Maximal Safe I-131 Dose Provides Effective Tx for Standard Non-Responders

Maximal Safe Dose of I-131 After Failure of Standard Fixed Dose Therapy in Patients With Differentiated Thyroid Carcinoma.

Lee JJ, Chung J-K, et al:


Maximal I-131 dosage based on dosimetry measures is an effective way to treat subjects who have failed prior empiric treatments with I-131.

**Background:** Patients with metastatic well-differentiated thyroid cancer (WDTC) are often treated with radiiodine based on an empiric-dosing scheme that was recommended many years ago by Dr Beierwaltes (1978) from the University of Michigan. However, not uncommonly, this approach does not completely eradicate disease, particularly in the bone and, to a lesser degree, the lung and regional lymph nodes. Using dosimetric measurements from the blood and whole body, patient-specific administration of I-131 may be used to deliver a much larger safe dosage of radioiodine to these individuals.

**Objective:** To evaluate the effectiveness of this dosimetric approach in patients who had failed therapy with empirically fixed levels of I-131.

**Participants:** 47 patients with WDTC who had failed to respond to >1 treatment of I-131 based on an empiric fixed dosing scheme were eligible for study.

**Methods:** At the time of diagnosis, 13 patients had stage IV disease. There were 28 patients with stage II or III, and only 6 with stage I disease. Each patient underwent a tracer administration of I-131 with multiple blood samples obtained subsequently over 72 hours to determine the radiation dose to the blood per unit of administered radioactivity. Administered activity levels of I-131 were delivered so as not to exceed 2 Gy (200 rads) to the blood. Baseline serum thyroglobulin (Tg) levels were measured in all subjects when thyroid-stimulating hormone levels were >30 U/mL. Follow-up Tg levels and imaging exams including diagnostic radioiodine imaging were used to establish response to treatment. In some cases, treatments were repeated at 6 months.

**Results:** Of 47 patients, 7 achieved complete remission, 15 were classified as partial response, 19 had stable disease, and 6 had disease progression following dosimetry-based individualized treatment. Of 21 patients with lung metastases unresponsive to empiric treatment levels, 9 demonstrated either partial or complete responses following individualized dosimetry-based therapy. The mean single treatment-administered activity level for the 47 subjects was 12.5 GBq (338 mCi). There were clinically insignificant drops in blood counts in 26 patients except for 1 who developed a grade IV pancytopenia.

**Conclusions:** According to the authors, "the maximal safe dose provides an effective means of treatment in patients who failed to respond adequately to conventional fixed dose therapy."

**Reviewer’s Comments:** Along with several of my colleagues, I have used this approach to successfully treat a number of patients with WDTC who had not responded to prior "fixed" dose therapy. I have never witnessed a grade IV blood count toxicity but, unlike the authors, we have never given repeat therapies prior to a 1-year interval.  (Reviewer-David Bushnell, MD).

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Keywords: Thyroid Cancer

Print Tag: Refer to original journal article
Is the V/Q Lung Scan a Dying Breed?

To PIOPED, or Not to PIOPED.
Reinartz P:


The PIOPED classification system, due to its "non-diagnostic" cases, its indeterminate probability groups, and the overall complexity of the classification, has led to the decline of V/Q lung scintigraphy for pulmonary embolism diagnosis.

This invited commentary blames the PIOPED II report for the unjustified decline of the ventilation-perfusion (V/Q) lung scan and questions the usefulness of the PIOPED classification system. The PIOPED—due to its "non-diagnostic" cases, its indeterminate probability groups, and its overall complexity of the classification—led to the decline of V/Q lung scintigraphy for pulmonary embolism diagnosis. The PIOPED investigators disregarded SPECT. CT angiography (CTA) also yields indeterminate results, as well as some false-positive and even more false-negative diagnoses. PIOPED II, in fact, reported a sensitivity for CTA of only 83%. V/Q scintigraphy is highly sensitive, is easy to perform, and produces a low radiation exposure. In Europe, Technegas is available and makes the acquisition of ventilation rapid and almost effortless. Recent reports suggest that CT examinations substantially increase the risk of radiation-induced cancer. Radiation dose from CTA more than doubles when the lower extremities are scanned in addition to the chest. The positive-predictive and negative-predictive values of approximately 85% and 95% are the same for CTA and scintigraphy. The ALARA principle would hold that, since lung scintigraphy and CTA are comparable diagnostically, the lower radiation exposure makes the lung scan the method of choice.

Reviewer's Comments: To comment on this commentary, I find the author's observations clearly conveyed, cogent, and convincing. Although one might debate the course of decline of the V/Q scan, the PIOPED classification system that regards "low probability" as diagnostically useless was bound to concede that V/Q scintigraphy with its preponderance of low-probability results as diagnostically useless. Many emergency departments, including our own, consider a low-probability result quite useful when combined with the pretest clinical probability. Also, in young patients with clear chest x-rays, the chances of getting near-normal or high-probability readings are excellent. This is especially important in women of childbearing age who benefit from the V/Q; 60 times lower than CT breast irradiation, we are currently reviewing the outcome of patients who discharged from our emergency department following a low-probability lung scan result. The PIOPED II study, I doubt, tells the total clinical story. (Reviewer-C. Richard Goldfarb, MD).

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Keywords: Lung Scintigraphy

Print Tag: Refer to original journal article
Increased diffuse hepatic uptake after radioiodine administration is most closely related to hepatosteatosis and elevated liver enzymes.

**Objective:** To examine the relation between post-radioiodine administration diffuse hepatic uptake with laboratory values and clinical follow-up.

**Design/Participants:** Retrospective study of 732 patients (604 females, 128 males; mean age, 45 years) with differentiated thyroid carcinoma who had undergone post-radioiodine administration imaging (dose range, 75 to 200 mCi).

**Methods:** All patients had undergone either total or subtotal thyroidectomy prior to I-131. Images were acquired 6 to 10 days after I-131 administration. A scale regarding the amount of visual uptake compared to background in the thyroid bed, in the liver, and any distant metastatic disease was used to evaluate images and was as follows: 0 - no uptake, 1 - close to background activity, 2 - low uptake, 3 - moderate uptake, and 4 - intense uptake. An uptake score for thyroid remnant and liver was calculated with this information. The correlation between this score, dose of radioiodine, serum thyroglobulin, liver function tests, liver ultrasound, presence of metastatic deposits, and recurrent disease were evaluated.

