Moderate I-131 Ablation Doses Seem to Do the Job

Thyroid Remnant Ablation in Patients With Papillary Cancer: A Comparison of Low, Moderate, and High Activities of Radioiodine.
Kuna SK, Samardzic T, et al:

In this series of >450 patients with papillary thyroid cancer who underwent total or near-total thyroidectomy, ablative doses of 50 mCi I-131 achieved an ablation rate statistically the same when doses of 120 mCi were used.

Background: The optimal I-131 activity needed for successful thyroid remnant ablation is not established. Some practice dosimetry, but most centers administer fixed doses that range from 30 mCi of I-131 to as high as 150 mCi.

Objective: To compare the ablation success rate with low, moderate, and high activities of I-131.

Design/Participants: Retrospective study of 464 patients with papillary thyroid cancer who underwent total or near-total thyroidectomy with ablative doses of I-131 at 4 to 6 weeks after surgery.

Methods: Group A (168 patients) received 24 mCi, group B (125 patients) received 40 mCi, group C (65 patients) received 50 mCi, and group D (108 patients) received 120 mCi. The 2 lower-dose groups (A and B) were ablated with I-131 without previous diagnostic whole-body scanning. The higher-dose groups had diagnostic whole-body scans after either 2 mCi (group C) or 5 mCi (group D) of I-131. Whole-body scans were obtained at 72 hours after ablation activity. Follow-up diagnostic I-131 scintigraphy was obtained 6 to 9 months after ablation and then at 18 to 21 months.

Results: On the first follow-up scan, there was no neck uptake in 60% of patients who received 24 mCi I-131. On the second follow-up scan, that number reached 75%. With 40 mCi (group B), 67% of patients on first follow-up reached 71% in the next examination. Group C (50 mCi) achieved no activity in the neck region of 74% and 88% on first and second follow-ups, respectively. Group D (120 mCi) patients were free of activity in the neck region in 81% at 6 to 9 months, which reached 91% on the second examination. There was no significant difference between groups C and D.

Conclusions: The optimum outcome can be attained with a moderate I-131 ablation dose of 50 mCi. High ablative doses (>50 mCi) are not justified except in patients with advanced disease.

Reviewer's Comments: The comparison of respectably large-sized groups receiving specified doses provides convincing evidence that 50 mCi is an adequate ablative dose. I am fond of the authors’ recommendation because frequent side effects with high doses, such as sialitis and gastritis, rarely occur at doses as low as 50 mCi I-131. However, I wonder whether the authors believe their own data: their treatment groups A through D were established according to their changing practice. At first, they used 120 mCi and gradually reduced it to 50 mcCi, then 40 mCi, and now they are down to 24 mCi. (Reviewer-C. Richard Goldfarb, MD).

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Keywords: Radioiodine, I-131 Ablation, Thyroid Remnants, Optimum Dose

Print Tag: Refer to original journal article
Qualitative myocardial perfusion scans cannot diagnose balanced disease where blood flow is reduced uniformly. Simplified quantitative techniques, therefore, have the potential to extend diagnostic capabilities of this test.

**Background:** Qualitative interpretation of myocardial perfusion studies is sometimes insensitive to multi-vessel disease. Rb-82 PET may be able to quantify cardiac blood flow, providing a richer and more sensitive test.

**Objective:** To evaluate 2 methods for determining myocardial blood flow from PET-CT Rb-82 studies in dogs with induced coronary stenosis.

**Methods:** 9 dogs with artificially induced stenoses in either the left anterior descending artery or left circumflex artery were included in this study. Each animal had dynamic, gated adenosine stress PET-CT studies acquired in the 2-dimensional (2D) imaging mode using list mode. Radiolabeled microspheres were administered along with the Rb-82 tracer. Immediately after the PET study, CT angiography was performed to identify compromised regions of the myocardium. The time activity behavior of the myocardium was determined from the collected PET study, and the arterial input function was generated from a region placed within the left ventricular cavity. This information was used to determine myocardial blood flow from a 2-compartment tissue model as well as from a simplified retention ratio defined by the average tissue concentration of the Rb-82 in the 4- to 8-minute interval divided by the 2-minute integral of the time activity curve. Results were directly compared with blood flow values found from the microspheres.

**Results:** The CT angiographic study found evidence of stenosis in 7 of 9 dogs. In these 7 dogs, there was good concordance between territories defined by the PET and CT angiography results. Mean blood values averaged over all animals were very similar for the 2-compartment model and the microspheres, but retention ratio results underestimated blood flow, especially at very high flow rates. The correlation between blood flow found from the microspheres and compartmental model was 0.92, while the correlation with the retention ratio flow was 0.75. However, all techniques showed good discrimination between normal and stenotic regions.

**Conclusions:** Quantitative determination of myocardial blood flow is feasible with 2D PET-CT imaging. The retention ratio approach appears to provide practical, diagnostic results in the physiologic range of blood flow.

**Reviewer’s Comments:** This is a very encouraging study, and it will be interesting to see if the positive results found in this paper persist when implemented on humans. One important component that was not investigated is 3-dimensional (3D) PET imaging. Although 3D PET imaging provides a factor of 4 improvement in count sensitivity, required corrections for scatter, random coincidences, and presence of an additional 776 keV gamma from Rb-82 may present additional challenges to quantitation. (Reviewer-Mark T. Madsen, PhD).

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**Keywords:** Cardiology PET, PET-CT Hybrid Imaging, Myocardial Blood Flow, Rubidium-82

**Print Tag:** Refer to original journal article
Indeterminate CT Findings May Be Solved With Help of FDG-PET

18F-Fluorodeoxyglucose Positron Emission Tomography for the Diagnosis of Adrenocortical Tumors: A Prospective Study in 77 Operated Patients.
Groussin L, Bonardel G, et al:

J Clin Endocrinol Metab 2009; (May): 1713-1722

FDG-PET is particularly helpful in assessing adrenal masses in patients with indeterminate CT results.

**Background:** Incidental findings in the adrenal glands on CT are relatively common. In many cases, CT can determine whether these lesions are benign or malignant. However, in some instances, CT scan results are considered indeterminate for these unexpected adrenal findings.

