Low-Dose Radiation Increases Risk of Solid Tumors

_Cancer Risks Associated With External Radiation From Diagnostic Imaging Procedures._


Medical radiation comprises almost 50% of the per capita radiation dose (was 15% in early 1980s). Pooled studies reveal some increased risk of solid tumors at low-dose levels of radiation exposure.

The 600% increase in medical radiation exposure to the US population since 1980 is mostly from diagnostic imaging procedures, comprising almost half of the per capita radiation dose, compared with 15% in the early 1980s. Initially, the radiation dose was measured in “radiation absorbed dose” (rad) and, more recently, in “gray” (Gy) or “milligray” (mGy; 1 Gy = 100 rad; 1 rad = 10 mGy). The relative effectiveness of a given type of radiation to produce a specific biological outcome compared with x-rays or gamma rays, formerly the Rem, is now the sievert (Sv), which is the biological equivalent dose. **Cellular Damage:** Radiation produces 2 types of cellular damage, deterministic and stochastic effects. Deterministic effects occur above a threshold dose and are dose-related. Examples include radiation-induced dermatitis, radiotherapy-associated erythema, and cataract formation. Stochastic effects include cancer and hereditary effects, caused by a mutation or other permanent damage to the viable cell. The probability of a stochastic effect increases with dose (probably with no threshold), but the severity is not related to the dose. **Low-Dose Rate Effects:** Based on studies of the atomic bomb survivors and of patients treated with moderate- to high-dose radiation, national and international radiation expert committees have concluded that dose response at low levels occurs in a linear pattern without a threshold. But recent reports suggest greater complexity regarding low-dose rate effects. The epidemiologic literature on low-dose rate effects has limited statistical power at cumulative lifetime radiation levels of <100 mSv, but pooled studies reveal some increased risk of solid tumors at low-dose levels. **Leukemia:** There is a latency period of 2 to 5 years between radiation exposure and the onset of leukemias, with many leukemias occurring within the first 2 decades of exposure. The risks of radiation-related leukemia in childhood decline sooner and in a more pronounced manner than in adults. **Solid Tumors:** Minimum latency periods for solid tumors range from 10 years to many years after the initial radiation exposure and continue to increase throughout the patient’s life. Radiation-related cancers occur at the same ages as nonradiation-related cancers.

**Reviewer’s Comments:** The increasing attention to medical radiation exposure by the public, regulatory agencies, and congressional committees compels diagnostic imaging personnel to enhance our knowledge of the trendy topic. The very name "nuclear" medicine saddles us with the burden to justify our procedures. This is more than a bit ironic since most of our diagnostic tests are less risky than contrast radiographic studies and involve less radiation, except for MRI. The bottom line is that there could be real risk in rejecting a scintigraphic study for unjustified radiation fears. (Reviewer-C. Richard Goldfarb, MD).

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Keywords: Medical Radiation, Cellular Damage, Cancer Risks

Print Tag: Refer to original journal article
PET Helpful for Diagnosing Large Vessel Vasculitis

The Impact of 18F-FDG PET on the Management of Patients With Suspected Large Vessel Vasculitis.

Fuchs M, Briel M, et al:


FDG-PET is highly sensitive for detecting large vessel vasculitis in patients not already receiving immunosuppressive therapy. PET results alter the medical management of a significant number of patients.

**Background:** Results from a number of studies now indicate that FDG-PET is an accurate method of assessing giant cell arteritis.

**Objective:** To determine the effect of PET on patient management in the setting of suspected large vessel arteritis.

**Methods:** Patients with suspected large vessel vasculitis were eligible for this study. All patients underwent FDG whole-body PET imaging. A group of 3 rheumatologists considered to be experts on vasculitis reviewed 67 cases of suspected large vessel arteritis. The diagnosis was established by consensus using the American College of Rheumatology classification criteria. The group then evaluated the management of each case first without PET findings and then again with PET findings to determine whether individual patients would have had better management had PET results been used.

**Results:** Of the 67 cases reviewed, 61 were considered to have adequate clinical, biopsy, or imaging follow-up to establish or rule out the diagnosis of vasculitis. Thirty of these 61 individual received a final diagnosis of large vessel vasculitis (giant cell arteritis, n=24; Takayasu disease, n=6). The 31 subjects without vasculitis were then used as a control group. PET had an overall sensitivity of 73% and a specificity of 84% for diagnosing large vessel vasculitis. However, all 8 false-negative PET results were found in patients already receiving immunosuppressive therapy for clinically suspected vasculitis. The addition of PET results significantly improved diagnostic accuracy in the group as a whole as well as in the subgroup of patients with giant cell arteritis. PET results altered the biopsy indication from “indicated” to “not indicated” in 4 patients and from “not indicated” to “indicated” in 7 individuals. The panel of experts found that using the PET results would appropriately alter medical management with steroids and/or immunosuppressive drugs in 8 of the 61 cases. **Conclusions:** FDG-PET has an impact on the medical management of a significant fraction of patients with suspected large vessel vasculitis.