**Results:** Mean follow-up was 7.4 ± 6.2 years. A pattern of diffuse liver uptake was seen in a total of 873 scans. Median hepatic uptake score was 1. There was positive correlation between hepatic uptake of radioiodine with the dose of I-131 and the level of serum liver values. There was no significant correlation between hepatic and thyroid remnant uptake scores. In addition, there was no significant correlation between hepatic uptake visualization and serum thyroglobulin, presence of metastatic disease, or recurrence. Interestingly, patients with fatty infiltration of the liver had higher liver uptake scores.

**Conclusions:** The authors found no correlation between radioiodine uptake in the liver and most of the other factors they evaluated. They state that the positive correlation between hepatic uptake of radioiodine with hepatic enzymes and hepatosteatosis supports the fact that this may be related to other mechanisms.

**Reviewer's Comments:** As the authors go on to discuss, it is a well-known fact that radioiodine is metabolized in the liver, and this may simply be the reason for this uptake. This study showed that it is not due to residual thyroid tissue. (Reviewer-Twyla Bartel, DO).

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Keywords: Diffuse Hepatic Uptake

Print Tag: Refer to original journal article
With a proper protocol, short-acting insulin can be administered prior to FDG injection to lower glucose levels.

**Objective:** To evaluate the impact of insulin use on glucose level, images, and clinical management.

**Participants:** 63 patients were included in this study due to a glucose level >10 mmol/L and having received IV insulin as part of a standardized protocol prior to FDG-PET imaging. There were 106 control patients with glucose levels <10 mmol/L.

**Methods:** The insulin given was short-acting and was given as follows: 2 units for glycemia of 10.0 to 12.0 mmol/L, 3 units for 12.1 to 14.0 mmol/L, and 4 to 6 units for ≥14.1 mmol/L. Glucose levels were measured before insulin injection, at 30 and 60 minutes after insulin injection, and before the patient left the department. About 0.02 mCi/kg (7.5 MBq/kg) F-18-FDG was injected intravenously at least 60 minutes after the last insulin injection. For each scan, images extended from the base of the skull to the mid-femurs. The biodistribution was evaluated by 2 experienced PET readers and was based on a 5-point scale regarding muscular uptake as follows: 0 - normal, 1 - mild muscular uptake, 2 - involving >1 muscular group, 3 - diffuse uptake of moderate intensity, and 4 - diffuse, intense uptake. Based on these visual scores, patients were stratified into subgroups: A - adequate biodistribution (0, 1, or 2) or B - altered biodistribution (3 or 4). Standardized uptake values (SUVs) were calculated from gluteal muscle uptake. Patients were followed up clinically to allow evaluation of diagnostic accuracy.

**Results:** Greater uptake was seen in patients who received insulin compared to controls. Of these patients, 25% had altered biodistribution. The time interval between insulin and FDG injection and the level of glucose reduction after insulin administration were the 2 most important factors that increased muscular uptake. Muscle SUV values were lower in insulin patients.

**Conclusions:** 75% of patients who received IV insulin had an acceptable biodistribution pattern on FDG-PET. Increased uptake was seen in muscles as well as low uptake in the liver, indicating altered biodistribution.

**Reviewer’s Comments:** As the authors state, 75% of patients in this study who had short-acting IV insulin administration had an acceptable biodistribution of the radiotracer. However, 25% with an unacceptable biodistribution would warrant using a different standard protocol such as a longer interval between insulin and FDG administration. (Reviewer-Twyla Bartel, DO).

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Keywords: IV Insulin

Print Tag: Refer to original journal article
FDG PET-CT Highly Effective for Assessing Recurrent Head, Neck Cancer

Does 18F-FDG PET/CT Improve the Detection of Posttreatment Recurrence of Head and Neck Squamous Cell Carcinoma in Patients Negative for Disease on Clinical Follow-Up?

Abgral R, Querellou S, et al:


PET-CT is highly effective in surveillance of head and neck cancer patients after initial therapy.

**Background:** FDG PET-CT is highly accurate in the diagnosis of recurrent disease in head and neck cancer patients suspected of recurrence after initial therapy. There is, however, limited data in using FDG PET-CT for surveillance of head and neck cancer patients who have no clinical evidence for recurrent disease.

**Objective:** To evaluate the role of FDG PET-CT in detection of recurrent disease in head and neck cancer patients who otherwise have no clinical evidence of recurrence.

**Participants/Methods:** 91 patients with head and neck squamous cell carcinoma who had no clinical evidence of recurrence at their 12-month posttreatment follow-up were imaged with FDG PET-CT. The initial stage was stage I or II in 23 patients and stage III or IV in 68. The majority of patients received surgery as well as radiotherapy and concurrent chemotherapy. FDG PET-CT images were analyzed for local recurrence in the primary tumor, metastasis in the neck, and distant metastases. PET-CT results were correlated with histopathology for locoregional disease and conventional imaging with CT or MRI for distant disease. A finding was considered true positive if it was confirmed with histopathology or with follow-up imaging studies that demonstrated progression of disease. A negative study was considered true negative if no disease was found at 6-month clinical follow-up after PET-CT.

**Results:** FDG PET-CT scans were negative in 52 patients and positive in 39. Recurrence was confirmed in 30 of 39 patients with positive PET-CT scans. Fourteen patients had only local recurrence, 2 had cervical nodal disease, 2 had local recurrence and distant metastases, and 12 had only distant metastases. Distant metastases were found most commonly in the lungs but also in bone and liver. Overall, the sensitivity and specificity of PET-CT for recurrent disease was 100% and 85%, respectively, with an overall accuracy of 90%.

**Conclusions:** FDG PET is highly effective in the assessment of recurrence of head and neck cancer.

**Reviewer's Comments:** Head and neck cancers usually recur within 2 years after initial diagnosis. A longer follow-up to at least 2 years would be desirable to confirm the 100% sensitivity reported in this study. Nevertheless, findings of this study strongly suggest that FDG PET-CT should be part of the surveillance of head and neck cancer patients after initial therapy. (Reviewer-Yusuf Menda, MD).

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Keywords: Head & Neck Cancer

Print Tag: Refer to original journal article
Infarct Size Accurately Determined With PET, Delayed CT

Expanding the Versatility of Cardiac PET/CT: Feasibility of Delayed Contrast Enhancement CT for Infarct Detection in a Porcine Model.
Holz A, Lautamäki R, et al:


The results from this investigation suggest that infarct detection with delayed contrast CT can be performed with low-dose prospective gating.

Objective: To evaluate contrast CT for infarct detection in an animal model to find optimal imaging times and to compare CT results with PET perfusion infarct size estimates.