**Objective:** To assess the ability of FDG-PET to accurately characterize such lesions as benign or malignant.

**Participants/Methods:** 77 total subjects were prospectively enrolled. Each had an adrenal mass detected by CT that had been obtained for reasons other than evaluation of malignancy. Patients with a known primary malignancy were excluded. PET imaging was obtained in all patients, along with non-enhanced and enhanced CT. Histopathology was obtained in all cases.

**Results:** Of 77 subjects, the final pathology determination revealed 22 adrenal carcinomas (AC), 12 non-adrenal lesions, and 43 adrenal adenomas (AA). All ACs had a maximum standardized uptake value (SUV$_{\text{max}}$) of $\geq$3.4 in addition to an adrenal-to-liver (A/L) ratio of $\geq$1.45. There were only 5 of 43 AAs that demonstrated an A/L ratio $>$1.45. However, 16 of 43 adenomas had SUV$_{\text{max}}$ of $\geq$3.4. The sensitivity for detecting ACs was 100% for an SUV$_{\text{max}}$ cutoff of 3.4, with a specificity of 70%. This was improved somewhat using an A/L ratio of 1.45, which carried a sensitivity of 100% and a specificity of 88%. There were 16 subjects in a subgroup analysis with indeterminate findings on CT based on a combination of non-enhanced Hounsfield unit $>$10 plus slow contrast washout. Of these 16 cases, PET demonstrated an A/L SUV ratio of $<$1.45 in 13, and all 13 of these were found to be AAs. Of 3 masses with an A/L ratio $>$1.45, 1 was determined to be an AC.

**Conclusions:** FDG-PET is particularly helpful in assessing adrenal masses in patients with indeterminate CT results.

**Reviewer's Comments:** Other studies have found adrenal tumor/liver SUV$_{\text{max}}$ cutoff values of 1.53 to 1.8 for optimal distinction between benign and malignant incidental adrenal lesions. Keep in mind that, for patients with known malignancies where adrenal metastases are a major consideration, the best adrenal/liver cutoff value may be different. (Reviewer-David Bushnell, MD).

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Keywords: FDG-PET, Adrenal Tumors

Print Tag: Refer to original journal article
Presence of fat in a contour-deforming renal mass on CT is virtually pathognomonic of angiomyolipoma.

**Background:** The majority of renal cancers are today detected as incidental findings on a CT exam performed for some other indication. Those physicians involved in the interpretation of PET/CT or SPECT/CT imaging need to be familiar with potentially serendipitous findings such as a renal mass, which may have major clinical relevance.

**Objective:** To examine specific features on CT of both benign and malignant renal lesions. **Discussion:** Most masses due to renal cell carcinoma (RCC) will be seen on unenhanced CT, which reveals a rounded defect in the parenchymal contour of the kidney. The uncommon infiltrative type of RCC does not alter normal renal contours and is, therefore, usually only visible with arterial phase contrast enhancement. The less common transitional cell carcinomas usually arise from the renal pelvis and appear as a mass in the collecting system of the kidney. Centrally located calcification is seen in up to 30% of RCCs on CT, whereas thin peripheral calcifications indicate a benign, usually cystic lesion. Approximately 15% of RCCs have a dominate cystic component, and there are special criteria (Bosniak) used for categorization of such complex cystic lesions (see Hartman et al. A practical approach to the cystic renal mass. *RadioGraphics*, 2004; 24: S101-S115).

Angiomyolipoma (AML) is a benign tumor, more often seen in middle-aged women, consisting of varying amounts of angiomatous, myomatous, and lipomatous tissues. Presence of fat in a contour-deforming renal mass on CT is virtually pathognomonic of this lesion. Only about 5% of AML tumors have insufficient fat for detection on CT. Oncocytoma is a non-fat-containing benign tumor of the kidney. These lesions are difficult to distinguish from RCCs on CT, but a central scar is sometimes seen, which may be helpful. The central scar, however, may be apparent only on contrast-enhanced images. The authors remind us that the kidneys are not an uncommon site for solid tumor metastases, particularly from lung, breast, and gastrointestinal tumors along with melanoma. They represent the fifth most common site for hematogenous metastases.

**Reviewer's Comments:** As someone who reads PET/CT scans, I thought this was a useful article. There are multiple excellent image examples of lesions described by the authors in this review as well. I was struck by the frequency of renal metastases that they described. The description and examples of AML tumors is particularly worth a look. (Reviewer-David Bushnell, MD).

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Keywords: CT Features, Renal Tumors

Print Tag: Refer to original journal article
The U.S. Budget Office, in a December 2008 report, recommended implementation of preauthorization for advanced imaging services.

Preauthorization for MRI, CT, and PET scans 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. While "appropriateness" is the stated intention of RBMs, the real issue is increasing spending on diagnostic imaging. Five-year growth rates exceed 100% for Medicare imaging spending. Consequently, the U.S. Budget Office, in a December 2008 report, recommended preauthorization for Medicare and Medicaid imaging services. Medicare would then hire RBMs to approve specific imaging tests based on guidelines developed by medical specialty societies. Congress hopes for a $280 million reduction in spending over 5 years and $1 billion by 2019, thanks to preauthorization. However, from the broader perspective, with a proper scan, earlier diagnosis saves money in the long run and results in fewer tests and hospitalizations. Many physicians and medical imaging equipment manufacturers feel preauthorization interferes with the doctor-patient relationship. Also, preauthorization typically creates delays in treatment that could be problematic for sicker patients. Educating referring physicians about criteria used for approval or denial of imaging studies has been difficult because of the semi-secretive nature of criteria and algorithms used by RBMs in the preauthorization process. Another problem ordering physicians have with using RBMs is the approved facility may not be where the referring physician wants the exam to be conducted. RBMs typically approve low-cost providers and channel patients to those facilities only.

Reviewer's Comments: The American College of Radiology (ACR) has long viewed the growth of RBMs with skepticism, but rather advocates alternative processes such as referring physician education as a means of reducing cost without reducing quality of care. Recent proclamations regarding use of RBMs from Washington, including from the White House, may have moved the ACR into a "if you can't beat them, try to control them" mode. While pointedly not endorsing the RBM system, the ACR recently published a Best Practices Guidelines on Radiology Benefits Management Programs. A timely informative feature article on preauthorization can be found in the April 6, 2009, issue of Radiology Today written by Kathy Hardy, from which I called the data for my discussion.