**Reviewer's Comments:** The evidence continues to mount in support of the usefulness of PET for establishing the diagnosis of giant cell vasculitis. This article also has a very nice PET image showing the typical FDG pattern of uptake in this condition. (Reviewer-David Bushnell, MD).

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Keywords: Large Vessel Vasculitis, Assessment, PET Findings vs Patient Management

Print Tag: Refer to original journal article
PET During RT Not Accurate for Monitoring HNC Response

Can 18FDG-PET During Radiotherapy Replace Post-Therapy Scanning for Detection/Demonstration of Tumor Response in Head-And-Neck Cancer?

Ceulemans G, Voordeckers M, et al:

Int J Radiat Oncol Biol Phys 2011; 81 (November 15): 938-942

FDG-PET results obtained during radiation therapy do not accurately predict treatment response in patients with head and neck cancer

**Background:** FDG-PET imaging to evaluate treatment response in head and neck cancers (HNC) is routinely performed 3 to 4 months after completion of radiation therapy (RT). The data are limited regarding the use of FDG-PET during RT to monitor treatment response.

**Objective:** To evaluate the accuracy of FDG-PET obtained at 4 weeks of RT to predict treatment outcome in HNC.

**Design:**Prospective study.

**Participants:** 40 patients with HNC treated with intensity-modulated RT.

**Methods:** Patients underwent 3 PET scans. The first scan was obtained before initiating RT, and the second scan was done 4 weeks later, which corresponds to 40 Gy of a total of 70 Gy. The third scan was obtained 4 months after completion of RT. PET scans were read as complete response (CR, no residual uptake) or non-CR (residual uptake). Scan results were compared to clinical outcomes and available pathology.

**Results:** All primary tumors were visualized on the pretherapy PET scan. The median follow-up after completion of RT was 26 months (range, 7 to 56 months). On the second PET scan obtained during RT, 11 scans showed no residual uptake and 29 scans showed residual FDG uptake. Of the 11 scans with no residual uptake, 8 patients had CR at the end of therapy and 3 patients had residual disease. Among 29 patients with residual uptake on the second scan, 20 patients had no residual disease at follow-up. Overall, the accuracy of FDG PET at 4 weeks into RT was 42.5%. PET scans obtained 4 months after completion of RT were significantly more accurate: 25 scans showed no residual disease, with 22 of them reflecting the true disease status. Among 15 scans with residual uptake, 9 patients were found to have residual disease. Overall, the accuracy of PET at 4 months after RT was 77.5%. The 2-year overall survival rate was significantly worse in patients with residual uptake on the posttherapy scan. The PET scans obtained during RT, however, did not show significant correlation with the overall survival rate.

**Conclusions:** For predicting response to radiation therapy in head and neck cancer, posttherapy PET scans obtained at 4 months after completion of RT are more accurate than PET scans obtained during RT.

**Reviewer’s Comments:** Radiation-induced inflammatory changes reduce the specificity of the PET scan during therapy. The investigators of this study, however, did a binary evaluation of presence or absence of uptake: analysis of change in uptake with SUV may be more accurate for monitoring response during RT. At this time, no sufficient data exist to support the clinical use of FDG-PET during RT for response assessment in head and neck cancer. (Reviewer-Yusuf Menda, MD).

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Keywords: Head & Neck Cancer, Radiotherapy Treatment Response, Early Response Assessment Using FDG-PET/CT

Print Tag: Refer to original journal article
**CAE Risk Low When See ST Depression on Stress Testing**

*ST-Segment Depression During Vasodilator Stress Is of Minor Clinical Importance in Women With Normal Myocardial Perfusion Imaging and Low or Intermediate Risk of Coronary Artery Disease.*

Apostolopoulos DJ, Davlouros P, et al:


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In low- to intermediate-risk patients, ST-segment depression during vasodilator stress testing is associated with a low prevalence of significant coronary artery disease and a low cardiac event rate.

**Background:** The diagnostic and prognostic value of vasodilator ECG stress test results in patients with a normal myocardial perfusion scan is unclear, and the incidence of obstructive coronary artery disease (CAD) associated with significant ST-segment depression on vasodilator stress is not known.

**Objective:** To determine the cardiac adverse event (CAE) rate among patients with significant ST-segment depression on vasodilator stress testing but a normal nuclear myocardial perfusion scan. Secondly, to determine the incidence of obstructive CAD in this population.

**Design:** Case-control study.

**Participants:** 109 patients with a normal perfusion scan, ST-segment depression on vasodilator stress testing, and no known CAD.

**Methods:** Patients were analyzed for pretest probability of disease, underwent vasodilator (dipyridamole or adenosine) stress testing in conjunction with myocardial perfusion scintigraphy, and were advised to undergo coronary angiography. The case group consisted of patients with a normal scan but abnormal ST-segment changes with vasodilator stress testing. The control group consisted of a matched group of patients with similar risk factors but both a normal perfusion scan and a normal vasodilator stress test. Follow-up was done by telephone.

