately 1% per year. This rate increases to 1.3% to 2.3% per year in those assessed using adenosine who have normal MPI. In patients with both an abnormal adenosine stress electrocardiogram (ECG) test and an abnormal adenosine stress perfusion scan, the risk is greater than an abnormal scan alone.

**Objective:** To determine if an abnormal adenosine stress ECG test in patients with normal MPI carries a worse prognosis.

Design: Retrospective cohort study.

**Participants:** Patients presenting for clinical reasons for MPI were retrospectively reviewed; 76 patients met inclusion criteria of a normal myocardial perfusion scan, abnormal adenosine stress ECG, no known coronary artery disease, and follow up >6 months.

**Methods:** A 6-minute infusion adenosine stress ECG test was performed. Ischemic ECG was defined as either  $\geq$ 1.5 mm upsloping ST-depression or  $\geq$ 1.0 mm horizontal or downsloping ST-depression at 80 ms beyond the J-point in at least 3 consecutive beats in at least 2 contiguous leads. Post-stress imaging started at 45 to 60 minutes post-infusion. Cardiovascular events were defined as cardiac death, nonfatal myocardial infarction (MI), or coronary revascularization.

**Results:** The mean age of participants was 66 years; 87% were women and 30% were diabetic. Follow-up was 24 ± 13 months. There were no cardiac deaths or nonfatal MIs in the cohort. Twenty two patients underwent angiography as a result of the adenosine stress myocardial perfusion scan. There were 11 patients who underwent revascularization; 10 occurred as a direct result of the initial perfusion scan, and 1 occurred 19 months later.

**Conclusions:** The rate of cardiac death and MI was 0% at a mean follow-up interval of 24 months in this cohort of patients with adenosine stress-induced ST-depression but normal MPIs. The authors state that, "In the presence of normal MPI, the specificity of ischemic ECG changes during adenosine infusion for the detection of severe obstructive coronary artery disease is poor, although patients with multiple coronary risk factors, particularly diabetes mellitus, should undergo further investigation."

**Reviewer's Comments:** The authors state that patients with an abnormal adenosine stress ECG but normal myocardial perfusion and who have multiple risk factors should undergo further investigation. Why? The rate of hard cardiac events (cardiac death or nonfatal MI) was 0% over 2 years in this cohort and in all subgroups of this cohort. They did not show that angiography was of benefit or that revascularization was of benefit in patients with a normal myocardial perfusion scan. On the contrary, the best conclusion from their data is that patients with a normal perfusion scan have a very low annual risk of a hard cardiac event, even if the stress adenosine test is positive. (Reviewer-Thomas F. Heston, MD).

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Keywords: Myocardial Perfusion Imaging, Adenosine, Pharmacologic Stress Testing

# Evaluating the Risks, Benefits of Cardiac Imaging Using Ionizing Radiation

Weighing the Risks and Benefits of Cardiac Imaging With Ionizing Radiation. Gerber TC, Gibbons RJ:

J Am Coll Cardiol Img 2010; 3 (May): 528-535

Carcinogenic risk of radiation exposure from cardiac imaging in symptomatic patients is minimal compared to the benefits.

**Background:** Rapid growth in medical imaging has increased concerns over patient radiation exposure. There is currently uncertainty over the carcinogenic potential of ionizing radiation.

**Objective:** To summarize current knowledge about the potential risks of radiation used in cardiac imaging as related to the expected benefits.

**Design:** Literature review. **Epidemiology:** The per-capita effective radiation exposure in the U.S. has increased 72% from the early 1980s to 2006. This increase is primarily due to an almost 6-fold increase in exposure from medical imaging. In 2006, in terms of nontherapeutic radiation to patients, CT scans represented 49% of the collective dose to patients, and nuclear medicine and conventional radiography represented 26% and 25%, respectively. Cardiac nuclear scans made up 85% of the overall exposure from nuclear medicine studies, resulting in an overall contribution of approximately 22% of overall nontherapeutic radiation exposure from imaging studies. Cardiac CT makes up about 12% of overall CT exposure, resulting in an overall contribution of approximately 6% to the collective exposure. Most nuclear medicine studies were performed in patients who were ≥55 years of age. **Risk of Cancer:** The intrinsic risk of cancer is much greater than the potential risk of cancer from medical imaging radiation exposure. Available studies of populations exposed to low-dose radiation to date are statistically weak and generally too low to exclude with certainty the possibility of zero risk (ie, the error bars include 0% increased risk). Low-dose radiation exposure, similar to what is received through medical imaging, in some studies has shown no increase in cancer rates. The primary data raising concern over radiation exposure are from atomic bomb survivors, where the mean dose was 200 mSv delivered at a very high-dose rate. The authors of this paper state that 10 mSv of exposure could add 0.05% absolute risk to the lifetime risk of 21% of dying from cancer in the US. This is a relative increase of 0.2%.

**Conclusions:** The authors propose that the risk of radiation-induced cancer argues against the widespread use of cardiac CT or nuclear medicine imaging in asymptomatic patients. However, in symptomatic patients, the available evidence strongly suggests that the benefits greatly outweigh any potential risk of radiation-induced cancer.

**Reviewer's Comments:** The "linear no-threshold" model and the as-low-as-reasonably-achievable (ALARA) principle still dominate thinking in this field; however, these are not universally held beliefs. One of the more reasonable websites for radiation information I have found is the Health Physics Society at http://www.hps.org. This article on the subject from the Mayo Clinic presents the existing data very well and is highly recommended reading. (Reviewer-Thomas F. Heston, MD).

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Keywords: CT, Myocardial Perfusion Imaging, CAD, Tx, Radiation Dose/Risk



Revised American Thyroid Association Management Guidelines for Patients With Thyroid Nodules and Differentiated Thyroid Cancer.

Cooper DS, Doherty GM, et al:

Thyroid 2009; 19 (11): 1167-1214

The 2009 revision of the American Thyroid Association Management Guidelines for Thyroid Cancer devotes much attention to the role of FDG-PET and emerging therapies.