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Keywords: Preauthorization, Diagnostic Imaging Tests

Print Tag: Refer to original journal article
CTA Is Powerful Predictor of Cardiac Events

Background: Coronary CT angiography (CTA) has been shown to be an accurate noninvasive tool using conventional coronary angiography as the gold standard.

Objective: To evaluate clinical outcomes of patients undergoing coronary cardiac CTA.

Design: Retrospective review of patients referred for clinical indications to cardiac CTA.

Participants: 493 outpatients with an average age of 58 years; 70% were male, and 14% were diabetic. Patients were all determined to have an intermediate (20% to 80%) pretest probability of obstructive coronary artery disease (CAD).

Methods: Coronary calcium scores along with CTAs were obtained. Obstructive CAD was defined as a >50% stenosis.

Results: 8% (n=39) of studies were non-diagnostic, and 19% of patients had obstructive CAD. Of patients, 89% in the obstructive CAD group and 12% in the non-diagnostic group underwent invasive coronary angiography. The remaining patients underwent medical treatment. There were no hard cardiac events in those with normal CTAs and those with nonobstructive CAD on CTA. There were no deaths in any group; however, for those with obstructive CAD, 22% suffered a nonfatal myocardial infarction.

Conclusions: A normal or nonobstructive cardiac CTA is associated with an excellent prognosis over a 40-month period. Obstructive disease on CTA was associated with a 20% event rate during the follow-up period.

Reviewer's Comments: This well-done study indicates, in a compelling fashion, that CTA is a powerful predictor of cardiac events. The only concern is the effect invasive CTA had; however, this is likely to have had a minimal effect that did not change outcomes of the analysis. (Reviewer-Thomas F. Heston, MD).

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Keywords: CT Angiography, Coronary Artery Disease

Print Tag: Refer to original journal article
For asymptomatic patients at moderate risk, an abnormal gated SPECT study approximately doubles the risk of mortality.

**Background:** Appropriateness criteria guidelines established by the American Society of Nuclear Cardiology give SPECT myocardial perfusion imaging (MPI) a rating of uncertain for detection and risk assessment of coronary artery disease (CAD) in asymptomatic patients at moderate risk.

**Objective:** To assess clinical outcomes of asymptomatic patients at moderate risk undergoing MPI.

**Design:** Retrospective review.

**Participants:** 260 asymptomatic patients (aged 67 ± 8 years, 72% men) without known CAD who were at moderate CAD risk according to the Framingham risk score.

**Methods:** SPECT MPI images were categorized using the summed stress score (SSS) and followed for a mean of 10 ± 3 years.

**Results:** Abnormal SPECT MPI scans were seen in 142 of 260 patients (55%). By SSS categories (low risk, 0 to 3; intermediate risk, 4 to 8; and high risk, ≥9), SPECT scans were low risk in 67%, intermediate risk in 20%, and high risk in 13%. Ten-year survival was 79%. Survival was 60% for patients with high-risk scans, 79% with intermediate-risk scans, and 83% with low-risk scans, including 84% (95% CI, 77% to 91%) with normal scans.

**Conclusions:** In asymptomatic patients at moderate CAD risk, stress SPECT MPI was effective for detection and risk stratification of CAD. Average annual mortality was 4.0% in patients with high-risk scans versus 1.6% in patients with normal scans. The authors conclude that, before SPECT MPI can be widely recommended, a more diverse study population is needed and benefits of early detection need to be demonstrated.

**Reviewer's Comments:** Gated SPECT imaging was not routinely performed during the study, so we are missing a valuable variable (left ventricular ejection fraction [LVEF]) in the determination of high versus low risk. The addition of LVEF would likely enhance risk stratification. Note that the study was performed in a fairly uniform population in Minnesota and thus may not be widely generalizable. (Reviewer-Thomas F. Heston, MD).

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Keywords: Coronary Artery Disease, SPECT, Nuclear Cardiology

Print Tag: Refer to original journal article
Is Pre-Ablation Radioiodine Scans Necessary for Thyroid Cancer?

The Utility of Radioiodine Scans Prior to 131I Ablation in Patients With Well-Differentiated Thyroid Cancer.

Van Nostrand D, Aiken M, et al:

Thyroid 2009; March 13 (epub ahead of print):

Pre-radioiodine ablation imaging in patients who are status post-thyroidectomy for well-differentiated thyroid carcinoma may change the management of these patients in >50% of cases.

Objective: To determine what the utility of radioiodine scans are prior to radioiodine ablation for well-differentiated thyroid carcinoma.

Design/Methods: Retrospective study including 355 radioiodine scans performed before I-131 ablation of well-differentiated thyroid cancer. Exclusion criteria were suspicion of or known locoregional disease, distant metastatic disease, ≥300 mg/L physiologic uptake that could potentially alter management prior to I-131 administration, recent large amount of iodine intake, thyroid-stimulating hormone (TSH) <25 mIU/mL within 4 days, or a spot urine iodine. For all patients, scans had been performed within 2 months of thyroidectomy. Each patient had been administered 1 to 4 mCi of I-123 (37 to 148 MBq) with images acquired 24 hours later or 1 to 4 mCi of I-131 (37 to 148 MBq) with imaging 48 hours later. Images were of the whole body, the thyroid bed/neck with a pinhole collimator, and the neck and chest with a parallel-hole collimator. Six criteria were used in evaluating scans: (1) number of foci of uptake in the thyroid bed/neck, (2) location of foci in thyroid bed/neck, (3) size of largest foci in thyroid bed/neck, (4) percent uptake in thyroid bed/neck, (5) possible distant metastases uptake, and (6) significant altered biodistribution.

Results: 55% of scans had findings that could have altered management as follows: 12.0% with ≥6 foci and 6.0% without focal uptake; 14.0% with probable lymph node metastases; 1.1% with at least 1 focus ≥1 lobe; 8.0% with ≥15.0% uptake; 4.0% with distant metastatic disease; and 16.0% with altered biodistribution (ie, breast, salivary, gastrointestinal tract, and urinary bladder).

Conclusions: There were a significant number of findings on pre-therapy radioiodine scans in patients with well-differentiated thyroid carcinoma who were post-thyroidectomy to warrant utilization of pre-ablation imaging to aid in management of these patients.