**Results:** Of the 109 patients with an ECG-positive vasodilator stress test, 100 were women. In this group, the pretest probability of disease was low in 56% of patients, intermediate in 39%, and high in 5%. Of the 109 patients with ST-segment depression on vasodilator stress testing, 52 subsequently underwent coronary angiography. Of these, 6 had obstructive disease (≥50% lumen stenosis). One had left main disease and 3 required revascularization. Telephone follow-up over 21 ±9 months was completed for 99 of the 109 patients with ST-segment depression. There was 1 nonfatal myocardial infarction and 1 revascularization in the 99 patients available for follow-up. There were no CAEs in the control group.

**Conclusions:** An ECG-positive vasodilator stress test is much more likely to occur in women compared to men. In the low- to intermediate-risk group, the subsequent risk of a CAE is low during the following 1 to 2 years.

**Reviewer's Comments:** If you look at the event rate of the combined outcome of revascularization or myocardial infarction in the ECG-positive group versus the ECG-negative group, the difference is statistically significant, indicating that the ECG-positive group is at a higher risk than the ECG-negative group. Nonetheless, it is also important to note that a positive vasodilator ECG stress test in combination with a normal perfusion scan is poorly predictive of obstructive disease on angiography (6 of 52 patients; 11%). (Reviewer-Thomas F. Heston, MD).

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Keywords: Myocardial Perfusion Imaging, Normal Vasodilator Stress Plus ST-Segment Depression, Diagnosis, Prognosis

Print Tag: Refer to original journal article
PET-CT Predicts Survival in Soft Tissue Sarcoma

18F-FDG-PET/CT Imaging as an Early Survival Predictor in Patients With Primary High Grade Soft Tissue Sarcomas Undergoing Neoadjuvant Therapy.

Herrmann K, Benz MR, et al:

Clin Cancer Research 2012; February 14 (): epub ahead of print

FDG-PET/CT performed early after the first cycle of chemotherapy may be able to predict tumor FDG response in patients with soft tissue sarcoma.

Background: The use of neoadjuvant chemotherapy is associated with substantial side effects in patients undergoing surgery for the treatment of soft tissue sarcomas (STS).

Objective: To determine if PET imaging, performed early after initiation of chemotherapy, can identify patients who have a good prognosis based on tumor FDG response.

Design: Prospective study.

Participants: Patients with high-grade STS.

Methods: In total, the study group was comprised of 57 patients who underwent neoadjuvant chemotherapy followed by curative-intent tumor resection. All patients underwent FDG-PET/CT imaging at baseline prior to initiation of neoadjuvant chemotherapy. A second early follow-up PET exam was performed on 39 individuals after the first cycle of chemotherapy. Of the 57 subjects in the study, 56 also had follow-up PET performed at the completion of all cycles of neoadjuvant chemotherapy.

Results/Conclusions: 17 patients died during a median follow-up of 55 months. The median baseline tumor SUV\text{max} was 7.5 (range, 2.5 to 31) and was not statistically different between survivors and nonsurvivors. ROC analysis determined that the optimal cutoff for determining response was a decrease in SUV\text{max} of 26% for early PET and 57% for PET obtained after completion of the entire neoadjuvant treatment protocol. Using these cutoff values, the 5-year survival rate was significantly better for early PET responders (82%) compared to early PET nonresponders. In addition, the overall 5-year survival rate was 85% for late PET responders versus 54% for late PET nonresponders. On CT, 80% of the total group showed stable disease after completion of neoadjuvant therapy. In univariate analysis, both early and late PET results were predictive of outcome. Histologic response to neoadjuvant treatment was, however, not predictive of survival. Only early PET metabolic response remained a significant predictor of survival in multivariate analysis.

Reviewer's Comments: In this study, the interval between injection of FDG and initiation of imaging ranged from 60 to 90 minutes, and we know this variability can impact the degree of FDG tumor uptake. In addition, the authors defined what they would consider to be tumor response from the study group data itself. They need to apply these response criteria to an entirely separate prospective cohort before drawing any definitive conclusions regarding survival. Still, as with many tumor types, these data seem to support a role for PET in predicting response to chemotherapy. (Reviewer-David Busnell, MD).

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Keywords: Soft Tissue Sarcoma, Early PET Imaging vs Prognosis, Tumor Response to Therapy

Print Tag: Refer to original journal article
Are BMD Studies Overutilized in Older Women?

Bone-Density Testing Interval and Transition to Osteoporosis in Older Women.

Gourlay ML, Fine JP, et al:


BMD testing intervals for postmenopausal women aged >65 years can be as long as 15 years for those with normal bone density or mild osteopenia.