If the thyroglobulin level becomes detectable while the patient is on thyroid suppression or if stimulated Tg levels rise to >2 ng/mL, search for metastatic disease, with neck US and helical chest CT without iodinated contrast. If US and CT are negative or if Tg is out of proportion to the identified surgically respectable disease, then 18FDG-PET imaging may be obtained, as long as the stimulated serum Tg is >10 ng/mL. If the 1311 18FDG-PET scan is negative, empiric therapy with 131I (100 to 200 mCi) will identify disease in half of the patients with persistent disease. 18FDG-PET/CT is superior to PET alone in patients with 131I-negative tumors. In a recent study, PET and CT images were scored blindly; accuracy was 93% for 18FDG-PET/CT and 78% for PET alone (P < 0.05). PET/CT added information to the side-by-side interpretation of PET and CT images in 75% of the patients. Fusion studies changed therapy in 50% of the patients. FDG positivity is <15% in patients with stimulated Tg levels <10 ng/mL. Recent studies suggest Tg levels after T<sub>4</sub> withdrawal require a dosage of 10 ng/mL or higher in order to merit treatment. A Tg level that is rising may also merit empiric therapy. External beam radiotherapy is reserved for unresectable localized or cervical disease that could cause fracture, neurological, or compressive symptoms (eq. vertebral metastases, central nervous system metastases, selected mediastinal or subcarinal lymph nodes, pelvic metastases). For the small subset of patients with progressive metastatic spread, a range of targeted therapies are now under investigation. Agents in phase II studies include axitinab, motesanib, sorafenib, pazopanib, and thalidomide; however, none of these have been specifically approved. These therapies can be grouped as follows, (1) Tyrosine Kinase Inhibitors – Target kinase pathways that are activated in papillary thyroid cancers. However, targeting for follicular thyroid cancer and Hürthle cell cancer awaits better understanding, although responses in such patients have been reported. (2) Modulators of Growth or Apoptosis – Clinical trials are underway. (3) Angiogenesis Inhibitors – Trials of these agents are proceeding for all subtypes. (4) Immunomodulators – May soon be studied in thyroid cancer. (5) Gene Therapy – Preclinical studies suggest potential efficacy in anaplastic thyroid cancer cell lines. For appropriate patients, participation in one of the available clinical trials may be the best option. Reviewer's Comments: For thyroid cancer today, a vital task of researchers is to develop a strategy to deal with PET-positive, 1311-resistant metastases. They are the metastases responsible for the small but significant incidence of disease-specific mortality from thyroid cancer. It is noteworthy that the sections on PET and emerging therapies probably contain the most that is new in the 2009 revision of the American Thyroid Association Management Guidelines for Thyroid Cancer. (Reviewer-C. Richard Goldfarb, MD).

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Keywords: Management, Revised ATA Guidelines, PET, PET/CT

# Important to Appreciate Significance of Uptake in Bone Scintigraphy

Soft Tissue Uptake on Bone Scintigraphy. Lionel S. Zuckier, MD

Lionel S. Zuckier, MD -Special Presentation

In addition to spurious uptake, there are at least 4 mechanisms of methylene diphosphonate uptake in soft tissues.

There are 4 mechanisms of actual uptake of diphosphonate in the soft tissues and a fifth category of spurious or artifactual uptake. Metastatic calcification refers to Ca++ deposition in normal tissues subjected to hypercalcemia and can be induced by a marked and rapid rise in serum Ca++ or PO4-. Metastatic calcification may be seen with increased secretion of parathyroid hormone, destruction of bone, vitamin D-related disorders, and renal failure. The distribution of calcification (and Tc-99m methylene diphosphonate [MDP] uptake) most frequently includes the lung, stomach, and kidney, which are tissues that exhibit an alkaline milieu. The second category of soft tissue uptake is dystrophic calcification, which occurs in patients with normal calcium and phosphate levels. In this category, calcium and MDP deposition is due to histologic disruption of the cells caused by trauma, ischemia, or cellular necrosis or in the enzymatic necrosis of fat. Examples of dystrophic calcification that are often associated with MDP uptake include infarctions of the brain, heart, and muscle. Splenic uptake may be observed in autoinfarction associated with sickle cell anemia. Finally, there is a collection of other assorted causes of soft tissue calcification and MDP uptake related to dystrophic calcification, such as in deep vein thrombosis, phlebitis, injection sites scars, and various soft tissue diseases (eq. dermatomyositis). The third category is uptake of MDP or calcification due to metabolic uptake. Several metabolic mechanisms are implicated in uptake of bone radiopharmaceuticals. Osteogenic sarcoma metastases produce osteoid matrix, which binds MDP. In a similar manner, myositis ossificans represents a dedifferentiation of muscle into osteoid-producing tissue. Fibrils of amyloidosis are said to have a physiologic affinity for calcium. Mucin-producing tumors have a glycoprotein that is biochemically similar to ossifying cartilage and binds Ca++ salts. In pediatric patients, neuroblastoma exhibits uptake of MDP related to an intrinsic metabolic characteristic of the tumor. The fourth category is the process of compartmental sequestration. We may visualize areas of MDP because the rate of washout from that location lags behind that of other compartments, such as in cases of venous or lymphatic obstruction, pleural effusions, or peritoneal ascites. Finally, spurious or artifactual uptake can originate due to problems with the radiopharmaceutical. Apparent uptake in unexpected locations is fairly commonly seen due to prior radiopharmaceutical on a previous day. In infiltrated injections, uptake can be seen in draining lymph nodes.

**Reviewer's Comments:** It is important to recognize soft tissue uptake when performing bone scintigraphy. Proper interpretation of these findings depends on identifying the involved organs and appreciating the significance of the uptake. (Reviewer-).

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Keywords: Bone Scintigraphy, Soft Tissue, Uptake, MDP

#### DEXA Scans Excellent for Assessing Fx Risk Based on BMD Measurement

An Update on Dual-Energy X-Ray Absorptiometry. Blake GM, Fogelman I:

Semin Nucl Med 2010; 40 (1): 62-73

Lumbar spine measurements from dual-energy x-ray absorptiometry are the best for establishing temporal changes in bone mineral density.

**Background:** Bone mineral density (BMD) measurement using dual-energy x-ray absorptiometry (DEXA) technology has been an important step in the past decade toward predicting and preventing hip fractures. **Objective:** To update the reader on the current state of opinion regarding the clinical use of results obtained from this technique.

**Results:** The T score compares the subject's BMD to a population of normal young adults, whereas the Z score is based upon a comparison to age-matched individuals. T scores should be used for patients >50 years of age and Z score for patients <50 years of age (including children). Spine measure requires 2 or more adjacent vertebra for optimal accuracy, and it is important to exclude vertebra that are significantly affected by degenerative disease. The lowest result from either the hip or spine measurement has been recommended for use in establishing the diagnosis of osteoporosis. Precision for BMD measurements from a DEXA machine is determined by the coefficient of variation (CV). The authors note that ideally each clinic should perform baseline-repeat scans on a minimum of 30 subjects to establish the specific CV for a given clinic. However, even with 30 subjects, there is still potential for a notably large statistical error in the derived CV. For the large majority of clinics, this approach to determining the CV is simply impractical. Instead, the authors recommend that a CV of 1% to 1.5% be used for the spine and total hip, and 2% to 2.5% for the femoral neck. The least significant change is then taken as 3 times the CV; so then, this would be 3% to 4.5% for spine and total hip compared to 6% to 7.5% for femoral neck. They further note that follow-up scans for assessment of response to therapy should not be performed for at least 1 year after initiation of treatment. They also point out that the lumbar spine BMD is the best measure for establishing response to therapy. Due to the effect on DEXA BMD results from variations in the relative soft tissue contribution from fatty tissue versus muscle or viscera, large changes in the weight of a patient between DEXA examinations can affect the accuracy of detecting significant BMD changes. The Fracture Risk Assessment Tool (FRAX) from the World Health Organization uses T score results for both genders >50 years old along with clinical data, most importantly age, to determine 10-year cumulative risk probability for femoral neck or other insufficiency fractures.

**Reviewer's Comments:** This was a very well-written review of the most recent thinking on BMD measurement and how to utilize the results. (Reviewer-David Bushnell, MD).