Reviewer’s Comments: One could argue that, if this patient population were aware of a potential management change in >50% of cases, they would all agree with the authors that pre-radioiodine imaging is necessary. (Reviewer-Twyla Bartel, DO).

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Keywords: Thyroid Cancer, I-131, Radioiodine, Ablation

Print Tag: Refer to original journal article
SPECT/CT with I-131 is superior to planar imaging as a diagnostic technique in patients with well-differentiated thyroid cancer.

**Background:** I-131 imaging is essential for proper management of many patients with well-differentiated thyroid cancer (WDTC). In recent years, with the availability of SPECT/CT, it has been suggested that this may be a better methodology than planar imaging.

**Objective:** To evaluate SPECT/CT in this clinical setting.

**Methods:** The authors evaluated 56 matched pairs of planar and SPECT/CT exams from 53 subjects with known WDTC following initial thyroidectomy. Fifty-two studies were diagnostic I-131 exams and 4 were post-therapy exams. Four studies were obtained using recombinant human thyroid-stimulating hormone. Images were assessed by 2 independent experienced readers.

**Results:** Planar exams detected a total of 147 foci. Of 122 lesions upon which there was observer agreement, a change in focus classification occurred for 53 based on utilization of SPECT/CT findings. In 26 cases, possible cervical lymph nodes were reclassified as thyroid remnant based on SPECT/CT and, in 11 instances, what was felt to be thyroid remnant on planar images was changed to lymph node metastasis based on SPECT/CT. An additional 6 individuals were reclassified as having dental or physiologic foci as opposed to remnant or nodal disease as first suspected by planar imaging. In 17 patients with distant metastases, SPECT/CT found lung disease not originally seen by planar images and, in a second case, SPECT/CT detected a metastatic mediastinal lymph node not seen on planar images. In 9 other foci, reader confidence improved from planar interpretation to SPECT/CT.

**Conclusions:** SPECT/CT with I-131 was superior to planar imaging as a diagnostic technique in patients with WDTC.

**Reviewer's Comments:** I have typically found it very difficult to distinguish a central compartment nodal metastasis from thyroid remnant. This issue is important since the treatment dosage of I-131 is notably different in these 2 situations. SPECT/CT is ideal for making this distinction. Moreover, I believe SPECT/non-contrast CT is the best technique for detecting pulmonary metastases. At some point, I expect I-124 PET/CT to take over imaging duties for thyroid cancer. However, until that time, SPECT/CT, preferably with I-123 (unless it's post-therapy of course), should be our preferred modality when/where available. (Reviewer-David Bushnell, MD).

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Keywords: Differentiated Thyroid Cancer, SPECT/CT Fusion

Print Tag: Refer to original journal article
SFOV SPECT Systems Provide Quality Results

Validation of Attenuation Correction Using Transmission Truncation Compensation With a Small Field of View Dedicated Cardiac SPECT Camera System.

Noble GL, Ahlberg AW, et al:

J Nucl Cardiol 2009; 16 (March/April): 222-232

View truncation can produce significant attenuation correction artefacts that would compromise myocardial SPECT results. The prevalence of small field of view SPECT systems requires validation of approaches that rely on truncated attenuation maps.

**Background:** Customized cardiac SPECT systems may not have a large enough field of view to capture the full extent of the body with radionuclide transmission studies. Truncation of transmission projections can lead to artefacts in attenuation maps, which could compromise attenuation-corrected SPECT images.

**Objective:** To evaluate a method for transmission truncation compensation on cardiac SPECT studies acquired on a small field of view system (SFOV) with direct comparisons of studies acquired on a large field of view (LFOV) gamma camera SPECT system.

**Participants/Methods:** 78 patients referred for stress and rest myocardial perfusion studies were included in this investigation. Subjects were imaged on both a LFOV SPECT system (51 cm) and SFOV SPECT system (37 cm) with radionuclide transmission used for attenuation. Standard image views were reconstructed with no attenuation correction and also with attenuation correction. The attenuation map was generated using compensation for view truncation. Images were interpreted by 3 experts blinded to the acquisition system using the standard 17 segments and 5-point abnormality scale. Paired t-tests were used to evaluate continuous variables, and Bland Altman plots were used to compare the summed scores generated with and without attenuation correction on the 2 SPECT systems.

**Results:** Evaluation of attenuation maps reconstructed without truncation compensation showed significant artefacts in 35% of cases. These were eliminated when truncation compensation was applied. Image quality assessments showed that SFOV SPECT images were preferred. Comparisons of SPECT interpretations between LFOV and SFOV images showed a substantial improvement in concordance for both overall diagnosis and territory classification when attenuation correction was applied (72% to 91%). There was also a significant reduction in summed score values when attenuation correction was applied, indicating appropriate compensation for attenuation artefacts.

**Conclusions:** With proper compensation for view truncation, attenuation correction with SFOV systems yield similar results to LFOV SPECT images where truncation is not a problem. Attenuation compensation significantly improves the agreement between the results from the 2 systems.

**Reviewer's Comments:** The results of this investigation indicate that SFOV SPECT systems can provide similar quality attenuation compensation when appropriate reconstruction software is available. The reader does need to be cautioned that these results are specific to devices and software used in this investigation. Similar validations should be performed for other commercial products. (Reviewer-Mark T. Madsen, PhD).

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Keywords: Attenuation Correction, Truncation Compensation, Small Field of View, SPECT

Print Tag: Refer to original journal article
Whole-body PET/CT imaging is associated with a significant radiation dose that increases cancer risk. PET/CT needs to be clinically justified, and the lowest-dose protocols should be used.

**Objective:** To calculate the likely radiation dose in those undergoing whole-body PET/CT scans and the increased cancer risk incurred.

**Methods:** PET/CT scans obtained using a 64-detector CT system from the base of the skull to the upper thigh were evaluated for the patients' dose using 1 of 3 CT protocols. The effective doses were calculated according to the organ and considering the factors recommended by the International Commission on Radiological Protection. Cancer risk due to radiation was estimated according to a report from the National Academies' Biological Effects of Ionizing Radiation.