Methods: This investigation was performed using pigs. Ten pigs (weight, 25 to 35 kg) had cardiac infarcts induced with balloon occlusion of the left anterior descending coronary artery under anesthesia. Approximately 5 weeks later, these animals were evaluated with PET/CT. Each animal had a 20-minute gated resting perfusion study with N-13 ammonia. After completion of PET imaging, the animals were injected with contrast agent, and high-dose (18 mSv per scan) retrospective ECG-gated CT studies were acquired at 0.5, 1.5, 10.0, and 15.0 minutes post-administration. On 6 pigs, a second set of studies with the same time delays was acquired 2 days later using a low-dose (2 mSv per scan) prospective gating technique. Co-registered polar maps were generated for both the N-13 ammonia and contrast CT studies. For N-13 ammonia maps, infarct defects were determined using a 60% count threshold and were expressed as a percent of the total left ventricular myocardium. Infarct size for the CT data was determined using thresholds that ranged from 2.5 to 4.5 standard deviations (SDs) above the mean for normal tissue.

Results: Perfusion defects were seen in the resting studies on all 10 animals, with an average infarct size of 31% with a standard deviation of 8%. When a CT threshold of 3.5 SD was used, average infarct size was nearly identical (30%) for both the low- and high-dose protocols, although individual correlation with PET results was modest (R = 0.65). Plots of the Hounsfield units (HUs) as a function of time show that, for both the low- and high-dose CT procedures, imaging should commence between 10 and 15 minutes post-contrast administration. A fair correlation (R = 0.84) was found in the HU in the infarcted area between the low- and high-dose techniques.

Conclusions: Infarct size can be accurately and reproducibly determined with both PET perfusion images and delayed CT contrast studies in controlled animal experiments. Low-dose prospective gating works as well as high-dose retrospective gating and can be started as early as 10 minutes after administration of contrast.

Reviewer’s Comments: The encouraging results from this paper indicate that delayed CT contrast imaging has the potential to provide useful information at a reasonable dose level. The authors point out in their discussion that the delayed CT contrast study could obviate the need for the resting PET perfusion study and may improve the prognostic power of the total exam. (Reviewer-Mark T. Madsen, PhD).

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Keywords: Cardiac PET/CT

Print Tag: Refer to original journal article
SPECT/CT is especially useful in reducing false-positive results through better localization of activity foci in areas where increased physiologic uptake is expected.

Objective: To investigate potential benefits of SPECT/CT in evaluating differentiated thyroid cancer (DTC) patients.

Participants/Methods: This study included 117 patients (28 males, 89 females) with previous thyroidectomies for DTC. Of these, 108 had whole-body anterior-posterior planar imaging 48 to 72 hours after oral administration of 185 MBq of I-131 sodium iodide, while the other 9 had their imaging 5 to 7 days after therapy (using 3700 MBq). All patients also had SPECT of the neck and chest region along with a low-dose CT on a commercial hybrid system (Millennium VG Hawkeye or Infinia Hawkeye 4; GE Healthcare). SPECT images were reconstructed iteratively with attenuation correction and fused with co-registered CT studies. Both whole-body and SPECT/CT images were read independently by 2 experienced nuclear medicine physicians who were blinded to clinical findings. Scintigraphic findings were compared against surgical histopathology, clinical examinations, and radiologic follow-up over at least 6 months.

Results: 116 hot lesions were found in the planar images from 52 patients. SPECT/CT found all of those lesions plus 42 more; 28 of the additional lesions were from the same 52 patients, while the remaining 14 lesions were found in 7 patients with no apparent planar lesions. In more than one third of patients with positive findings, SPECT/CT led to a more appropriate patient management. In two thirds of patients, more precise anatomical localization was provided by SPECT/CT.

Conclusions: SPECT/CT provides significant additional value over planar imaging, both in improved detection of disease and with localization. The improvement in localization is especially useful in reducing false-positive results.

Reviewer’s Comments: Because of the twin benefits of improved contrast and anatomic localization, it is no surprise that SPECT/CT outperformed whole-body planar imaging with I-131 in evaluating DTC patients. The results obtained in this study confirm those from several earlier investigations using similar imaging systems. Although not specifically recommended by the authors, it would seem apparent that clinics with access to SPECT/CT systems ought to forego whole-body planar studies and rely solely on the tomographic results. (Reviewer-Mark T. Madsen, PhD).

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Keywords: I-131 SPECT/CT

Print Tag: Refer to original journal article
PET Imaging Beneficial in Low-Grade NHL

Positron Emission Tomography Changes Management, Improves Prognostic Stratification and Is Superior to Gallium Scintigraphy in Patients With Low-Grade Lymphoma: Results of a Multicentre Prospective Study.

Scott AM, Gunawardana DH, et al:


PET imaging is useful for accurate staging of low-grade non-Hodgkin lymphoma.

**Background:** Patients with early stage low-grade non-Hodgkin lymphoma (NHL) may be curable with radiotherapy. FDG uptake is typically elevated in both low- and high-grade Lymphomas. PET/CT imaging with FDG is commonly used to assess response to therapy in aggressive lymphomas. However, its use in low-grade disease is less well defined.

**Objective:** To assess the value of initial PET imaging with FDG for patients with low-grade NHL.

**Design:** Prospective multicenter study.

**Participants:** Newly diagnosed patients with low-grade NHL with early stage disease based on conventional imaging.

**Methods:** PET or PET/CT was performed on each subject and, in some cases, gallium imaging was obtained as well. Patient management plans were recorded before and then again following completion of the PET exam. Patients were followed for 12 months following completion of PET exams.

**Results:** There were 74 patients eligible for data analysis upon completion of this study. Assessment of stage based on conventional workup before PET revealed 41 patients with stage I and 16 with stage II disease. Of these 74 patients, 55 had follicular NHL. Additional sites of disease were detected by PET in approximately 50% of patients. PET results led to an upstaging in 21 subjects and downstaging in 3. Overall 28% of patients who had initially been stage I or II prior to PET were reclassified as stage III or IV following PET. Clinicians considered results from PET to have had a high or medium degree of impact on management in 25 patients. Patients with additional disease sites detected by PET had a significantly higher disease-free progression rate than did those who did not have additional lesions detected by PET. Of 16 patients who also had gallium/SPECT exams, management was affected by the results from the gallium exam in 3, whereas PET findings in these 16 led to altered management in 7.