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Keywords: Osteoporosis, Bone Mineral Density, DEXA

# **Radiology Targeted to Cut Excessive Costs**

Appropriating Imaging: What is Radiology's Role in Controlling Utilization. Orenstein BW:

Radiol Today 2010; 11 (April): 12-15

It is estimated that approximately 30% of radiological tests do not meet the standard appropriateness criteria.

Governmental agencies and insurance companies are beginning to focus more on radiology to cut excessive health care costs. It is estimated that approximately 30% of radiological tests do not meet American College of Radiology appropriateness criteria. Furthermore, radiology is responsible for the 6-fold increase in medical radiation exposure over the last 25 years. Part of the problem is that physicians are not up-to-date on the appropriateness of a requested procedure for their patients. Some hospitals have computerized physician order entry (CPOE) systems that physicians can use to modify their orders accordingly. At Massachusetts General Hospital, this system has been effective in reducing the costs and number of imaging techniques. But the CPOE systems are expensive, and many hospitals do not have access to them. Another solution is to follow clinical prediction rules where physicians follow set evidence-based algorithms to plan their investigation techniques. Radiologists can themselves play a more direct role by discussing excessive or inappropriate tests with ordering physicians. While there may be concern of loss of revenue or compromise of professional relationships, it is imperative that the safety and comfort of the patient be the highest priority. Not only do these systems reduce health care costs and limit radiation exposure, they will also reduce the risk of putting patients through unnecessary and possibly invasive investigations for incidental findings.

**Reviewer's Comments:** Preauthorization for most high-cost radiographic examinations (especially PET and frequently nuclear cardiology) is an established feature of private health insurance. To administer preauthorization, insurance companies contract Radiology Business Management (RBM) organizations whose ostensible goal is to reduce the proliferation of unnecessary diagnostic imaging exams. Now, the U.S. Budget Office is on record as recommending preauthorization for Medicare and Medicaid imaging services. Many nuclear medicine physicians and radiologists have little interaction with RBMs because they interface, and frequently interfere, with potential referring physicians before the request for the study ever reaches us. We generally receive the request with authorization secured. The above article highlights the efforts of radiologists to compete with or eliminate the need for RBM organizations. (Reviewer-C. Richard Goldfarb, MD).

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Keywords: Appropriating Imaging, Utilization, Cost Control

# Effects of Obesity on Internal Doses Are Minor

Changes in Radiation Dose With Variations in Human Anatomy: Moderately and Severely Obese Adults.

Clark LD, Stabin MG, et al:

J Nucl Med 2010; 51 (June): 929-932

The internal size and location of most organs is relatively independent of body mass index.

**Background:** Dose factors calculated from standard organ geometries may not be appropriate for obese patients.

**Objective:** To investigate how radiation dose factors used for internal dosimetry are affected by body weight in obese individuals.

**Methods:** The size and geometry of organs in mildly and severely obese individuals were determined from published information and were used to generate digital phantoms based on non-uniform rational B-splines (NURBS). Ranges of obesity were modeled with the addition of surrounding adipose tissue. Standard Monte Carlo radiation transport simulations were done to obtain specific absorbed fractions and dose factors for each organ for gamma ray energies ranging from 10 keV to 4 MeV. A comparison of the factors from the simulated obese individuals and the standard person models was made.

**Results:** For most of the organs, there was little difference seen in the specific absorbed fraction as a function of obesity over the entire range of gamma ray energies. However, in the lower abdomen, the specific absorbed fractions were lower by a factor of 1.6 to 2 for the obese individuals because of the distribution of the adipose tissue. In the heart and large intestine, the specific absorbed fractions were approximately 20% to 50% higher in the moderately and severely obese individuals respectively.

**Conclusions:** The authors conclude that obesity has little effect on the organ factors associated with internal dose calculations. This is because the organs of obese individuals have roughly the same size and location as those in the standard model, and the layers of adipose tissue do not strongly affect specific absorbed fractions. **Reviewer's Comments:** This is a very interesting paper showing that the dose factors associated with specific tissues and organs are not strongly dependent on the patient body weight. However, in order to obtain actual doses, the dose factors are multiplied by the cumulated activity in the tissue or organ of interest. Since the cumulated activity depends on the concentration of the radiotracer, body weight often does have a big effect on the actual radiation dose. For example, the iodine space is 35% of the body weight. For a comparable glomerular filtration rate, a 60-kg person will have 2 times the blood dose per administered activity as a 120-kg person because of the dilution effect. (Reviewer-Mark T. Madsen, MD).

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Keywords: Radiobiology/Dosimetry, Radiopharmaceuticals, Anatomy, Radiation Dosimetry

# Technegas Has Some Strong Advantages Over DTPA

Ventilation–Perfusion SPECT With 99mTc-DTPA Versus Technegas: A Head-to-Head Study in Obstructive and Nonobstructive Disease.

Jögi J, Johnson B, et al:

J Nucl Med 2010; 51 (May): 735-741

Technegas is more evenly distributed in both obstructive and nonobstructive disease as compared to 99mTc- diethylenetriaminepentaacetate.

**Background:** Scintigraphy of ventilation in the U.S. is almost exclusively performed with 99mTcdiethylenetriaminepentaacetate (DTPA) aerosol. Technegas, (an ultrafine dispersion of carbon) is used in Europe but is not yet approved by the Food and Drug Administration in this country. Aerosol distribution depends on diameter of the particles. 99mTc-DTPA droplets have a size distribution between 0.5 and 2 μm; Technegas particles are of submicron size. Clumping creates hot-spots, particularly in chronic obstructive pulmonary disease (COPD), but also occurs when aerosol particles are relatively large. This would be more likely to occur with DTPA than with Technegas, but no direct comparison has been reported. **Objective:** To examine differences in ventilation studies performed with 99mTc-DTPA and Technegas. **Participants/Methods:** 65 patients were enrolled in the study; 35 were referred for ventilation–perfusion (V/Q) SPECT to evaluate suspected pulmonary embolism (PE; n=29) or alveolitis (n=3) or to assess lung function before surgery or after transplantation (n=3). The mean age of the patients was 57 ± 17 years; 51% were women, and 5 had known obstructive lung disease. Two of these 35 patients were later excluded because data had not been properly stored for re-evaluation. Also, 30 outpatients with known COPD (age, 65 ± 6.7 years; 63% women) were also recruited. A total of 126 sets of V/Q SPECT images were reviewed according to a standardized scoring system to characterize distribution. Ventilation images were rated by unevenness,

deposition in major airways, and focal peripheral deposition. These parameters were scored from 0 (none) to 10 (very high).

**Results:** In both obstructive and nonobstructive disease, unevenness of radiotracer deposition and the degree of central deposition were more pronounced in 99mTc-DTPA than Technegas studies. In obstructive disease, focal deposition in distal airways was more pronounced with 99mTc-DTPA. Mismatched perfusion defects were more frequent with Technegas in obstructive disease.

**Conclusions:** Technegas is preferred over DTPA radioaerosol, especially in obstructive disease. **Reviewer's Comments:** I have long wondered why Technegas is not approved for routine use in the United States. It may simply be that there has been no head-to-head comparison of the Technegas with 99mTc-DTPA aerosol. Well, now there is, and what has been anecdotally assumed for over a decade is now documented— Technegas has some strong advantages over DTPA aerosol. Perhaps, with the publication of this article and the growth of V/Q SPECT, there may be a push for commercial availability of Technegas in this country. (Reviewer-C. Richard Goldfarb, MD).