**Results:** The approximate CT effective doses of the 3 protocols A, B, and C were 7, 18.5, and 26 mSv, respectively. The effective dose from PET scanning was 6.23 mSv. The total effective doses of the combined PET/CT were approximately 13.5, 25, and 32 mSv, respectively. The CT component contributed 55% to 80% of the total combined dose. The lifetime attributable risk of cancer for 20-year-old U.S. women was between 0.23% and 0.51%; for 20-year-old U.S. men, the risk was between 0.16% and 0.32%. The induced cancer risks decreased when age at exposure increased.

**Conclusions:** Whole-body PET/CT imaging is associated with a significant radiation dose that increases the cancer risk. PET/CT needs to be clinically justified, and the lowest-dose protocols should be considered.

**Reviewer's Comments:** CT accounted for >80% of the PET/CT dose in some protocols for younger patients. For cancer staging and restaging (the usual PET/CT uses), radiation risk with any CT protocol is justified. The risk is likely much lower than the risk of incorrect staging due to suboptimal technique. For less-established compelling indications (eg, evaluating fever of unknown origin) in younger patients, it is prudent to explore reduced radiation CT protocols. (Reviewer-C. Richard Goldfarb, MD).

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Keywords: Whole Body PET/CT, Radiation

Print Tag: Refer to original journal article
Can FDG-PET Detect Alzheimer’s Before It Develops?

FDG-PET Changes in Brain Glucose Metabolism From Normal Cognition to Pathologically Verified Alzheimer’s Disease.

Mosconi L, Mistur R, et al:


FDG-PET possibly detects the early signs of cognitive decline before it becomes clinically apparent.

**Background:** Studies have shown that FDG-PET scans consistently depict a classic pattern of cerebral glucose hypometabolism that correlates with Alzheimer’s, with the degree of hypometabolism correlating to disease severity. These authors point out, however, that theirs is the first study to follow normal subjects to the development of cognitive decline and then to postmortem verification of the disease, with FDG-PET demonstrating development and worsening of the classical hypometabolic pattern with disease progression.

**Objective:** To present the first longitudinal study following patients who are initially cognitively intact to the clinical onset of Alzheimer’s disease to postmortem verification, using FDG-PET results as a marker and monitor of disease progression.

**Methods:** Of 7 patients, 4 demonstrated normal cognitive function on enrollment and 3 had clinical cognitive decline. Subjects were evaluated at baseline with several standard cognitive tests, as well as with FDG-PET. Patients were periodically re-evaluated, obtaining an average of 2 to 3 PET scans until death. Postmortem exams were performed on all subjects to verify the presence or absence of disease.

**Results:** Baseline normal patients all showed cerebral hypometabolism on PET before demonstrating clinical signs of the disease, with the pattern becoming more extensive and severe with cognitive decline as determined by testing. Baseline cognitive-impaired patients demonstrated hypometabolism as well in a more extensive pattern, again with increasing severity paralleling clinical disease progression. All patients had autopsy-verified disease.

**Conclusions:** FDG-PET findings showed a good correlation between clinical disease in life and the verification of disease at death. The authors also found that FDG-PET can detect pathology prior to clinical development of disease.

**Reviewer’s Comments:** This intriguing study shows the power of FDG-PET in detecting patterns of cognitive decline prior to the onset of clinically apparent disease. As the authors point out, several studies have shown that FDG-PET demonstrates a consistent pattern of hypometabolism in patients with clinically detected disease. However, this study goes one step further, using postmortem verification of disease as the gold standard for PET as a tool in detecting early signs of disease. Although a small group of patients were followed, this study shows promise of FDG-PET being a reliable detector of early metabolic patterns associated with subsequent cognitive decline. (Reviewer-Damita Thomas, MD).

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Keywords: Alzheimer’s, FDG-PET, Brain Glucose Metabolism

Print Tag: Refer to original journal article
FDG-PET May Indicate HCC Recurrence After Liver Transplant

Prediction of Tumor Recurrence by 18F-FDG PET in Liver Transplantation for Hepatocellular Carcinoma.

Lee JW, Paeng JC, et al:


FDG-PET may be used as a prognostic indicator of hepatocellular carcinoma disease recurrence in liver transplant patients.

**Background:** The authors reviewed current prognostic indicators of recurrence when evaluating hepatocellular carcinoma (HCC) patients as candidates for liver transplant. As living donor and cadaveric organs are a limited resource, it is important that this resource is allocated to those who have the best prognosis for disease-free survival.

**Objective:** To evaluate FDG-PET as a prognostic indicator of HCC recurrence in liver transplant patients.

**Methods:** Records of 59 patients with HCC who had undergone living donor or cadaveric liver transplantation were retrospectively reviewed. Only those with HCC and no other malignancies were included. Of 59 patients, 40 had localized therapy prior to transplant. All patients underwent FDG-PET imaging about 1 month prior to transplantation, after 6 hours of fasting, and 60 minutes after injection. Quantitative analysis of imaging was performed using regions of interest to measure the $SUV_{max}$ of the tumor ($TSUV_{max}$) and normal liver ($LSUV_{max}$), $SUV_{mean}$ of normal liver ($LSUV_{mean}$), and various ratios ($TSUV_{max}/LSUV_{max}$ and $TSUV_{max}/LSUV_{mean}$).

Histopathological analysis was done on all explanted livers to determine the T stage, Milan criteria (tumor number/size), vascularity, and pathological grade. Patients were followed up for at least 1 year.

**Results:** 14 patients (24%) had a recurrence, most within the first year after transplantation. The 1-year and overall recurrence-free survival rates were 83% and 76%, respectively. Of various quantitative FDG-PET imaging parameters, the $TSUV_{max}/LSUV_{max}$ ratio showed the highest AUC, with an optimal cut-off value of 1.15 in predicting recurrence after transplant. There were significant differences among the nonrecurrence and recurrence groups with respect to this ratio as well as all histopathological parameters. However, only the ratio and tumor vascularity were shown to show a significant correlation with disease recurrence in a multivariate analysis. The 1-year recurrence-free survival rate was 97.0% for those with a ratio <1.15 versus 57.0% for those with a ratio >1.15. There was a 100% recurrence rate among patients with both a ratio >1.15 and with positive tumor vascularity, but 0% recurrence among patients with negative vascularity and a ratio <1.15. In patients with either of the 2 and not both, recurrence rates varied widely (17% to 50%).