**Conclusions:** PET imaging is beneficial in patients with low-grade NHL.

**Reviewer’s Comments:** It is important to keep in mind that these results should be applied to only those patients with follicular lymphoma, since the number of patients with other histologic subtypes was too low to draw meaningful conclusions. (Reviewer-David Bushnell, MD).

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**Keywords:** Low-Grade Lymphoma

**Print Tag:** Refer to original journal article
Atrial fibrillation is a risk factor for reduced myocardial perfusion reserve and increased coronary resistance in nonischemic dilated cardiomyopathy.

**Background:** Atrial fibrillation (AF) is the most common form of sustained arrhythmia. AF is associated with increased morbidity and mortality, a diminished myocardial perfusion, and a decreased perfusion reserve.

**Objective:** To investigate the difference in myocardial perfusion and perfusion reserve in patients with nonischemic dilated cardiomyopathy (DCM) with and without AF.

**Design:** Cross-sectional study.

**Participants:** 30 patients with nonischemic DCM, defined as a left ventricular ejection fraction of <55%, left ventricular dilation, and no coronary artery disease. Of patients, 12 had AF and 18 were in sinus rhythm (SR). There were 22 healthy control subjects in SR.

**Methods:** Myocardial perfusion was assessed by dynamic PET (ECAT-921; Siemens/CTI) after a bolus injection of O-15 H2O. A 26-frame dynamic acquisition was obtained over 5 minutes. Hyperemic myocardial blood flow (MBF) was measured from a second injection of O-15 H2O after a 7-minute adenosine infusion. Coronary flow reserve was calculated as the ratio of hyperemic to baseline MBF. Coronary vascular resistance was calculated by dividing mean arterial pressure by the MBF. MBF corrected for the rate pressure product (RPP) was calculated as MBF/RPP x 10,000.

**Results:** Resting MBF-corrected in DCM/SR patients was comparable to that in controls. Baseline MBF was lower in DCM/AF compared to DCM/SR. The hyperemic MBF was lower in DCM/AF compared to DCM/SR to a greater degree. Coronary flow reserve was lower in DCM/AF patients and coronary vascular resistance was higher.

**Conclusions:** In patients with nonischemic DCM, those with AF have a reduced myocardial perfusion reserve and increased coronary vascular resistance.

**Reviewer’s Comments:** In patients with nonischemic DCM, this study found AF is associated with decreased myocardial perfusion both at rest and after adenosine stress. AF is also associated with an increased coronary vascular resistance in these patients. However, at rest, those in SR have a similar myocardial blood flow and coronary vascular resistance as those in the healthy control group. Researchers do not postulate as to the clinical implications of their findings. (Reviewer-Thomas F. Heston, MD).

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Keywords: Atrial Fibrillation

Print Tag: Refer to original journal article
Multi-slice cardiac CT adds incremental prognostic value to myocardial perfusion imaging in patients with suspected coronary artery disease.

**Background:** Previous studies have suggested that multi-slice cardiac CT (MSCT) provides complementary information to myocardial perfusion imaging (MPI); however, there is little information in regard to whether or not MSCT adds additional prognostic information beyond that obtained by MPI.

**Objective:** To assess any additional prognostic value of MSCT over MPI in patients with suspected coronary artery disease.

**Design:** Prospective cohort study.

**Participants:** 541 patients referred for clinical reasons to cardiac imaging. Patients underwent both MPI and MSCT within 3 months of each other. Age of patients was 59 ± 11 years. Risk factors included diabetes (30%), hypertension (56%), and current smoking (30%). Pre-test likelihood of coronary artery disease based on the Diamond and Forrester method was low (22%), intermediate (65%), and high (13%).

**Methods:** MPI was performed using gated SPECT. MSCT was performed using a 64-slice CT in most patients (94%), with the rest undergoing 16-slice MSCT (6%). Follow-up was performed by observers blinded to results of the imaging studies. Atherosclerotic lesions were determined to be significant at ≥50% diameter stenosis. Abnormal perfusion was defined as a stress myocardial defect of ≥5%. Severe abnormal perfusion was defined as a stress myocardial defect of ≥10%.

**Results:** MSCT obstruction of ≥50% was an independent predictor of cardiac-free survival (figure 4 in the article) as was an abnormal MPI (figure 3). The predictive value of each taken alone was approximately the same. However, the combination of the 2 variables was better than either alone (figure 5) in the prediction of event-free survival.

**Conclusions:** MSCT adds significant prognostic information to MPI. The predictive value of MSCT was found to be similar to that of MPI when considering perfusion data only.

**Reviewer’s Comments:** The major limitation of this study is that it compared only part of the findings from an MPI scan, namely, perfusion findings. It did not include left ventricular functional information, ventricular size, or stress test information when comparing MPI with MSCT. Every imaging study should be optimized to glean as much useful information from the test as possible. Not including left ventricular ejection fraction in this analysis leaves the reader to question whether or not MSCT adds any useful information to MPI, when both the nuclear perfusion and gated data are considered. (Reviewer-Thomas F. Heston, MD).

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Keywords: Cardiac CT, SPECT, Myocardial Perfusion

Print Tag: Refer to original journal article
Sestamibi scintigraphy remains the most popular and sensitive non-invasive localization method. Its greatest benefit is that it can localize both eutopic and ectopic parathyroid adenomas.

Patients with clinically and biochemically confirmed primary hyperparathyroidism (PHPT) should undergo imaging studies to localize abnormal parathyroid glands. Scintigraphy, sonography, and other non-invasive studies are not appropriate for confirming the diagnosis of PHPT or for selecting patients for surgical referral. Negative imaging does not exclude surgical intervention. In fact, experienced endocrine surgeons have performed consistently better than the best predictive rates of imaging. Sestamibi scintigraphy remains the most popular and sensitive non-invasive localization method. Its greatest benefit is that it can localize both eutopic and ectopic parathyroid adenomas. Predictive values vary widely with some institutions, reporting an accuracy rate of >90%, but most are closer to 50% or 70%. Furthermore, a large prospective study found the sensitivity for single adenomas to be 90%, but only 27% for double adenomas; 55% of hyperplastic glands were missed. Multi-gland disease, small parathyroid glands, or coexistent thyroid disease are the most frequent causes of failure to detect the adenoma. Sestamibi scans are the most useful method to localize parathyroid glands in the mediastinum. Preoperative ultrasound is popular because it is painless, non-invasive, free of radiation, inexpensive, and can be duplicated in the operating room. Sonography identifies coexistent thyroid pathology (as does dual-phase sestamibi/pertechnetate) but is quite operator dependent. Sonogram-guided fine-needle aspiration of presumed parathyroid adenoma can clinch the diagnosis by analysis for parathormone. Sonography's main limitation is inability to evaluate the mediastinum. CT and MRI lack the accuracy of scintigraphy but are improving and can be helpful when other methods fail to localize the adenoma. Fine-needle aspiration of presumed parathyroid adenoma can clinch the diagnosis by analysis for parathormone.