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Keywords: SPECT, Ventilation-Perfusion, Technegas, DTPA

# Bone Scans Retain Major Role in Work-Up of Metastatic Dz

ACR Appropriateness Criteria® on Metastatic Bone Disease. Roberts CC, Daffner RH, et al:

J Am Coll Radiol 2010; 7 (June): 400-409

According to the current American College of Radiology Appropriateness Criteria® on metastatic bone disease, Tc-99m methylene diphosphonate bone scanning remains the primary imaging examination used to detect osseous metastasis.

Radionuclide bone scanning remains the primary imaging examination used to detect osseous metastasis. Its major advantage is the feasibility of a total-body survey that is impartial, which is of significant importance as >10% of metastatic lesions occur in the extremities. Bone-scanning, FDG-PET, and PET/CT are useful in preoperative staging and follow-up of stages 2, 3, and 4 breast carcinoma. For breast carcinoma with single or multiple "hot" spots on bone scan, the panel recommends radiography, and if the radiography results are negative, then MRI is recommended. CT is recommended if a needle biopsy is warranted. SPECT is warranted to clarify planar bone scan results, especially in the spine. In a patient with a pathologic fracture of a long bone on radiography, the panel recommends a radionuclide bone scan to look for other metastatic sites. For prostate carcinoma, radionuclide bone scan is not necessary if the prostate-specific antigen (PSA) level is ≥20 ng/mL or if the primary tumor is poorly differentiated. In non-small-cell lung cancer, exclusion of bony metastases is imperative for preoperative staging. Current recommendations for bone scan are for staging after needle biopsy of lung nodules. However, in patients who will be undergoing FDG-PET studies as part of their initial work-up, radionuclide bone scanning is not necessary. For osteosarcoma, the presence of metastasis would substantially affect management. Bone scan is recommended for patients who have osteosarcoma at presentation for staging. Among those who have received adjuvant chemotherapy, >15% will develop asymptomatic osseous metastasis before lung metastasis. Bone scans are appropriate for routine follow-up and after tumor resection and chemotherapy. FDG-PET does not replace chest CT and bone scanning for staging osteosarcoma. The vertebral column is the most common site of skeletal metastasis, and cord compression from metastasis is a dreaded complication. MRI is the best modality, but cannot reliably differentiate benign (traumatic or osteopenic) compression fracture from a pathologic fracture caused by metastasis. FDG-PET has better specificity than bone scan but similar sensitivity. FDG-PET/CT has better specificity than FDG-PET because it provides improved localization and associates soft-tissue involvement with likely cord compression.

**Reviewer's Comments:** The American College of Radiology (ACR) Appropriateness Criteria® are assuming greater importance as preauthorization for imaging tests is becoming universal. Radiology business management organizations, hired by insurance companies to administrate preauthorization, make frequent use of ACR criteria. Utilization of imaging modalities is largely determined by these published criteria. It is comforting to note that the bone scan is holding its own in the PET/CT era. (Reviewer-C. Richard Goldfarb, MD).

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Keywords: Metastatic Bone Disease, ACR Appropriateness Criteria®

# Another Step Closer to Quantitative SPECT CT?

Quantitative Accuracy of Clinical 99mTc SPECT/CT Using Ordered-Subset Expectation Maximization With 3-Dimensional Resolution Recovery, Attenuation, and Scatter Correction.

Zeintl J, Vija AH, et al:

J Nucl Med 2010; 51 (June): 921-928

Quantitative SPECT requires careful attention to characterizing the spatial resolution of the imaging system, scatter correction, and attenuation correction.

**Background:** SPECT CT systems are commercially available with sophisticated resolution recovery reconstruction algorithms. How well can these systems quantify absolute activity in patient studies? **Objective:** To investigate the quantitative accuracy of a commercial SPECT CT system in phantom and patient studies.

**Methods:** All measurements were performed with a Siemens Symbia T SPECT CT system. A 3-step process was used to calibrate the system. First the SPECT imaging system spatial resolution properties were characterized to derive recovery coefficients for various sized objects. Next, image counts to activity calibrations were made from SPECT measurements of a large cylindrical phantom with a precisely known activity. These corrections and calibration factors were applied to phantom and patient studies. Attenuation and scatter correction was applied, and the images were reconstructed with the Siemens Flash 3D ordered-subset expectation maximization (OSEM) algorithm. The phantom had fillable spheres located in a cylindrical container. The 16 patient studies were technetium-99m methylene diphosphonate bone studies. SPECT studies were acquired of the lower abdomen, and bladder activity in the attenuation-corrected images was compared with measured activity concentration in the voided urine.

**Results:** The results from the phantom and patient studies were similar with a standard error of estimate of approximately 8%, (95% CI. -19% to +17%). The range of errors for the spheres in the phantom study was -6% to 7%. The range of errors for determining the radioactivity concentration of the urine was -8% to 17%. **Conclusions:** The authors conclude that accurate SPECT quantification with 99mTc is possible, but note that measurement uncertainties dominate clinical applications. They look toward future improvements in acquisition and processing methods to improve the situation.

**Reviewer's Comments:** There are several points that deserve comment. First, the method used to validate the quantitation in patients was very good. By collecting the patient's urine after the SPECT imaging, a direct comparison can be made between the image-based estimation and the actual activity concentration. In my summary, I only reported the standard error of estimate for the measurements, while the authors also include the "average" accuracy (1.1%) for the patient studies. This is both a meaningless and misleading parameter since positive and negative errors offset each other. As an example, 4 of the 16 patient measurements were off by >10% while 6 were off by more than -5%. The low average value of 1.1% reflects this distribution of errors and really provides no information about the accuracy of the approach. (Reviewer-Mark T. Madsen, MD).

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Keywords: Quantitative SPECT, SPECT/CT, OSEM-3D, System Calibration

# **Bowel Preparation Not Useful Before PET-CT**

Influence of Bowel Preparation Before 18F-FDG PET/CT on Physiologic 18F-FDG Activity in the Intestine.

Soyka JD, Strobel K, et al:

J Nucl Med 2010; 51 (April): 507-510

Bowel preparation prior to FDG PET/CT does not appear to enhance diagnostic acumen in patients with bowel neoplasms.

**Background:** Physiologic bowel uptake on PET/CT is usually recognized as mild and diffusely distributed, causing no concern for malignancy. However, bowel uptake can sometimes be focal and quite intense raising alarm that a pathological process is at play. Although many recommendations have been made regarding reducing bowel uptake of FDG, few studies have shown the benefit, if any, of bowel preparation in patients undergoing FDG PET/CT.

Objective: To evaluate the effects of bowel preparation on bowel activity seen on FDG PET/CT.

**Methods:** Patients with a history of a primary abdominal malignancy undergoing initial staging or follow-up with FDG PET/CT were enrolled. Patients were randomized into 2 groups: those receiving (n=26) and not receiving (n=39) bowel preparation prior to PET/CT scanning. Regions of interests were drawn around the small bowel as a whole, as well the large bowel in segments (ascending, transverse, descending, and sigmoid/rectum) on each scan, and maximal standardized uptake values (SUVmax) were compared between the groups. Diameters of the colonic segments were also measured and compared between groups.