**Background:** Dual-energy x-ray absorptiometry (DXA) scan is recommended for screening all postmenopausal women, including those aged >65 years. However, there is no agreement for a follow-up testing interval.

**Objective:** To estimate appropriate bone mineral density (BMD) testing intervals for older postmenopausal women.

**Design:** Prospective study that lasted 15 years.

**Participants:** 4957 postmenopausal women (age ≥67 years) who had T scores ranging from -2.4 to -1.0 (osteopenia or normal BMD) not requiring medications and who had no history of vertebral and hip fractures.

**Methods:** Participants were subdivided into 1 of 4 groups according to their T-scores: normal BMD (T-score, -1.1 to -1.4), moderate osteopenia (T-score, -1.5 to -1.9), and advanced osteopenia (T-score, -2.0 to -2.4). The follow-up examinations were performed at 2, 6, 8, 10, and 16 years. The BMD testing interval was considered to be the time required for 10% of participants to make the transition to osteoporosis before a hip or vertebral fracture occurred and before treatment for osteoporosis was initiated.

**Results:** The estimated BMD testing intervals for women with normal BMD and mild osteopenia were both approximately 17 years. The estimated BMD testing intervals for women with moderate and advanced osteopenia were 4.7 and 1.1 years, respectively. Before the transition to osteoporosis, 2.4% women had a hip or clinical vertebral fracture.

**Conclusions:** BMD testing intervals for postmenopausal women aged >65 years can be as long as 15 years for those with normal BMD or mild osteopenia, 5 years for those with moderate osteopenia, and 1 year for those with advanced osteopenia.

**Reviewer's Comments:** On the surface, the results of this study are all well and good. The problem is that, in their discussion, the authors refer to overutilization of diagnostic testing, and one could come away with the notion that this includes DXA. The study does not include the main group of women undergoing DXA (perimenopausal or postmenopausal women aged <65 years). Because the study appeared in the New England Journal of Medicine, it gained enormous, attention, which motivated the International Society for Clinical Densitometry (ISCD) to e-mail its membership citing evidence to confirm the need for more frequent BMD testing intervals in most peri- and postmenopausal women. The e-mail also provided statistics showing that, in current practice, DXA is not at all overutilized. Even in the over-65-year-old age group, there were important limitations to the study cited by the authors themselves and emphasized by the ISCD letter. Take a good look at both if you have the time and interest. (Reviewer-C. Richard Goldfarb, MD).

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**Keywords:** Osteoporosis, Bone Density Testing, Rescreening Intervals

**Print Tag:** Refer to original journal article
Lateral compartment nodal metastases are associated with an increased likelihood of cancer recurrence in patients treated for well-differentiated thyroid cancer.

**Background:** Though the years, we have had conflicting evidence regarding whether metastases to regional cervical lymph nodes are associated with an adverse outcome in patients with well-differentiated thyroid cancer (WDTC). The consensus probably is that disease recurrence is more likely in these patients, although it may not have an effect on survival.

**Objective:** To determine whether the location of and number of nodal metastases have an impact on disease recurrence and/or survival in patients who have undergone treatment for WDTC.

**Design:** Retrospective study.

**Methods:** All patients had been treated with near-total thyroidectomy and postoperative radioiodine therapy ranging from 100 mCi to 200 mCi of I-131. Lateral and central compartment nodal dissections were performed if preoperative ultrasound of the neck was positive for nodal disease. Disease recurrence was based on serum thyroglobulin levels during follow-up and/or results of imaging exams, including radioactive iodine imaging, ultrasound, and/or PET.

**Results:** The median follow-up was 49 months. At the time of initial surgery, cervical nodal metastases without distant metastases were found in 97 of the 402 subjects. These 97 patients represented the actual study group. During follow-up, recurrent disease developed in 45 of these 97 patients and was present in regional lymph nodes in 37 of the 45 patients. The authors found that neither the likelihood of recurrence (at any location) nor the disease-free survival was related to the number of disease-positive lymph nodes at initial presentation. However, after multivariate analysis, the single significant predictor of recurrence and disease-free survival was the presence of metastatic disease in the lateral compartment lymph nodes. Recurrence developed in 60% of patients with lateral compartment nodal metastases and in only 30% of patients with central compartment nodal metastases. All 4 patients who died from their disease in this study had lateral compartment nodal disease. However, due to the low number of deaths, this was not found to be statistically significant.

**Reviewer's Comments:** These authors present compelling data that disease recurrence is more likely in patients with lateral compartment nodal disease versus those with only central compartment disease. Based on the data in this study, it would seem reasonable to take a more aggressive approach with I-131 therapy in patients with lateral compartment nodal metastases. (Reviewer-David Bushnell, MD).

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Keywords: Thyroid Cancer, Cervical Lymph Node Metastases vs Recurrence Risk

Print Tag: Refer to original journal article
PET Distinguishes Benign, Malignant Parotid Tumors

Parotid Gland Tumors: Preliminary Data for the Value of FDG PET/CT Diagnostic Parameters.