**Reviewer's Comments:** Little more than a decade ago, some surgical organization endorsed the recommendation: "All that's needed for parathyroid surgery is a good parathyroid surgeon." It is refreshing to note that, at this most recent international gathering, surgeons have not only endorsed preoperative imaging but they also advocate scintigraphy as the most essential. (Reviewer-C. Richard Goldfarb, MD).

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Keywords: Hyperparathyroidism

Print Tag: Refer to original journal article
In gastric emptying studies, the stomach frequently overlaps the colon, making delayed measurements of residual food in the stomach problematic.

Objective: (1) To compare parameters for gastric emptying using oatmeal versus scrambled egg meals; and (2) to assess overlap of stomach with colon or jejunum in the anterior and left anterior oblique (LAO) projections.

Participants/Methods: 15 consecutive patients with suspected gastric emptying problems agreed to participate in this research study. Meals for gastric emptying studies were compared. The first meal consisted of instant oatmeal, mixed with 500 μCi of 99mTc-sulfur colloid, heated in a microwave. The caloric content is 100 kcal and contains 2 g of fat, 4 g of protein, and 19 g of carbohydrate. The second meal consisted of 1 egg mixed with 500 μCi of 99mTc-sulfur colloid and scrambled in a skillet. Serial 1-minute images were obtained every 15 minutes in the LAO projection with the patient standing. Imaging times were 60 minutes for the oatmeal meal and 90 minutes for egg meal. Delayed imaging was performed if the half time of emptying was not reached by the end of routine imaging. One hundred CT studies with oral contrast material were evaluated for overlap of the stomach and the colon or jejunum in the anterior and LAO projections.

Results: The oatmeal and scrambled egg studies were performed 1 day apart. When 1 outlier was excluded, the correlation coefficient in the remaining 14 patients was 0.77 ($P<0.01$). Overlap of the stomach and colon occurred in 74% of patients in the anterior projection and 82% in the LAO projection; the difference was not significant. Overlap of the stomach and jejunum occurred in 77% of patients in the anterior projection and 52% in the LAO projection. The difference was significant ($P<0.05$).

Conclusions: The half time for emptying instant oatmeal correlates well with that of a more complex scrambled egg meal. The stomach frequently overlaps the colon, making delayed measurements of residual food in the stomach problematic. The stomach frequently overlaps the jejunum, but less in the LAO projection than in the anterior projection. Protocols with complex meals and delayed 4 hours in the anterior projection are probably unnecessary and possibly misleading. Oatmeal has the advantage of being easy to prepare, semisolid so it requires no chewing, and meals enters the stomach as a bolus.

Reviewer's Comments: The practical applications of this study are substantial, and I would have preferred to see this paper in a journal read predominantly by physicians rather than technologists. To implement useful suggestions in this paper requires protocol changes by those having the authority to do so. Regrettably, few nuclear medicine physicians read the Journal of Nuclear Medicine Technology since it's not a free perk for a physician member of the Society of Nuclear Medicine. (Reviewer-C. Richard Goldfarb, MD).

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Keywords: Gastric Emptying Studies

Print Tag: Refer to original journal article
FDG-PET may potentially be used to assess active and inactive atherosclerotic plaque burden and response to statin therapy.

Background: Studies have demonstrated that accumulation of FDG occurs in atherosclerotic plaques that harbor active inflammatory cells. It is felt that inflammation plays an important role in the stability or instability of these plaques.

Objective: To evaluate the prevalence of FDG-positive plaques in patients who have multiple risk factors for cardiovascular disease.

Participants/Methods: There were 200 asymptomatic subjects in this study in age groups ranging from 20 to 90 years. PET/CT was performed in each individual. CT was performed with and without IV contrast. Regions of the aorta and iliac and carotid arteries were evaluated for calcification and FDG uptake. FDG activity in a plaque above blood pool level was considered positive. Most patients had been referred for PET exams due to known or suspected malignancy. Cardiovascular risk factors were obtained from the medical records.

Results: There were 18 of 200 patients who were being actively treated with statin medication. The authors found that calcified FDG-negative and non-calcified FDG-positive plaques increased significantly with age. The authors reported a positive correlation between the number of FDG-positive plaques and the presence of multiple cardiovascular risk factors. In addition, the subgroup of individuals receiving statin medications demonstrated a significantly reduced number of both FDG-positive and FDG-negative plaques.

Conclusions: FDG-PET may potentially be used to assess active and inactive atherosclerotic plaque burden and PET may be useful for monitoring therapy with statin drugs in these patients.

Reviewer's Comments: We may be witnessing the birth of an important new application for FDG-PET/CT imaging. There are now numerous studies demonstrating the promise of PET for determining plaque inflammation and stability. Clearly, large prospective studies will be needed to determine whether PET predicts cardiovascular events in specific FDG-positive plaques. (Reviewer-David Bushnell, MD).

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Keywords: Atherosclerosis

Print Tag: Refer to original journal article
The authors of this study suggest using HU >10 and SUV >3.1 to accurately identify metastatic disease in adrenal glands.

**Background:** Benign adrenal nodules are not uncommonly seen on CT exams performed in the process of staging known malignancies. PET/CT exams are used routinely for staging many malignancies including lung cancer. Various criteria have been proposed for using PET and CT findings to determine if an adrenal nodule is malignant or not.

**Objective:** To evaluate the optimal approach in establishing metastases in patients with lung cancer using PET/CT.

**Participants/Methods:** This study included 147 patients with lung cancer, in which there were 187 total adrenal nodules. All patients had undergone PET/CT imaging as part of the staging process for lung cancer. CT follow-up or biopsy was used to establish the presence or absence of malignancy. Of 187 adrenal nodules, 95 could be characterized in this way.

**Results:** A mean CT attenuation >10 Hounsfield units (HUs) had a sensitivity of 100%, but only a 60% specificity for detecting malignancy. An SUV$_{\text{max}}$ of 3.1 carried a sensitivity of 97% with a specificity of 76%. Using a combination of SUV$_{\text{max}}$ >3.1 and HU >10, the sensitivity and specificity were 97% and 86%, respectively. Using ROC curve analysis, the ratio of adrenal SUV$_{\text{max}}$ to liver SUV$_{\text{mean}}$ yielded the highest area under the curve. An adrenal SUV$_{\text{max}}$ >9.0 or SUV ratio (with the liver) >2.5 always indicated malignancy.