**Results:** Colonic segment diameters (except for the descending colon) were significantly larger among those who did not use the bowel prep. Colonic SUVmax was significantly higher among the bowel prep group, with the exception of the sigmoid rectum (although the SUVmax in this segment was higher than in the non-prep group, just not significantly so). Although fewer prep patients (6 vs 11 in the non-prep group) had focal bowel FDG uptake leading to diagnostic impairment (ie, inability to distinguish normal variant from pathologic uptake), this did represent a significant difference between the 2 groups.

**Conclusions:** Bowel preparation prior to FDG PET/CT significantly increases bowel FDG uptake but does not result in diagnostic impairment.

**Reviewer's Comments:** This interesting study evaluated the impact of bowel cleansing on bowel FDG uptake prior to FDG PET/CT. The authors demonstrate that, although all bowel segments show an increase in FDG uptake, in the bowel prepped patients versus the non-prepped patients, this increase in uptake did not affect diagnostic acumen. This suggests that although the uptake was higher, it was not distributed in a pattern that was suggestive of disease. However, the study also suggests that bowel prepping prior to FDG PET/CT scanning does not increase the ability to detect/exclude bowel disease in that there was no significant difference in diagnostic impairment between the 2 groups. As such, there does not appear to be any benefit to having patients undergo this inconvenience. As the reason for focal uptake in the bowel is still unknown, more research is needed to elucidate its cause, which could potentially resolve the diagnostic dilemma it occasionally causes. (Reviewer-Damita Thomas, MD).

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Keywords: FDG PET/CT, Physiologic Bowel Activity, Bowel Preparation

# Vitamin C of No Help

Influence of Vitamin C on Salivary Absorbed Dose of 1311 in Thyroid Cancer Patients: A Prospective, Randomized, Single-Blind, Controlled Trial.

Liu B, Kuang A, et al:

J Nucl Med 2010; 51 (April): 618-623

Salivary gland stimulation with vitamin C may not significantly reduce radioactive dose to the glands following radioactive iodine therapy.

**Background:** It is postulated that in post-thyroidectomy patients receiving radioactive iodine therapy for thyroid cancer, the salivary glands receive a substantial 131I dose, which can subsequently lead to significant morbidity related to the effects of xerostomia (ie, dental caries and significant change in taste). Different schema using sialogogues of varying types have been used to diminish the radioiodine dose to the salivary glands and thus reduce the untoward side effects.

**Objective:** To assess the effect of vitamin C on salivary gland absorbed dose following radioactive iodine therapy in post-thyroidectomy thyroid cancer patients.

**Methods:** Patients with well-differentiated thyroid cancer who had undergone thyroidectomy with no prior history of 131I external radiation therapy, diabetes, collagen tissue disorder, or a pre-existing salivary gland condition were included. Patients were divided into 4 groups that varied based on when they were to start oral vitamin C (1, 5, 13, and 25 hours after radioactive 131I ingestion); all patients were imaged 48 after radioactive 131I therapy. Salivary gland residence times and absorbed doses were also calculated for each patient. **Results:** The absorbed dose to the salivary glands was highest within the first 24 hours post-therapy (particularly the first 3 hours), and there was no significant difference in absorbed dose after 24 hours. There was also no significant difference among groups.

**Conclusions:** Vitamin C as a sialogogue does not significantly affect absorbed dose to the salivary glands following radioactive iodine therapy in post-thyroidectomy thyroid cancer patients.

**Reviewer's Comments:** This well-designed study strongly suggests that vitamin C does not significantly alter the absorbed dose to the salivary glands following radioactive iodine therapy. The authors show that the residence time within the glands is very short, with the vast majority of activity being cleared by 24 hours following therapy. As such, they suggest that vitamin C (or any sialogogue for that matter) may be of little benefit if started after 24 hours. This suggests that evaluation of salivary stimulation within the first 24 hours following therapy may be useful to assess. However, there may be a catch-22 with this approach in that the increased salivary flow induced by sialogogues in the immediate period following radioactive iodine therapy will deliver more dose to the glands. The authors suggest that striking the right balance may be difficult if trying to truly diminish the 1311 dose delivered to the glands. (Reviewer-Damita Thomas, MD).

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Keywords: Thyroid Cancer, Vitamin C, Salivary Glands,1311 Radioiodine Tx

#### More Study Needed on Benefit of Amifostine

Does Amifostine Have Radioprotective Effects on Salivary Glands in High-Dose Radioactive Iodine-Treated Differentiated Thyroid Cancer.

Ma C, Xie J, et al:

Eur J Nucl Med Mol Imaging 2010; February 4 (): epub ahead of print

There is no significant difference in salivary gland absorbed dose in patients receiving amifostine versus placebo following 131I therapy post-thyroidectomy for thyroid cancer.

**Background:** Radioactive iodine therapy (RAIRx) has been a mainstay of adjunctive therapy in patients with well-differentiated thyroid cancer (WDTC) following thyroidectomy as it has been shown to reduce recurrence rates as well as facilitate long-term follow-up with serum thyroglobulin. However, RAIRx is not without side effects, the most significant being salivary gland dysfunction, which is a sequelae of the radiation dose to the glands. The associated side effects of xerostomia, dental caries, and change in taste can impact quality of life and also lead to significant morbidity in terms of dental health. As such, this study aims to search the literature pertaining to the use of amifostine for its radioprotective effects of salivary glands to determine its efficacy. **Objective:** To query the available literature regarding the significance of the radioprotective effects of amifostine on salivary glands following RAIRx in well-differentiated thyroid cancer (WDTC) patients after thyroidectomy.

**Methods:** An extensive search of major literature databases (Cochrane Library, Medline, and Embase) was done, using patients status following near or total thyroidectomy for WDTC and having received amifostine as adjunct to therapy as search criteria. The authors also included as a requirement at least 3 month follow-up. **Results:** The authors found only 2 studies meeting the criteria, which were comprised of 130 patients total. Meta-analysis showed that there was no significant difference among patients treated with amifostine and those treated with placebo in terms of development of side effects or subsequent salivary gland function as determined by 99mTc-pertechnetate scintigraphy 12 months later.

**Conclusions:** The authors' findings suggest that amifostine has no significant radioprotective effects on salivary gland function in patients with WDTC undergoing RAIRx.

**Reviewer's Comments:** It is unlikely that real conclusions regarding amifostine's efficacy as a radioprotective agent for salivary glands following RAIRx can be gleaned from only 2 studies, the details of how each were performed being largely unknown. However, more importantly, this meta-analysis highlights the paucity of studies on the use of amifostine for this purpose. As amifostine has been shown to be useful in salivary gland protection following external beam radiation therapy in head and neck cancer patients, the nuclear medicine community adopted its use following RAIRx in post-thyroidectomy WDTC patients presuming a similar benefit. However, it seems that very little is known about the efficacy of amifostine for this purpose. This study suggests that, although there are studies on the subject, the studies varied widely in their patient population, dosage of radioactive iodine used, definition of salivary gland effects, and administration of amifostine, which is likely why only 2 were included in this meta-analysis. It is clear that the benefit of amifostine needs to be better characterized, perhaps by studies that control for the dose of amifostine used, timing of its use following RAIRx, and dose of RAIRx given. (Reviewer-Damita Thomas, MD).