Hadiprodjo D, Ryan T, et al:

AJR Am J Roentgenol 2012; 198 (February): 185-190

FDG-PET metabolic imaging parameters can differentiate benign and malignant tumor uptake in parotid glands. There is some overlap in SUV$_{\text{max}}$ levels for benign and malignant parotid tumors.

**Background:** The 10-year disease-free survival rate is much better for early stage malignant parotid tumors than for late-stage disease.

**Objective:** To determine whether FDG-PET can identify malignant parotid tumors with a high level of accuracy.

**Design:** Retrospective study.

**Participants:** 49 subjects with abnormal parotid uptake of FDG on PET and an additional 49 control patients with no evidence of parotid disease on PET/CT.

**Methods:** In addition to measuring SUV$_{\text{max}}$, the authors determined the following parameters for the parotid glands: (1) metabolic tumor volume, which simply represents the volume of tumor that shows abnormal FDG uptake; and (2) total glycolytic activity for a tumor, which is defined as the metabolic tumor volume times the mean SUV of the tumor. Image interpretation was performed by an experienced interpreter without knowledge of the final diagnosis.

**Results/Conclusions:** Of the 49 subjects with abnormal parotid FDG uptake, 24 had focal lesions and 25 showed abnormal diffuse parotid uptake (according to the authors). Of the 24 patients with focal FDG abnormalities on PET, 18 underwent biopsy, and the remaining 6 had imaging and clinical follow-up to establish a diagnosis. The 25 subjects with abnormal diffuse uptake were followed up clinically and with imaging; some cases were followed up for up to 1 year. For the entire group of 49, the mean follow-up was 15 months. In the control group, the median SUV$_{\text{max}}$ for parotid gland uptake of FDG was 1.25 (range, 0.63 to 1.87). The median SUV$_{\text{max}}$ was 2.55 (range, 1.03 to 4.07) in the 25 subjects with abnormal diffuse uptake, 6.4 (range, 3.4 to 9.0) in the 15 benign parotid tumors, and 11.8 (range, 4.45 to 19.15) in the 9 malignant parotid tumors. These differences were statistically significant. Using an SUV$_{\text{max}}$ cutoff of 4.2 yielded the optimal sensitivity (89%) and specificity (80%) for diagnosing malignant tumor with PET. An SUV >11.6 was seen only in malignant tumors, and all malignant lesions showed an SUV$_{\text{max}}$ >3.2. Both metabolic tumor volume and the total glycolytic activity were significantly greater in malignant versus benign parotid tumors. Of the 3 imaging parameters, ROC curve analysis showed a significantly higher area under the curve for SUV$_{\text{max}}$ compared to the other 2 parameters.

**Reviewer’s Comments:** Although the authors present a group of 49 subjects and another 49 matched controls, this study primarily focuses on results from a group of 24 subjects with focal parotid tumors. I am not certain that the 25 subjects identified as having abnormal diffuse FDG parotid uptake actually had abnormal parotid uptake. Nonetheless, some of the data in this study are very useful. (Reviewer-David Bushnell, MD)

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Keywords: Parotid Tumors, PET’s Ability to Differentiate Malignant vs Benign Tumors

Print Tag: Refer to original journal article
F-18 DOPA May Be New Imaging Test for NB

Comparison of 18F-DOPA PET/CT and 123I-MIBG Scintigraphy in Stage 3 and 4 Neuroblastoma: A Pilot Study.

Piccardo A, Lopci E, et al:


Background: I-123 MIBG imaging has been an extremely useful imaging technique for initial staging, detection of recurrence, and evaluation of response to chemotherapy in children with neuroblastoma (NB). PET/CT using F-18 DOPA, has been found to be extremely sensitive for detecting carcinoid tumors and pheochromocytoma in adults.

Objective: To compare PET DOPA imaging to I-123 MIBG for detecting NB.

Design: Prospective study.

Methods: The authors compared results of PET/CT F-18 DOPA to those of I-123 MIBG in 19 children diagnosed with NB. Most subjects had been referred for suspected disease recurrence. For MIBG studies, both planar and SPECT imaging (n=15) were performed. Of note, carbidopa premedication was not used for any of the PET DOPA imaging exams. The final diagnosis was established based on clinical information, histology, and/or results from CT/MRI exams.

Results/Conclusions: NB was present in 17 of the 19 individuals. PET/CT F-18 DOPA detected disease in 16 of these 17 patients, whereas I-123 MIBG detected disease in 11. Of the 28 paired exams, the sensitivity was 95% for PET/CT F-18 DOPA and 65% for MIBG. This difference was statistically significant. The authors reported a specificity of just under 100% for DOPA imaging and noted that there was no significant difference in the specificity of the 2 techniques in the analysis of the 28 paired studies. However, it is notable that the 2 disease-free patients had shown false-positive results on the initial MIBG studies and later demonstrated true-negative findings with DOPA. In addition, PET DOPA findings were believed to alter management in approximately a third of the subjects. From the 28 paired exams, there were 156 NB sites, 141 (90%) of which were detected by PET DOPA and 88 (56%) which were detected by MIBG. On a per-lesion basis, the authors reported a specificity of 75% for PET/CT and 62% for 123I-MIBG, which was not found to be a significant difference.