**Conclusions:** The authors favor an approach using an adrenal SUV cutoff of 3.1 combined with HU >10. In instances where very high specificity is required, they suggest using an adrenal/liver SUV cutoff of 2.5.

**Reviewer’s Comments:** This is a reasonably large study addressing the best way to use PET/CT to assess adrenal metastases in lung cancer. The way I understand the author’s recommendation, if either the HU are <10 or the SUV$_{\text{max}}$ is <3.1, the adrenal finding should be considered benign. (Reviewer-David Bushnell, MD).

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Keywords: Adrenal Metastases

Print Tag: Refer to original journal article
The Significance of Cardiac Sympathetic Nervous System Abnormality in the Long-Term Prognosis of Patients With a History of Ventricular Tachyarrhythmia.

Akutsu Y, Kaneko K, et al:

I-123 MIBG imaging can help risk-stratify patients at risk for ventricular arrhythmias.

**Background:** Patients with recurrent ventricular arrhythmias may be difficult to treat. Predicting the likelihood of ventricular arrhythmias has important clinical implications. There is evidence to suggest that MIBG imaging of the heart may be able to identify those subjects at risk for future cardiac arrhythmic events.

**Objective:** To assess the ability of I-123 MIBG imaging to predict ventricular arrhythmias.

**Design/Methods:** The authors prospectively enrolled 86 subjects with a history of ventricular tachycardia and followed them for a mean period of 11 years. Each subject underwent imaging of the chest with I-123 MIBG with determination of heart/mediastinum (H/M) activity levels.

**Results:** 24 patients from the group of 86 developed recurrent cardiac ventricular arrhythmias and/or cardiac death. Using a cutoff of 2.8 for the H/M ratio definition of normal, values less than this were strongly associated with risk of recurrent arrhythmias ($P <0.05$). There were 40 subjects with values <2.8. In a multivariate analysis, an abnormal H/M ratio remained a strong indicator of future arrhythmic events, with a hazard ratio of 3.6. Patients with severely depressed cardiac ejection fractions also had a significantly increased risk of arrhythmic events. The combination of low cardiac output and low MIBG cardiac uptake was additive in predicting arrhythmias. The use of anti-arrhythmic drugs did not seem to be a good predictor of future events.

**Conclusions:** Use of I-123 MIBG scintigraphy may be an option for screening patients who are at risk for ventricular arrhythmias.

**Reviewer's Comments:** Other studies in the past few years have also demonstrated a strong association between diminished cardiac sympathetic activity as depicted by MIBG and a risk of ventricular arrhythmias and death. It will be important to determine whether MIBG imaging can help improve outcomes by leading to better treatment of high-risk patients. (Reviewer-David Bushnell, MD).

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Keywords: MIBG Imaging

Print Tag: Refer to original journal article
Imaging at Later Time Point Allows Accumulation of FDG Activity Within Tumor

Objective: To compare FDG uptake in normal tissue at 1 hour as compared to 3 hours.
Design/Methods: In this retrospective study, 99 patients with known or suspected malignancy underwent FDG-PET/CT imaging. For each PET scan, each patient was administered 0.18 mCi/kg (6.7 MBq/kg) of FDG intravenously with imaging occurring at approximately 1 hour and then again at 3 hours. All images were first reviewed by an experienced nuclear medicine physician to ensure that the normal tissues of interest did not have malignant involvement, were influenced by artifact (i.e., misregistration, brown fat, and focal muscle uptake), focal atherosclerotic disease, no dose infiltration, and absence of abnormally high red marrow or splenic uptake of the radiotracer. The normal tissues of interest that were evaluated were the aortic blood pool, fatty tissue, bone marrow, cerebellum, liver, lungs, muscle, and spleen. These areas were evaluated with CT guidance to calculate the mean SUVs based on body weight using 1-way analysis of variance.
Results: For aortic blood pool, the 3-hour SUVs were significantly lower than for those at 1 hour as was also the case for adipose tissue. However, in the cerebellum, there was significant increase in SUVs at 3 hours as compared to 1 hour. This was also the case for bone marrow, muscle, and spleen. No difference in SUVs was seen between the 2 imaging time points for liver and lung.
Conclusions: Overall, only modest changes were noted regarding FDG uptake in normal tissues at 1 and 3 hours. The authors suggested that improved tumor image contrast by imaging at a later time point is most likely related to tumor accumulation of FDG rather than reduction of activity in the background.
Reviewer's Comments: As the authors state, the main purpose of imaging tumors at a later time point is to allow accumulation of FDG activity within that tumor and not necessarily to allow a decrease in background activity. (Reviewer-Twyla Bartel, DO).

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Keywords: FDG Uptake

Print Tag: Refer to original journal article
A calculated high dose regimen for older patients and a calculated low dose protocol for younger patients produce better outcomes as compared to fixed doses for treatment of toxic nodule-associated hyperthyroidism.

**Objective:** To compare fixed, calculated, low, and high doses of radioiodine in treating toxic thyroid adenoma.  

**Design/Methods:** This was a prospective study where patients with known hyperthyroidism and a single hot nodule noted on a thyroid scan as well as 24-hour radioiodine uptake >25% were randomly treated by 1 of the following protocols: (1) fixed low dose (FLD [481 MBq]), (2) fixed high dose (FHD [832 MBq/g]), (3) calculated low dose (CLD [3.33 to 3.70 MBq/g]), or (4) calculated high dose (CHD [6.66 to 7.4 MBq/g]). All patients had undergone prior ultrasound examination to exclude multiple nodules and were followed by their endocrinologist at 2 and 6 months after radioiodine therapy and every 6 months thereafter. Radioiodine therapy was considered curative when there was absence of thyroid stimulating hormone (TSH) suppression >0.3. Only 2 patients in this study had a second treatment with I-131 due to continued symptoms of hyperthyroidism.  

**Results:** 97 patients were included, of which 8 were male and 89 were female (mean age, 43.3 years). The mean 24-hour thyroid uptake value was 48.07%. The highest cure rate was seen in the CHD group at about 10 months after therapy. However, hypothyroidism was more frequent in this group (8.3 times more). Utilizing the Kaplan-Meier method, no significant difference in survival was seen among the groups. The cure rate in those aged >50 years was 47.6%, while it was 70.5% in younger patients ($P =0.06$).  