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Keywords: Salivary Glands, Amifostine, 131I Tx, Well-Differentiated Thyroid Ca

## **Obese Patients With Suspected CAD, Normal MPI Have Lower Mortality Rates**

Impact of Weight on Long-Term Survival Among Patients Without Known Coronary Artery Disease and a Normal Stress SPECT MPI.

Uretsky S, Supariwala A, et al:

J Nucl Cardiol 2010; 17 (May/June): 390-397

Despite a great number of risk factors, overweight and obese patients with suspected coronary artery disease and normal myocardial perfusion imaging have lower mortality rates.

**Background:** The "obesity paradox" is a well-known phenomenon in which obesity seems to be protective among patients with known coronary artery disease (CAD); obese patients with known CAD actually have lower mortality rates. However, the extent of this finding is not known in patients with suspected CAD who have normal myocardial perfusion imaging (MPI).

**Objective:** To determine if obese patients with suspected CAD and normal MPI have lower mortality rates. **Participants/Methods:** 3673 patients with suspected ischemia who underwent stress-rest SPECT were evaluated. Those with a history of CAD and abnormal MPI were excluded. Age, weight (normal, overweight, and obese categories based on body mass index [BMI]), and several other variables were recorded for each patient (ie, history of hypertension, diabetes mellitus, smoking, family history, and chest pain to name a few). Patients were followed for a mean of 7.5 years.

**Results:** Of the total 3673 patients, 26%, 35%, and 40% were normal weight, overweight, and obese, respectively. The obese patients tended to be younger, female, and have a greater number of risk factors for CAD, though even among the older patients, obesity was associated with greater survival rates. A significantly smaller number of obese patients died when compared to normal weight patients (9% vs 24%). In fact, normal weight, smoking, and diabetes mellitus were associated with poorer survival.

**Conclusions:** Overweight and obese patients have better survival rates despite having more CAD risk factors. **Reviewer's Comments:** This interesting study shows that despite having more CAD risk factors, obese patients with suspected CAD but normal MPI actually have lower mortality rates compared to their normal-weight counterparts. This begs the question, why is this so? The authors give possible explanations as cited from the literature, including earlier and more aggressive medical therapy in the overweight population, larger coronary arteries, and increased metabolic reserve among the obese. The authors point out, however, that these theories have been ascribed to the obese with known CAD, not suspected CAD. Therefore, these reasons may not be the factors at play in the patients in this study. Another plausible explanation suggested in the paper is that their definition of obese based on the BMI may not be an accurate reflection of obesity, as often muscular, short statured people can have an elevated BMI and not be obese. Also, other studies have shown that whereas BMI does not correlate with increased risk of myocardial infarction, an elevated waist-to-hip ratio does. It would be interesting to know the survival rates of patients with/without CAD who have increased waist-to-hip ratios versus those with normal values. (Reviewer-Damita Thomas, MD).

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Keywords: SPECT Myocardial Perfusion, Obesity, Mortality



The Prognosis of a Normal Stress-Only Tc-99m Myocardial Perfusion Imaging Study. Duvall WL, Wijetunga MN, et al:

J Nucl Cardiol 2010; 17 (May/June): 370-377

Normal Tc-99m–based stress-only myocardial perfusion imaging has similar mortality rates to the conventional rest-stress imaging protocol.

**Background:** Tc-99m-based, rest-stress myocardial perfusion imaging (MPI) has long been used to detect obstructive coronary artery disease (CAD). It is not, however, without undesirable aspects, including its time requirement and the relatively high radiation dose to the patient. As such, innovation of imaging techniques and protocols are underway to address these issues.

**Objective:** To determine the prognosis of stress-only Tc-99m MPI using Tc-99m in order to ascertain whether it is as useful as the conventional MPI imaging protocol.

**Design/Participants:** This retrospective study examined patients who underwent routine stress-only MPI (as is the protocol at the investigational institution) or conventional rest-stress MPI that were interpreted as normal. Patients with a history of CAD as well as undergoing MPI for transplantation clearance were excluded. **Methods:** As per the investigational institution, stress-only MPI was performed if there was a low pre-test probability for CAD, weight indices in the extreme (ie, underweight or >250 pounds), a negative cardiac catheterization or other cardiac evaluation within the previous 3 years, advanced age, or a condition that makes it difficult for the patient to undergo the conventional protocol. Average follow up was 40 months. **Results:** 4910 patients were evaluated (34% rest-stress and 66% stress-only MPI). Most patients were low risk and were outpatients. The rest-stress group tended to be older with more CAD risk factors when compared to the stress-only group. The 1-year mortality rate was 1.2% for each cohort. At the end of follow-up, the overall mortality rates of 2.7% and 3.7% for the stress-only and rest-stress groups, respectively, were not significantly different. There was also no significant difference between the 2 groups when risk-adjusted analysis was performed.

**Conclusions:** A normal stress-only MPI has a similar prognostic profile to conventional rest-stress MPI. **Reviewer's Comments:** This interesting study suggests that a normal stress-only MPI has a just as favorable prognosis as does a normal MPI using conventional rest-stress imaging. The study further suggests that in select patients, resting imaging may not add additional information and, therefore, may not be necessary. Although one could argue that TID (a factor that is associated with multivessel disease even in the absence of perfusion defects) is not evaluated with stress-only imaging, those eligible for stress imaging only are those with a lower likelihood of having disease to begin with. During an era when throughput is important and radiation dose is in every headline, this approach for selected patients as outlined in this study may prove useful in cutting cost, saving time, and decreasing radiation dose to the patient. (Reviewer-Damita Thomas, MD).

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Keywords: Myocardial Perfusion Imaging, SPECT, Prognosis

#### Individual Patient Prediction of Radiation-Induced Malignancy Is Complex, Uncertain

Low-Level Ionizing Radiation From Noninvasive Cardiac Imaging: Can We Extrapolate Estimated Risks From Epidemiologic Data to the Clinical Setting?

Laskey WK, Feinendegen LE, et al:

J Am Coll Cardiol Img 2010; 3 (May): 517-524

Risk estimates of medical radiation exposure are highly uncertain and based upon incomplete and speculative mathematical modeling.

**Background:** Concerns over the late carcinogenic effects of exposure to radiation from medical imaging in the range of <100 mSv come from extrapolation of exposure-outcome data in survivors of World War II atomic bomb blasts. The parameter of interest in determining radiation exposure is "effective dose," which is a calculated (not measured) quantity based upon the average age, average gender, and average relative tissue radiosensitivities in a given population. Applying these estimates to individual patients is associated with a high degree of uncertainty.

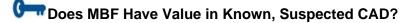
**Objective:** To assist the clinical decision making when weighing the risks of medical radiation versus the benefits of medical imaging.