Reviewer’s Comments: The primary limitation for this study, as I see it, was the absence of SPECT/CT (as opposed to SPECT, which was performed) for MIBG imaging. In addition, the fact that the authors did not use carbidopa to premedicate patients before the PET exam may have reduced the accuracy of this technique. I would also emphasize that the apparent low specificity (on a per-lesion basis that the authors reported for both MIBG and DOPA) is most likely related to the actual low sensitivity of the gold standard techniques used.

(Reviewer-David Bushnell, MD).

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Keywords: Neuroblastoma, Diagnosis, PET/CT, Sensitivity of I-123 MIBG vs F-18 DOPA

Print Tag: Refer to original journal article
**FDOPA-PET Superior for Imaging Brain Tumors**

18F-FDOPA PET Imaging of Brain Tumors: Comparison Study With 18F-FDG PET and Evaluation of Diagnostic Accuracy.

Chen W, Silverman DH, et al:

J Nucl Med 2006; 47 (June): 904-911

Using striatum as standard reference can yield optimal thresholds for determining brain tumor viability with F-18 FDOPA-PET imaging.

**Objective:** To determine the diagnostic accuracy of PET-based glucose (F-18 FDG) versus amino acid (F-18 FDOPA) analog radiotracers for the detection of brain tumors.

**Participants:** 30 patients with newly diagnosed (n=7) or previously treated (n=23) brain tumors.

**Methods:** All patients underwent PET exams and brain MRI (with and without contrast).

**Results:** Based on a standard tumor SUV greater than background SUV (T/N >1.0), the direct comparison of F-18 FDOPA and F-18 FDG-PET evaluations suggested that both studies were comparable in specificity (43% versus 43%, respectively) but that F-18 FDOPA was superior in sensitivity (96%) compared with F-18 FDG (61%). Both demonstrated no visible uptake in the 3 reported cases of long-term remission but demonstrated low-level uptake in the 4 reported cases of radiation necrosis. Differences in tumor detection may be attributed to each radiotracer's signal-to-noise characteristics. F-18 FDOPA generally yielded greater T/N ratio values for high-grade (2.50 ± 0.73; n=18) and low-grade (1.95 ± 0.69; n=5) tumors, whereas the relatively indiscriminant localization of F-18 FDG to normal cortical brain tissue limited the conspicuity of the high-grade (1.23 ± 0.69) and low-grade tumors (0.66 ± 0.33).

**Conclusions:** F-18 FDOPA is better than F-18 FDG for visualizing residual high-grade and low-grade brain tumors, in general. **Discussion:** Of the patient outcomes in this study, half were derived from reports of clinical follow-up, which included 6 deaths, 5 cases of clinical stability after 27 months, and 3 cases of radiation necrosis confirmed by MRI. The other half of these patient outcomes were based on histologic findings, which were not presented in detail. Consequently, minor discrepancies arise during subsequent statistical analysis, such as why merely 7 patients were classified as disease-free and why only 3 of these were considered to be in long-term remission. However, semiquantitative ROC analysis of the 30 comparison patients yielded more conclusive criteria for interpreting abnormal F-18 FDOPA localization, which were then validated in an additional 51 patients. Ultimately, F-18 FDOPA PET scans (n=81) showing focal uptake greater than normal striatum tissue (T/S >1.0) correlated to residual tumor with overall sensitivity, specificity, and accuracy values as high as 92%, 95%, and 93%, respectively. These promising numbers may portend essential use of F-18 FDOPA-PET for distinguishing residual disease from radiation necrosis.

**Reviewer’s Comments:** Although this is an older article, it deals with an important application of a PET radiopharmaceutical that is becoming more widely used. Time-activity curves demonstrate concurrent peak accumulations of F-18 FDOPA to tumor, cerebellum, and cerebral cortex at 10 to 30 minutes. This precedes peak localization to striatum (around 50 to 70 minutes) and ensures reliable T/S ratios. T/N ratios are significantly less time dependent. (Reviewer-Parren McNeely, MD).

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Keywords: Brain Tumor Imaging, PET, Accuracy of F-18 FDOPA vs F-18 FDG

Print Tag: Refer to original journal article
F-18 florbetapir has a high test-retest reliability and yields adequate images that differentiate AD from normal controls at a lower dose (3 mCi) compared to a higher one (10 mCi).