**Conclusions:** The highest cure rate for a toxic nodule in hyperthyroid patients was with administration of a calculated high dose regimen. This protocol was also preferable in older patients, while the calculated low dose was more appropriate in younger patients.  

**Reviewer's Comments:** These data suggest that, regardless of the age of the patient, a calculated radioiodine dose is more appropriate than a fixed dose for treatment of hyperthyroidism from a toxic nodule. (Reviewer-Twyla Bartel, DO).  

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Keywords: Toxic Thyroid Adenoma  

Print Tag: Refer to original journal article
WBS Effective in Detecting Recurrence, Metastasis Regardless of Serum Tg Results

Post-therapy radioiodine imaging will detect thyroid cancer metastases in a small fraction of patients with normal thyroglobulin levels.

**Background:** In recent years, serum thyroglobulin (Tg) levels have largely replaced radioiodine imaging in the routine follow-up of patients with well-differentiated thyroid carcinoma (WDTC). Most centers reserve radioiodine imaging for those individuals in whom Tg levels become positive after initial therapy. However, it is well known that post-therapy imaging with I-131 is more sensitive than imaging following diagnostic dosages of radioiodine.

**Objective:** To evaluate the sensitivity of I-131 post-therapy whole body scan (WBS) in comparison to serum Tg levels.

**Design/Methods:** This was a retrospective study of 824 patients with WDTC who had been treated with I-131 following thyroidectomy. Serum Tg levels were obtained at the time of imaging when TSH levels were >30. Tg levels >2 ng/mL were considered positive.

**Results:** Of 824 patients, 752 had a positive scan; 59 were excluded from further analysis for lack of sufficient clinical information. Of the remaining 693 subjects, 365 had a negative Tg level, but 110 of these had positive Tg antibodies. Of the 255 with negative Tg and TgAb, 203 showed thyroid remnant on radioiodine images and 52 (6% of the total group) demonstrated either locoregional or distant metastases with the majority being nodal metastases.

**Conclusions:** The authors concluded, “Based on these findings, we recommend the complementary use of post-therapy I-131 WBS for the detection of functioning recurrence/metastasis regardless of serum Tg results.”

**Reviewer’s Comments:** I confess that the results of this study will not likely change patient management paradigms since almost all centers use post-therapy radioiodine imaging anyway; however, it was interesting to see that a small but significant number of patients with disease may be Tg negative. I might also point out that, in my experience, and there is literature to support this, changes in serum Tg measurements are often most reliable in assessing the presence of disease, particularly when levels are relatively low. (Reviewer-David Bushnell, MD).

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Keywords: Thyroglobulin

Print Tag: Refer to original journal article
PET with co-registered enhanced CT is better at identifying recurrent uterine cancer than either modality alone.

**Background:** The detection of recurrent and metastatic disease in uterine cancer is important as it can change overall survival. When management strategies are implemented, disease is detected earlier. Physical exam and biochemical tumor markers are often nonspecific, as they can also be detected in the presence of benign lesions. Conventional imaging (CT and MR) are often not sensitive or specific as nodal metastases/disseminated disease are missed and post-therapeutic changes are mischaracterized as disease. Several studies have shown that FDG-PET is accurate in the detection of recurrent/metastatic disease in uterine cancer. However, the authors point out that these studies used nondiagnostic CTs for co-registration. The authors sought to determine if the combination of FDG-PET with a diagnostic, contrasted CT improved accuracy when compared to each modality alone.

**Design/Methods:** This retrospective study was comprised of 90 patients with proven uterine cancer, who had undergone PET imaging for suspected recurrence. Suspicions of recurrence were based on abnormal physical exams/Pap smears, elevated biochemical markers, and abnormal CT/MR imaging. The gold standard included a combination of histopathology and clinical follow-up (based on tumor markers and FDG-PET/enhanced CT). FDG-PET with the use of a low-dose CT for attenuation correction (AC) was performed, followed by the acquisition of a contrast-enhanced CT. The CT-AC PET images were then fused with the contrast-enhanced CT for the final FDG-PET/enhanced CT images. Two independent readers interpreted the studies, which were all displayed simultaneously for the reader.

**Results:** Of 90 patients in the study group, 44 had recurrent disease and 46 did not. On a per-patient basis, the PET/enhanced CT study identified 40 true positives and 43 true negatives, for an accuracy of 92%. This compared to 77% and 78% for PET and contrasted CT images, respectively. It was found that PET/enhanced CT generally missed lesions <5 mm, while mischaracterizing negative hilar/lung findings, degenerative bone changes, and physiologic bowel uptake findings as disease. PET alone tended to be nonspecific, mischaracterizing negative findings as disease, whereas enhanced CT alone was not sensitive. The authors found that PET/enhanced CT imaging changed the management in 38 of 90 patients.

**Conclusions:** FDG-PET/enhanced CT is more accurate at detecting recurrent/metastatic uterine cancer than either modality alone.

**Reviewer's Comments:** As some centers use FDG-PET with a low-dose CT for AC and localization, it would have been interesting to see how that compared with a fused PET/contrast CT. The comparison between the latter would have been more useful, as the dilemma currently is not whether CT is useful, but rather if contrast adds more to the diagnostic interpretation of the study. (Reviewer-Damita Thomas, MD).

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Keywords: FDG-PET/Contrast-Enhanced CT

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C-11 Acetate PET identified RCC >1.5 cm

Background: Renal cell carcinomas (RCC) are sometimes difficult to evaluate noninvasively because they often contain complicated cysts that belie their malignancy. The authors state that as many as 8% to 10% of RCC with such cystic components are judged indeterminate by US and CT, thereby necessitating an invasive procedure for definitive diagnosis. The ability of PET to noninvasively detect other malignancies sparked interest in the development of tracers that allow optimal visualization of the genitourinary system, as FDG does not as it is renally excreted. Several smaller studies have shown that C-11 acetate is quite effective in detecting RCC, and this studies aims to support this assertion with a larger study population.

Objective: To investigate the effectiveness of C-11 acetate PET in detecting RCC.

Methods: 20 patients with suspected RCC were prospectively studied with a C-11 acetate PET scan followed by surgery. Surgical histopathology results served as the gold standard by which C-11 acetate PET imaging was measured. Prior CT studies were also used for correlation of PET study results. PET images were acquired 30 minutes post-injection without CT co-registration. Images were read by 2 readers blinded to patient clinical information, with agreement on discrepant readings reached by consensus.