**Design:** Literature review. **Epidemiology:** Radiation risk estimates as presented in the Biologic Effects of lonizing Radiation (BEIR) VII report come from population-based data. BEIR VII estimates a 2% increase in risk with 0.1 Gy (approximately 20% per Sv), whereas the International Commission for Radiation Protection (ICRP) estimates an overall risk of 5% per Sv, a 4-fold difference. Such large differences are not unexpected, given the large uncertainties contained in the data. **Concept of Dose:** The effective dose (ED) reflects absorbed dose, age, gender, cellular radiosensitivity, biological effectiveness of the specific type of radiation, and a mathematical relationship between absorbed dose and biological response. At absorbed doses <100 mGy, meaningful extrapolation of the data from atomic bomb explosions is highly uncertain, and further extrapolation down to the individual patient risk of a single nuclear myocardial perfusion scan (approximately 10 mSv) or cardiac CT angiogram (approximately 5 to 15 mSv) relies on mathematical modeling and not observational evidence. The modeling relies upon the linear no-threshold hypothesis, but recent discoveries on low-dose effects in biological systems do not always support this hypothesis.

**Conclusions:** Prediction of radiation-induced malignancy for an individual patient is highly complex and highly uncertain. Current estimates of risk are based upon incomplete data and a controversial mathematical model. **Reviewer's Comments:** This article looks at the medical radiation controversy from a medical decision-making standpoint, highlighting the high statistical uncertainty of existing estimates that have been made by BEIR VII and ICRP. Making risk estimates for individual patients undergoing a specific study is not recommended. There is even some evidence that low-dose radiation may lower health risks, and the validity of this hypothesis has not been refuted. The assumptions being made in the lay press are quite dramatic. This article helps give the issue a more balanced perspective. (Reviewer-Thomas F. Heston, MD).

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Keywords: Ionizing Radiation, Cancer, Epidemiology, Cardiac Imaging, CAD



The Clinical Utility of Assessing Myocardial Blood Flow Using Positron Emission Tomography. Ziadi MC, Beanlands RSB:

J Nucl Cardiol 2010; 17 (August): 571-581

Absolute myocardial blood flow is altered in patients with microvascular disease as well as severe large-vessel obstructive coronary artery disease.

**Background:** It is possible to measure the absolute myocardial blood flow (MBF) with positron emission tomography. PET remains the most accurate noninvasive modality for MBF quantification. With the ongoing global shortage of Tc-99m, there is growing interest in cardiac PET and PET/CT.

**Objective:** To evaluate the potential clinical utility of MBF quantification and potential future directions. **Design:** Literature review. **Resting MBF:** The absolute amount of blood flow the myocardium receives per minute per gram of tissue. Normal is approximately 1 ± 0.2 mL/min/g. **Stress MBF:** Usually measured after pharmacologic stress testing since the early time frames post-tracer injection cannot be acquired with treadmill stress and bicycle stress results in excessive artifacts. **Myocardial Flow Reserve:** This refers to the ratio of stress to rest MBF. The normal ratio appears to be 2 to 2.5 or greater, although the literature is not yet settled. It is often used interchangeably with the term coronary flow reserve. **Myocardial Flow Difference:** Sometimes used; equals stress minus rest MBF. **Clinical Applications:** MBF appears to add prognostic and diagnostic value, but the clinical impact is unclear given the limited amount of data in the existing medical literature. A major application is in the identification of microvascular disease; patients with this have a worse prognosis and may benefit from a more aggressive management strategy. An additional application is in the identification of balanced triple-vessel disease.

**Reviewer's Comments:** PET-derived MBF is able to assess microvascular disease in a manner superior to previous technologies. Due to the limited research currently available, its clinical value remains uncertain although the data so far are promising. (Reviewer-Thomas F. Heston, MD).

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Keywords: CAD, Myocardial Blood Flow, PET/CT, Nuclear Cardiology

# PET-CT Has Low Diagnostic Accuracy for Intrathoracic Staging of Mesothelioma

Integrated Positron Emission Tomography-Computed Tomography Does Not Accurately Stage Intrathoracic Disease of Patients Undergoing Trimodality Therapy for Malignant Pleural Mesothelioma.

Pilling J, Dartnell J-A, Lang-Lazdunski L:

Thorac Cardiov Surg 2010; 58 (June): 215-219

PET-CT has high specificity and low sensitivity for the detection of ipsilateral mediastinal lymph nodes in malignant mesothelioma.

**Background:** Malignant pleural mesothelioma (MPM) has a median survival of <1 year. Trimodality therapy (induction chemotherapy, extrapleural pneumonectomy, and radical hemithoracic radiotherapy) can prolong survival in some cases. Patients with ipsilateral mediastinal nodal disease (N2) do not benefit from extrapleural pneumonectomy (EPP).

**Objective:** To assess the ability of PET-CT with 18F-FDG to stage intrathoracic disease in patients with MPM undergoing trimodality therapy.

**Methods:** Patients being considered for trimodality therapy underwent PET-CT imaging. Some patients underwent imaging twice (before and after induction chemotherapy). Patients with extrathoracic disease were excluded. Images were interpreted by 2 readers. T and N stage of thoracic disease was determined from the PET-CT report using the International Mesothelioma Interest Group System and compared with pathologic stage. Following induction chemotherapy, patients underwent EPP with mediastinal nodal dissection. Radiation therapy occurred 6 to 8 weeks postoperatively.

**Results:** The study included 20 consecutive patients who underwent 24 PET-CT scans. Sixteen scans were performed a median of 55 days following talc pleurodesis, while the remaining 8 were performed in patients who did not receive talc. PET-CT yielded the correct T stage in only 2 patients who received talc and in only 1 patient who did not receive talc. PET-CT over staged the T stage in 4 scans, under staged it in 17 scans, and was correct in 3 scans. T4 disease was not identified by PET-CT in any of the patients who had it. PET-CT had a sensitivity of 11.1%, specificity of 93%, and accuracy of 66.6% for N2 disease.

**Conclusions:** PET-CT is insufficiently sensitive to stage mediastinal disease in patients with MPM. **Reviewer's Comments:** PET-CT was performed a median of 119 days prior to surgery. This long interval may account for some of the discrepancy between PET-CT staging and pathologic staging, but it likely accurately represents a typical clinical scenario where imaging is performed prior to induction chemotherapy, which in turn is performed before surgery. (Reviewer-Shayne Squires, MD).

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Keywords: Malignant Mesothelioma, PET-CT, Staging

# PET-CT May Be Superior in Detecting Osseous Metastatic Breast Ca

Integrated Positron Emission Tomography/Computed Tomography May Render Bone Scintigraphy Unnecessary to Investigate Suspected Metastatic Breast Cancer.

Morris PG, Lynch C, et al:

J Clin Oncol 2010; 28 (July 1): 3154-3159

PET-CT is more likely to detect lesions missed by bone scan than vice versa.

**Background:** Bone scan (BSc) has relatively high sensitivity for osteoblastic bone metastases due to breast cancer, but its sensitivity for lytic bone metastases is poor. In contrast, FDG PET-CT has higher sensitivity for lytic bone metastases and lower sensitivity for osteoblastic metastases.

**Objective:** To compare the diagnostic performance of FDG PET-CT with BSc for the detection of osseous metastases due to breast cancer.

**Design/Participants:** This retrospective study included women who underwent both BSc (using technetium-99m methylene diphosphonate (99mTc MDP) and PET-CT for the evaluation of suspected breast cancer metastases.