**Background:** Despite the various diagnostic criteria developed to aid in its diagnosis, Alzheimer disease (AD) still poses a diagnostic conundrum to physicians. As such, functional imaging with C-11 PiB targeting β-amyloid brain plaques characteristic of the disease has been developed. Because C-11 PiB’s short half-life restricts its use to facilities with an on-site cyclotron, this radiotracer has proven to be quite limited in its use. F-18 florbetapir was developed in response to this concern.

**Objective:** To evaluate the effective dose (3 vs 10 mCi) of F-18 florbetapir in differentiating AD from normal subjects and to evaluate this radiotracer's test-retest intrasubject reliability.

**Methods:** A total of 40 patients were evaluated: 9 AD patients and 11 normal control subjects were evaluated for the dose-determination portion of the study, and 10 AD patients plus 10 normal control subjects were evaluated in the reliability testing portion of the study. In the dose-determination study, all patients underwent florbetapir imaging twice — once with 3 mCi and again with 10 mCi of the radiotracer. In the reliability study, each subject also underwent imaging twice approximately 4 weeks apart with both semiquantitative and visual assessments measured.

**Results:** The image quality did not differ significantly between 3 versus 10 mCi of florbetapir. However, 3 mCi of florbetapir yielded images with slightly reduced image quality. Regardless of dose, visual and semiquantitative measures were higher in AD versus controls. In the reliability study, there was a high degree of agreement between the both the visual and semiquantitative measures in both patient groups as well as between imaging times.

**Conclusions:** F-18 florbetapir has both a wide effective dose range as well as high test reliability. Therefore, it is a good imaging biomarker of AD.

**Reviewer's Comments:** The results of this interesting study demonstrate the efficacy of low-dose florbetapir in accurately differentiating AD from normal controls. With facilities becoming more conscious when it comes to radiation exposure, this study shows that florbetapir can be administered at a smaller dose with resulting less radiation exposure, without sacrificing image quality. The study also demonstrates the reliability of florbetapir in not only differentiating disease from normal states but also in doing so reliably and with visual and semiquantitative interpretive criteria. Because AD is such a daunting disease to definitely diagnose until further into the disease process, finding a fluorine-based PET biomarker for AD is a huge step forward in the use of PET in the diagnosis of this disease. (Reviewer-Damita Thomas, MD).

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Keywords: Alzheimer Disease, Diagnosis, Florbetapir PET Test-Retest Reliability

Print Tag: Refer to original journal article
Predicting improvement after bypass surgery is highly inaccurate when based on clinical and angiographic findings alone. Compared to scintigraphy, surgeons’ pre-op predictions of post-op improvement are unreliable.

**Background:** In Europe, the current standard of practice before a patient undergoes coronary artery bypass grafting (CABG) is to rely almost exclusively on the clinical findings and anatomic details from coronary angiography to determine the prognosis.

**Objective:** To compare the clinically predicted outcome of patients undergoing CABG with the actual changes identified by gated myocardial perfusion scintigraphy (MPS).

**Design:** Prospective observational study.

**Participants:** 12 cardiac surgeons participated in this study of 92 patients undergoing CABG.

**Methods:** MPS and angiography were performed on all patients before and again 6 months after CABG. Cardiac surgeons were blinded to the results of the initial myocardial perfusion scan. Just before operating, the surgeons filled out a questionnaire inquiring about the predicted effect of the procedure in terms of myocardial perfusion (by territory), left ventricular ejection fraction (LVEF), and clinical symptoms. These completed questionnaires were compared with clinical and myocardial perfusion findings at 6 months post-op.

**Results:** The sensitivity for the surgeons’ prediction of freedom from angina was good (94%), although the specificity was poor (0%). Compared to MPS, the overall accuracy for surgeons correctly predicting improvement versus no improvement was 68%. When looking at the 3 major vascular territories, no significant correlations were found between the surgeons’ preoperative predictions of improvement compared to changes seen on MPS for the left anterior descending and circumflex territories. There was only a weak correlation between predictions and perfusion findings for the right coronary artery ($r=0.244$, $P<0.05$). No correlation was found between clinically predicted and observed changes in LVEF.

**Conclusions:** Clinical and angiographic findings are poorly predictive of improvements after CABG in terms of cardiac perfusion and LVEF.

**Reviewer’s Comments:** The results of this study suggest that patients should routinely undergo MPS before undergoing CABG, even if angiography has already been performed. The authors of this study found that the correlation between predicted versus actual outcomes was poor when based on clinical findings and angiography alone. These findings support the hypothesis that improved results might come about if MPS was a routine part of the workup performed prior to CABG. (Reviewer-Thomas F. Heston, MD).

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Keywords: Myocardial Perfusion Scintigraphy, Coronary Angiography, Bypass Surgery, Predicting Outcomes

Print Tag: Refer to original journal article
SUV Changes Predict Survival in NSCLC

Large Decreases in Standardized Uptake Values After Definitive Radiation Are Associated With Better Survival of Patients With Locally Advanced Non–Small Cell Lung Cancer.
Lopez Guerra JL, Gladish G, et al:

Following chemotherapy in patients with non-small cell lung cancer, higher SUV_{\text{max}} values on FDG-PET/CT are associated with lower overall and disease-free survival rates.