Results: 20 patients had 22 tumors (1 patient had 3 tumors). Eighteen of those patients with 20 tumors showed RCC on histopathology. Of 20 RCC tumors, 19 were of the clear-cell variety and 1 was of the papillary cell variant. C-11 acetate PET demonstrated 14 true positives and 6 false-negative studies. All 6 false-negative studies were of patients with tumors <1.5 cm, regardless of histological grade. Time-activity curves (TAC) showed that the initial radiotracer uptake was higher in malignant versus normal renal tissue, likely due to the hypervascularity of the malignant tumors. TACs also found that normal renal tissue showed a higher radiotracer concentration in malignant tissues at 10 minutes post-injection versus 15 minutes, favoring an imaging protocol of at least 15 minutes post-injection.

Conclusions: The authors show that C-11 acetate PET effectively identifies relatively larger RCC tumors when imaged 30 minutes post-injection.

Reviewer’s Comments: Overall, this is a good study showing that C-11 acetate PET effectively identifies RCC in tumors >1.5 cm when imaged 30 minutes post-injection. Although the authors do state that histopathologic grade does not correlate with positivity, they identified scans as either only positive or negative, not attempting to grade a ‘positive’ result to determine if there was indeed a correlation between degree of uptake and histopathologic grade. Also, it would be interesting to know if, and how, co-registration with CT for localization purposes affects the ability of C-11 acetate to effectively identify RCC lesions. (Reviewer-Damita Thomas, MD).

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Keywords: Renal Cell Carcinoma

Print Tag: Refer to original journal article
Molecular imaging with F-18-FDG and Tc99m-annexin both show promise in the identification of vulnerable plaque in coronary artery disease patients.

**Discussion:** Pre-clinical molecular imaging studies have predominantly targeted the identification of plaque inflammation as a marker for the vulnerable plaque, ie, the atherosclerotic plaque most likely to break free and cause a downline obstruction with subsequent distal myocardial infarction. **Pathophysiologic Basis:** Vulnerable plaques are substantially inflamed, with macrophages being associated with a thin fibrous cap over the plaque, making it more prone to rupture. This inflammation is accompanied by cytokine release, such as interleukin-1, tumor necrosis factor-α, and MCP-1. These unstable plaques demonstrate cell death, with a necrotic core. More than 40% of macrophages at a rupture site are in the process of cellular death by apoptosis, whereas macrophages remote from the site do not show much apoptosis. **FDG Imaging for Plaque Inflammation:** Glucose uptake in atherosclerotic plaques appears to be due to the uptake by cytokine- or lipopolysaccharide-activated macrophages, in parallel to the extent of cellular respiratory burst. FDG uptake is able to serially monitor plaque inflammation, giving it the potential to assess response to therapy, eg, statin therapy. With proper patient preparation (eg, high fat diet with restriction of carbohydrates for 24 hours), it has been shown that measuring the FDG uptake of coronary arteries is feasible. **Annexin Imaging of Plaque:** Annexin has a high affinity for binding to phosphatidylserine, which is expressed by apoptotic cells. Annexin uptake has been correlated to the extent of cell death in carotid endarterectomy specimens. Radiolabeling annexin with PET-compatible tracers such as I-124 and F-18 is currently being researched. **Conclusions:** Not all plaques are likely to rupture and cause an infarction. The likelihood of rupture appears to be related to inflammation and degree of apoptosis within the plaque. In research studies, these conditions have been able to be imaged with F-18 FDG and Tc99m-annexin. **Reviewer's Comments:** Serial imaging to assess response of atherosclerotic plaques to statin therapy may be cost-effective if it helps decrease the unnecessary use of medications and if the imaging also helps in risk stratification. If gamma camera-based imaging can do this, then we will have a valuable and reasonably priced tool to assist in clinical care. (Reviewer-Thomas F. Heston, MD).
Cardiac CT Has Excellent Specificity for Detection of SPECT-MI

*Detection of Myocardial Infarction by Dual-Source Coronary Computer Tomography Angiography Using Quantitated Myocardial Scintigraphy as the Reference Standard.*

Rubinshtein R, Miller TD, et al:
Heart 2009; February 5 (epub ahead of print):

In this study, dual-source cardiac CT had a sensitivity of 75% in the diagnosis of previous MI when using myocardial perfusion SPECT as the reference standard.

**Background:** Myocardial hypo-enhancement during first-pass cardiac CT is thought to represent myocardial infarction (MI). This is presumably caused by a reduced microvascular blood flow in the infarct area, leading to a decreased concentration of the contrast material. Dual-source cardiac CT has 2 source/detector combinations at a 90° angle which simultaneously collect a data set during one heartbeat.

**Objective:** To determine the accuracy of first-pass dual-source cardiac CT in the detection of MI using myocardial perfusion SPECT as the reference standard.

**Design:** Retrospective review of patients referred for clinical reasons to both cardiac CT and myocardial perfusion SPECT within 120 days of each other.

**Participants:** 122 patients aged 60 ±11 years; 36% were female.

**Methods:** For the cardiac CT scans, patients were given an oral β-blocker if the heart rate was >80 beats per minute. Patients received sublingual nitroglycerin unless contraindicated. Stress rest myocardial perfusion SPECT was performed using technetium 99m sestamibi. For both modalities, infarct size was expressed as a percentage of the left ventricular mass.

**Results:** On a per-vessel territory basis, cardiac CT had a sensitivity of 75% and specificity of 98%. On a per-patient basis, sensitivity of cardiac CT was 77% and specificity 94%. The difference in measurements of MI size between modalities was 0.5% ± 4.6%.

**Conclusions:** First-pass dual-source cardiac CT has a moderate sensitivity and excellent specificity in the detection of MI when using myocardial perfusion SPECT as the reference standard. The agreement in the estimation of infarct size between the modalities is excellent.

**Reviewer's Comments:** The agreement in the estimation of infarct size by myocardial perfusion SPECT was excellent when compared to the infarct size by first-pass cardiac CT. The authors state that CT had an excellent negative predictive value; however, this was primarily due to the low prevalence of disease (5%) found in their study population. In general, if the prevalence of disease is in a mid range (30% to 70%), a cardiac CT scan when positive almost always represents true disease (since the specificity is so high). However, when the test is negative (and the pretest probability of disease is moderate), a significant percentage of infarctions will be missed (approximately 20%). (Reviewer-Thomas F. Heston, MD).

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Keywords: Dual-Source Cardiac CT

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