**Methods:** Imaging studies were completed within 30 days of each other. Imaging results were compared with bone biopsy or fine-needle aspiration results that were completed within 30 days of scanning. When tissue diagnosis was equivocal or unavailable, investigators reviewed all clinical notes and correlative imaging studies and then determined the presence or absence of osseous metastases by consensus.

**Results:** The study included 163 patients. Both PET-CT and BSc were positive in 32 patients and negative in 100 patients, for an overall concordance of 81%. In 18 cases, PET-CT was positive and BSc was negative. Bone metastases were ultimately confirmed in 16 of the 18 cases. In only 2 cases was BSc positive and PET-CT negative. These 2 patients did not undergo biopsy, but one of them appeared to have sclerotic osseous metastases by a follow-up CT scan. PET-CT detected soft tissue metastases in 62% of patients with positive PET-CT scans in this study.

**Conclusions:** PET-CT may be superior to BSc in evaluating women with suspected breast cancer metastases. A prospective study is warranted.

**Reviewer's Comments:** Although bone scan can detect osseous metastases that are not FDG avid, these can often be detected on CT as sclerotic lesions. Careful review of the CT portion of the exam in the bone window would be warranted in patients that undergo PET-CT without bone scan. (Reviewer-Shayne Squires, MD).

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Keywords: Breast Cancer, Bone Metastases, PET, Bone Scan

# Mechanical Dyssynchrony Detected on MPI Predictive of Death, Arrhythmia

Relation of Left-Ventricular Dyssynchrony by Phase Analysis of Gated SPECT Images and Cardiovascular Events in Patients With Implantable Cardiac Defibrillators.

Aljaroudi WA, Hage FG, et al:

J Nucl Cardiol 2010; 17 (May/June): 398-404

Lack of mechanical dyssynchrony on myocardial perfusion imaging carries a good 1-year prognosis in patients with left ventricular dysfunction.

**Background:** Dyssynchrony is delayed electrical activation and contraction of the left ventricle (LV). Patients with dyssynchrony may respond to cardiac resynchronization therapy. Electrical dyssynchrony (prolonged QRS complex on electrocardiography [ECG]) is often used as a surrogate for the presence of mechanical dyssynchrony, but it is an imperfect indicator. Mechanical dyssynchrony can be assessed on echocardiography.

**Objective:** To examine the relationship between the degree of dyssynchrony on SPECT myocardial perfusion imaging (MPI) and outcome (death or appropriate shocks) in patients with implantable cardiac defibrillators (ICDs).

**Design/Participants:** This retrospective study included 70 patients with an ejection fraction (EF) <40% who underwent SPECT MPI (exercise or pharmacologic) within 6 weeks of having an ICD placed. The study also included 157 control patients who underwent SPECT MPI for clinical reasons but who had normal EF and perfusion and no electrical dyssynchrony.

**Methods:** SPECT images were acquired using Tc-99m sestamibi according to American Society of Nuclear Cardiology guidelines. Dyssynchrony was assessed by phase analysis of the gated perfusion images. The 3-dimensional count distributions from the short axis images were subjected to Fourier phase analysis. The phase of the cardiac cycle during which contraction occurs was superimposed on the appropriate region of myocardium in a polar plot. Additionally, data were used to generate histograms where the x-axis represents one cardiac cycle and the y-axis represents percentage of myocardium contracting at a given phase in the cardiac cycle. Standard deviations (SD) were calculated from the histograms. Patient outcomes were defined as death from all causes or appropriate shocks delivered by ICD.

**Results:** The ICD patients had significantly greater phase SD (mean,  $51^\circ \pm 20^\circ$ ) than control patients. At the end of 1 year, 3 patients died, 5 patients had an appropriate shock, and 3 patients had inappropriate shocks due to supraventricular tachycardia. Patients with events had a higher phase SD than those without ( $60^\circ \pm 5^\circ > 50^\circ \pm 21^\circ$ ; *P* =0.002). No patient with phase SD <50° died or had an appropriate shock during the first year of follow-up, while 18% of patients with phase SD ≥50° had an event (*P* =0.02). Mean QRS duration was not statistically different between those with and without events. Correlation between QRS duration and phase SD was only fair (*r* =0.25; *P* =0.04).

**Conclusions:** Patients with ICD who have more LV dyssynchrony as measured by phase SD on MPI are at higher risk of events (death or appropriate shocks).

**Reviewer's Comments:** This is the first study to provide correlative outcome data for severity of LV dyssynchrony as measured by phase analysis using a method other than echocardiography. (Reviewer-Shayne Squires, MD).

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Keywords: Dyssynchrony, Myocardial Perfusion Imaging, ICD, Arrhythmia

# **Combining SPECT MPI With CTA Improves Diagnostic Accuracy**

Incremental Value of Combining 64-Slice Computed Tomography Angiography With Stress Nuclear Myocardial Perfusion Imaging to Improve Noninvasive Detection of Coronary Artery Disease.

Sato A, Nozato T, et al:

J Nucl Cardiol 2010; 17 (January/February): 19-26

SPECT myocardial perfusion imaging can improve diagnostic accuracy in cases where CT angiography is limited by artifacts.

**Background:** CT angiography (CTA) has relatively high negative predictive value for the detection of significant coronary artery disease (CAD), but specificity and positive predictive value are not as high. Some vessels are not evaluable on CTA due to calcification, motion artifact, or insufficient opacification. CTA shortcomings could be offset by combining it with SPECT myocardial perfusion imaging (MPI). **Objective:** To compare the diagnostic accuracy of combined 64-slice CTA and stress MPI for the detection of CAD with that of 64-slice CTA alone.

Participants/Methods: This study included 130 patients who underwent both MPI and CTA followed by invasive coronary angiography within 1 month. CTA studies were interpreted by readers blinded to the results of MPI. Stenoses of ≥50% luminal narrowing were defined as significant. Patients underwent 1-day stress/redistribution MPI using thallium within 1 week of CTA. Eighty seven patients underwent exercise stress, while the remainder received adenosine. MPI studies were interpreted by readers blinded to the results of CTA.

**Results:** Using the results of invasive angiography as a reference standard, MPI had a per vessel sensitivity of 81% and a specificity of 87%. CTA could not be used to evaluate 14% of 390 vessels due to motion artifact (n=16), calcification (n=32), or insufficient opacification (n=6). Of the evaluable vessels, CTA had a sensitivity of 94% and a specificity of 91%. CTA per patient sensitivity was 99%. If patients not evaluable by CTA (23/130) were considered positive, CTA per patient specificity was 70%. If results of MPI were used to classify patients not evaluable by CTA, combined specificity increased to 87%, and the positive predictive value increased from 82% to 91%. **Conclusions**: Combining stress nuclear MPI with CTA improves diagnostic accuracy over CTA alone, particularly when vessels are not evaluable by CTA.

**Reviewer's Comments:** This study suggests that patients with suspected CAD can undergo CTA first followed by MPI if there are nonevaluable vessels. (Reviewer-Shayne Squires, MD).

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Keywords: CT Angiography, SPECT Myocardial Perfusion Imaging, CAD