**Conclusions:** A $TSUV_{max}/LSUV_{max}$ ratio with a cut-off value of 1.15 is an effective predictor of disease recurrence in HCC transplant patients, more so than the conventionally used Milan criteria.

**Reviewer's Comments:** Interesting and well-designed study that appears to demonstrate the efficacy of FDG-PET as a prognostic indicator of HCC disease recurrence in patients after liver transplantation. The authors raise the concern of normal heterogeneity seen on FDG-PET. However, they propose that using ratios and not just singular SUV more accurately reflects abnormal hepatic glucose metabolism, citing literature to this effect. (Reviewer-Damita Thomas, MD).

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Keywords: FDG-PET, Liver Transplantation, Hepatocellular Carcinoma Recurrence

Print Tag: Refer to original journal article
Can FDG-PET Identify Benign vs Malignant Chromaffin-Derived Tumors?

18F-FDG Avidity of Pheochromocytomas and Paragangliomas: A New Molecular Imaging Signature?

Taleb D, Sebag F, et al:


Malignant and benign chromaffin-derived neoplasms demonstrate similar FDG-avidity.

Background: FDG-PET is not widely used to evaluate endocrine oncological processes because it is thought to lack the specificity for certain markers that characterize these diseases (ie, somatostatin receptors, neurotransmitters). According to the authors, most endocrine neoplasms exhibit a pattern of FDG avidity that is low during its early course, becoming more avid with disease progression and dedifferentiation, but this uptake pattern is not typical of chromaffin-derived neoplasms. They cite their work and that of other investigators showing that, although FDG-PET can detect additional disease compared to other molecular imaging studies, FDG avidity does not seem to be associated with the malignant potential of the disease.

Objective: To evaluate FDG avidity among nonmetastatic and metastatic chromaffin-derived tumors, and whether it reflects a specific metabolic pattern regardless of its clinical behavior.

Methods: Records of 28 patients (18 and 10 patients with nonmetastatic and metastatic disease, respectively) were retrospectively evaluated (16 and 12 patients with newly diagnosed and recurrent disease, respectively). In 9 patients, predisposing factors were known, such as an association with neurofibromatosis type 1 (NF1), Von-Hippel Landau (VHL) disease, multiple endocrine neoplasia type 2A (MEN-2A), and presence of predisposing succinate dehydrogenase subunit mutations. The "gold standard" was comprised of CT imaging as well as a combination of the following molecular imaging modalities: I-131 MIBG, In-111 OctreoScan, or F-18 fluorodopa PET. FDG-PET scans were performed after 6 hours of fasting and 60 minutes after injection and were interpreted independently by 2 nuclear medicine physicians. Visual (using liver and background for comparison for pheochromocytomas and extra-adrenal disease, respectively) and quantitative analyses using SUV_max were performed.

Results: Among patients with nonmetastatic disease, there were 2 false-negative results with FDG-PET, both also negative by I-131 MIBG but positive with F-fluorodopa. PET. FDG-PET identified all 10 patients with metastatic disease, identifying additional disease that was missed by both MIBG and F-fluorodopa PET in 5 patients. FDG, however, did underestimate disease in 5 patients that was detected by fluorodopa PET. There was no statistical difference between FDG avidity of nonmetastatic/metastatic disease. In general, patients with succinate dehydrogenase subunit mutations and with VHL disease had higher uptake values compared to those with NF1 or MEN-2A.

Conclusions: FDG avidity is a hallmark of chromaffin-derived neoplasms, with differences reflecting not only disease dedifferentiation, but also variations of altered metabolic pathways in these neoplastic tissues.

Reviewer's Comments: It is already known that chromaffin-derived neoplasms demonstrate variable FDG avidity regardless of malignity/benignity. As such, as the authors point out, dedifferentiation alone can't explain FDG avidity in these neoplasms. They hypothesize that other variables (an adaptive response to a growing hypoxic environment vs genetic mutations that result in a shift to glycolysis) account for increased FDG avidity. Although interesting, more studies are needed to prove these theories. As for the present, FDG-PET likely cannot be used to differentiate benign from malignant chromaffin-derived neoplasms. (Reviewer-Damita Thomas, MD).

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Keywords: Pheochromocytoma, FDG-PET

Print Tag: Refer to original journal article
FDG-PET/CT Superior to CECT for Detecting Hepatic Metastases

Prospective Evaluation of CECT and 18F-FDG-PET/CT in Detection of Hepatic Metastases.

D'Souza MM, Sharma R, et al:

Nucl Med Commun 2009; 30 (February): 117-125

FDG-PET/CT imaging of liver lesions is superior to contrast-enhanced CT in detecting metastatic lesions.

Objective: To compare contrast-enhanced CT (CECT) with integrated F-18-FDG-PET/CT in the detection of metastatic disease of the liver.

Participants/Methods: 45 patients (26 females, 19 males; age range, 16 to 78 years) with suspected liver metastases were included. The liver metastases were suspected based on clinical findings or ultrasound examinations. Forty-three of these patients had a known extrahepatic primary malignancy, and 2 patients had an unknown primary malignancy. All patients had both a CECT and FDG-PET/CT study within a period of 72 hours. For each PET scan, the patient was administered 10 mCi (370 MBq) of the radiotracer intravenously with imaging 60 minutes after injection. For each CECT, a noncontrast CT was followed by an arterial-phase CT of the hepatic region and then a portal venous phase scan of the entire abdomen. The imaging studies were reviewed by an experienced nuclear medicine physician and a radiologist. The number of liver lesions and their associated SUVs were evaluated. These findings were compared to histopathology as well as clinical and imaging follow-up findings over 6 to 12 months.

Results: The sensitivity of CECT in detecting liver metastases was approximately 88%, and its specificity was about 17%. These rates were 97% and 75%, respectively, for FDG-PET/CT. The primary malignancies that metastasized to the liver in these patients were breast, colorectal, gastric, esophageal, gallbladder, head and neck, lymphoma, cervical, ovarian, pancreatic, malignant melanoma, bronchogenic, testicular, Wilm's tumor, and 2 unknown primaries. Concordance between the 2 types of imaging studies was seen in about 62% of cases. There were more false-positive findings on CECT, particularly with lesions <1.5 cm in size. There were 4 false-negative results on CECT. Three false-positive results were noted on PET/CT, 2 of which were due to postoperative inflammation. One false-negative result was noted on PET/CT and was due to a metastatic mucinous adenocarcinoma of the colon.

Conclusions: FDG-PET/CT was superior to CECT in detecting metastatic lesions to the liver. This was particularly true for lesions <1.5 cm. The authors also state that a larger study is needed with correlative pathology findings to confirm these initial findings.

Reviewer's Comments: In addition to performing a larger study, it seems worthwhile to also evaluate FDG-PET/CT imaging at a time point beyond 60 minutes. (Reviewer-Twyla Bartel, DO).

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Keywords: FDG-PET, Contrast-Enhanced CT, Hepatic Metastases

Print Tag: Refer to original journal article
Attenuated heart rate response to dipyridamole in diabetic patients is associated with depressed left ventricular ejection fraction and chronic renal failure.

Background: Several studies have shown an increased risk of mortality among diabetic patients with an attenuated heart rate (HR) response to both commonly used pharmacological stress agents, adenosine and dipyridamole, as well as to physical exercise. Although the mechanism behind this phenomenon has been previously attributed to autonomic dysfunction, no known investigations have proven this. Therefore, the authors sought to identify certain factors that might account for the HR attenuation to dipyridamole seen in diabetic patients.

Objective: To identify clinical, hemodynamic, and myocardial perfusion parameters associated with an attenuated HR response to dipyridamole in diabetic patients.

Participants/Design: 102 patients with a medically recorded history of diabetes without a history of arrhythmias, heart failure, or other cardiomyopathies were prospectively studied.

Methods: Other pertinent medical histories (hypertension, hyperlipidemia, or chronic renal failure) and medications were also identified. All patients underwent same-day TI-201 rest/Tc-99m tetrofosmin stress with dipyridamole, followed by reversal with aminophylline. The standard 17-segment semiquantitative analysis method was performed using the summed rest score (SRS), summed stress score (SSS), and summed difference score (SDS) measurements. An attenuated HR response was defined as a peak HR-to-rest HR ratio of 1.2 (previously derived by Bhateja et al. Am J Cardiol 2005).

Results: Approximately 46% of patients demonstrated a peak-to-rest HR ratio of ≤1.2. Multivariate regression analysis of various factors (ie, resting HR, left ventricular ejection fraction [LVEF], presence of chronic renal failure, certain cardiac medication use, hypertension, hyperlipidemia, smoking, SSS/SRS/SDS, end-diastolic and end-systolic volume, and prior myocardial infarction and/or angioplasty) revealed that the only factors independently associated with an attenuated HR response were chronic renal failure, a low post-stress LVEF, and a higher resting HR.

Conclusions: The authors’ findings are similar to those of others, and these findings, particularly the low post-stress LVEF, could reflect LV dysfunction in addition to autonomic neuropathy.

Reviewer’s Comments: As the authors point out, their study reiterated what was already known about attenuated HR response to pharmacological and exercise stress in diabetic patients. It is interesting, however, that this response was not independently associated with ischemic changes on perfusion imaging. The authors propose that this response could be due to LV dysfunction and not autonomic dysfunction. The investigation merely showed an association between this response and chronic renal failure, depressed post-stress LVEF, and high resting HR; in terms of investigation, it did not address if LV or autonomic dysfunction is the etiology. Also, the authors seem to imply that the 2 processes are exclusive of each other, when it may be that the former is a cardiac manifestation of the latter. Studies specifically defining and testing these processes and determining them as causes of attenuated HR in diabetic patients are needed. (Reviewer-Damita Thomas, MD).

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Keywords: Myocardial Perfusion Scintigraphy, Heart Rate

Print Tag: Refer to original journal article
By reserving V/Q scanning for patients with normal chest x-ray and no history of asthma or chronic lung disease, diagnostic results should be achieved in >95% of pregnant patients.

Pulmonary embolism (PE) is among the most frequent causes of maternal death in pregnancy. Increased venous stasis, pregnancy-related hypercoagulability, prolonged bed rest, and diminished fibrinolysis result in a 5-fold increased risk of PE in pregnant patients. D-dimer assay plays a limited diagnostic role since pregnancy itself produces a rise above baseline levels, resulting in false-positive results. Because of the lack of specific clinical signs and the absence of reliable laboratory assessment for PE in pregnancy, diagnostic imaging plays an important role. A main concern is fetal and maternal radiation exposure. To better choose among imaging tests, consider the following. Fetal risks from radiation doses of <50 mGy are negligible. Doses of 100 mGy result in a combined risk of organ malformation and cancer of only 1%. Even a combination of chest x-ray, lung scintigraphy, CT pulmonary angiography, and x-ray angiography exposes the fetus to only 1.5 mGy. Disadvantages of CT include radiation exposure to the maternal breasts and risk related to iodinated contrast material. Ventilation-perfusion (V/Q) scintigraphy is now used less frequently than CT, but PIOPED II investigators recommend V/Q scanning in pregnant patients. The majority of V/Q scans in pregnant patients yield normal results. By reserving V/Q scanning for patients with normal chest x-ray and no history of asthma or chronic lung disease, diagnostic results should be achieved in >95% of pregnant patients. Eliminating the ventilation portion and decreasing the perfusion dose by 50% substantially decreases the already low radiation exposure to the pregnant patient. To further reduce fetal radiation dose at lung scintigraphy, the patient should be encouraged to void frequently or a Foley catheter should be inserted to reduce fetal exposure to radiotracer in the bladder.

**Reviewer's Comments:** The editorial aspect of this state-of-the-art review emphasizes the importance of reducing maternal radiation exposure during diagnostic imaging for PE but is reassuring regarding the limited radiation risks to the fetus. V/Q scintigraphy—even with ventilation—results in a tiny fraction of the CT dose to the maternal breast. It seems most appropriate to prefer V/Q over CT in all women of child-bearing age, and even in older women who have normal chest x-rays and no other known lung problems. (Reviewer-C. Richard Goldfarb, MD).

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Keywords: Pulmonary Embolism, Pregnancy

Print Tag: Refer to original journal article
New appropriateness criteria endorsed by the Society of Nuclear Medicine and American College of Radiology provide guidelines for use of cardiac radionuclide imaging.

**Background:** Appropriateness criteria include guidelines about which patients should undergo a specific medical procedure. These guidelines are likely to be adopted by insurance companies and government entities in the evaluation of medical imaging programs. **Grading:** Cardiac radionuclide imaging was determined to be appropriate, inappropriate, or uncertain for the specific patient groups examined. **Pretest Probability:** This is based on the type of chest pain, age, and gender (see table A). Very low is defined as a <5% risk of coronary artery disease (CAD); low is defined as a <10% risk of CAD; intermediate is a 10% to 90% risk of CAD; and high is >90% risk of CAD. **Ischemic Equivalent:** Many of the criteria are dependent on presence or absence of an ischemic equivalent, which is defined as any constellation of clinical findings that the clinician believes is consistent with obstructive CAD. The guidelines provide examples but do not exclude other variables. Some examples given are chest pain, chest tightness, jaw pain, dyspnea, ECG abnormalities suggestive of ischemia, and worsening of effort tolerance.

**Results:** 8 tables are provided covering 8 different categories of patients. These tables outline appropriate, inappropriate, and uncertain indications. Figures 2 through 6 provide a good overall picture of the guidelines. **Conclusions:** The document concludes by saying, "It is hoped that payers would use these criteria as the basis for the development of rational payment management strategies. It is expected that services performed for appropriate indications will be considered reimbursable. In contrast, services performed for inappropriate indications should likely require additional documentation to justify reimbursement because of the unique circumstances or the clinical profile that must exist in such a patient." These criteria have been endorsed by the American College of Radiology and the Society of Nuclear Medicine, along with several other medical groups.

**Reviewer's Comments:** This is an important document to read and share with your referring clinicians. It is important that the referring clinicians state clearly, when appropriate, that the clinical picture is thought to be an ischemic equivalent. Presence or absence of an ischemic equivalent is a critical juncture for many of the decision pathways. For example, in a patient with fatigue and dyspnea worrisome for obstructive CAD, the referral should not just state "patient with fatigue and dyspnea" but rather "patient with clinical symptoms considered to be an ischemic equivalent." This allows a more rapid and accurate categorization of patients. (Reviewer-Thomas F. Heston, MD).

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Keywords: Coronary Artery Disease, Nuclear Imaging

Print Tag: Refer to original journal article
Imaging at 1 hour after injection of FDG is just as accurate as imaging at 3 hours for assessment of vascular inflammation by PET/CT.

**Background:** The best time to image vascular inflammation after FDG injection using PET/CT is not known, with some advocating a 3-hour delay to improve image contrast.

**Objective:** To compare FDG PET/CT imaging 1 hour after injection versus 3 hours after injection in the evaluation of vascular inflammation.

**Design/Participants:** Observational study involving 17 asymptomatic patients referred for clinical reasons for the routine surveillance of abdominal aortic aneurysm.

**Methods:** After a 6-hour fast, dynamic imaging using 2-minute frames was performed starting at 45 minutes, 1 hour, 2 hours, and 3 hours after injection of FDG. Imaging was focused on the abdominal aorta. For each period of dynamic imaging, the vessel wall and lumen uptake were measured using the body mass-corrected SUV$_{\text{max}}$ and a target-to-background ratio (TBR).

**Results:** No statistically significant difference was found in TBR across all time points. There was a significant difference in lumen uptake with time (decrease of 26% from the 45-minute images to the 3-hour images). No significant difference was found between aortic wall uptake at 60 minutes (SUV$_{\text{max}}$, 2.15 ± 0.11 SE) and 180 minutes (SUV$_{\text{max}}$, 1.99 ± 0.18 SE).

**Conclusions:** There was no significant advantage in imaging vascular inflammation of the abdominal aortic wall at 3 hours versus 1 hour after F-18 FDG injection.

**Reviewer’s Comments:** Because the authors did not perform a power analysis, we do not know if the lack of significance was due to low numbers (a sample size of 17) or a true lack of difference. It appears that for a variation of ± 25% in SUV$_{\text{max}}$ of the lumen wall, there is no statistically significant difference between 1 and 3 hours. If smaller variations (<25% change) in the SUV$_{\text{max}}$ are thought to be clinically significant, then this study was underpowered to detect such a difference. (Reviewer-Thomas F. Heston, MD).
Contrast-enhanced CT/PET may be preferable to non-contrast-enhanced CT/PET for detection of hepatic metastases.

**Background:** FDG-PET/CT is very effective for the evaluation of hepatic metastases from most types of solid tumors. The issue of whether to utilize IV contrast with the CT component continues to be debated. At present, most centers perform only non-contrast CT with PET. However, there are merits to contrast enhancement that may outweigh the disadvantages.

**Objective:** To assess the effectiveness of contrast-enhanced CT (CECT) compared to non-CECT performed with PET in patients with suspected hepatic metastases.

**Design/Methods:** This was a retrospective review of the records of 39 patients. FDG-PET, non-CECT, and CECT were performed, including arterial and portal vein phases. Images were interpreted by multiple readers as PET plus non-CECT and then again as PET plus CECT.

**Results:** 178 liver lesions were found. Of these, 41 were eventually determined to be benign based on histopathologic or clinicoradiographic follow-up. Colorectal cancer was the most common primary (n=27), followed by breast cancer. PET plus CECT detected 114 of 137 metastases, whereas PET plus non-CECT detected 92 of 137 ($P = 0.01$). Overall, CECT/PET correctly characterized 131 of 178 lesions compared to 101 of 178 for non-CECT/PET ($P = 0.004$).

**Conclusions:** The authors conclude, "IV iodinated contrast material administration improves the detection of hepatic metastases and the characterization of focal hepatic lesions at PET/CT."

**Reviewer's Comments:** While this study seems to support use of contrast-enhanced CT with PET, at least in this particularly clinical setting, I must take issue with the authors' interpretation of the non-CECT/PET exam presented in figure 1. I suppose this may raise a bit of a red flag regarding their findings. In any case, I suspect CECT should be performed in some cases, whereas non-CECT would suffice in others. Neuroendocrine tumors, which strongly enhance with contrast and are prone to disseminate to the liver, should probably be studied with CECT/PET when this study is performed. At our institution, at least at present, we continue to perform CT exams without contrast with our FDG-PET studies except for certain cases of head/neck cancer. (Reviewer-David Bushnell, MD).

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Keywords: IV Contrast PET/CT, Liver Metastases

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