Background: FDG-PET/CT is an established staging tool used both before and after therapy in patients with advanced non-small cell lung cancer (NSCLC). However, its use as a predictor of outcome following therapy is not as well established.

Objective: To determine whether the change in SUV_{\text{max}} between pre- and post-chemotherapy FDG-PET/CT scans in the primary lesion and within the most metabolically active regional lymph node is predictive of overall and disease-free survival in patients undergoing treatment for NSCLC.

Design: Retrospective review.
Participants: 49 patients with advanced NSCLC.
Methods: All patients underwent baseline FDG-PET/CT scans approximately 26 days before therapy and again at approximately 3 months after therapy. SUV_{\text{max}} in the primary lesion and in the “hottest” regional lymph node were noted on both scans, and the changes in SUV_{\text{max}} of the respective lesions were calculated. Standard statistical methods were used to assess the overall and disease-free survival rates.

Results: Overall and disease-free survival rates were significantly lower among patients who had higher SUV_{\text{max}} in the primary lesion and the hottest regional lymph node following therapy. Optimal SUV_{\text{max}} cutoffs were 3.7 in the primary lesion and 3.1 in the hottest lymph node. The overall and disease-free survival rates were lower for patients having an SUV_{\text{max}} after therapy >3.7 in the primary lesion and >3.1 in the hottest lymph node. Also, a reduction in SUV_{\text{max}} >72% between pretherapy and posttherapy scans was associated with better survival rates compared to reductions <72%.

Conclusions: In patients with NSCLC, the posttherapy SUV_{\text{max}} and the change between pre- and post-therapy SUV_{\text{max}} on FDG-PET/CT following therapy is predictive of disease-free and overall survival rates.

Reviewer’s Comments: Although limited by its retrospective nature and small study size, the results from this study are compelling. They suggest that the semiquantitative SUV_{\text{max}} measure can be used to predict survival outcomes. This may have important clinical implications because posttherapy SUV_{\text{max}} may be useful in identifying those at a higher risk of recurrence. This use of SUV_{\text{max}} may also help identify those in whom a more aggressive treatment strategy is warranted. In the case of the latter, it remains to be seen whether an actual change in therapy will translate into improved outcome. Further evaluation with larger patient numbers is required to further elucidate the findings of this study as well as to answer the questions it poses. (Reviewer-Damita Thomas, MD).

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Keywords: Non-Small Cell Lung Cancer, Radiation Therapy, PET Standardized Uptake Values vs Survival

Print Tag: Refer to original journal article
GBP-SPECT Compares Well With Cardiac MRI

Evaluation of Left and Right Ventricular Ejection Fraction and Volumes From Gated Blood-Pool SPECT in Patients With Dilated Cardiomyopathy: Comparison With Cardiac MRI.

Xie BQ, Tian YQ, et al:


In patients with dilated cardiomyopathy, gated blood pool SPECT tends to underestimate left and right ventricular volumes in comparison with cardiac MRI.

**Background:** Cardiac MRI has become the reference standard for evaluating left ventricular (LV) and right ventricular (RV) end-systolic volume (ESV), end-diastolic volume (EDV), and ejection fraction (EF). Gated blood pool SPECT (GBP-SPECT) correlates significantly with echocardiography and gated radionuclide ventriculography. However, its performance in patients with dilated cardiomyopathy (DCM) has not been previously compared with cardiac MRI.

**Objective:** To determine the accuracy of GBP-SPECT for measuring RV and LV indices in patients with DCM using cardiac MRI as the reference standard.

**Design:** Prospective cohort study.

**Participants:** Consecutive patients with idiopathic DCM. This diagnosis was based on an LVEF <45%, diffuse hypokinesis, LV end-diastolic diameter >55 mm for men and >50 mm for women, and normal coronary arteries by angiography or CT. Patients were excluded if they had clinical instability, uncontrolled arrhythmias, pacemakers, or defibrillators. **Methods:** Patients underwent GBP-SPECT and cardiac MRI within 48 hours. **Results:** The study included 32 patients. LV volume measurements by GBP-SPECT and cardiac MRI were significantly correlated (r =0.83 and 0.88 for EDV and ESV, respectively; P<0.001). LV volumes were statistically lower by GBP-SPECT than by cardiac MRI (EDV: 229 mL ± 68 mL vs 261 mL ± 69 mL; P<0.001; ESV: 188 mL ± 68 mL vs 216 mL ± 70 mL; P<0.001). Assessment of mean LVEF was not statistically different for the 2 methods (19% ± 7%, P =0.23). The Pearson correlation coefficient for LVEF determined by each method was 0.89 (P<0.001). Mean RV-EDV and RV-ESV were significantly lower by GBP-SPECT than by cardiac MRI (170 mL ± 36 mL vs 195 mL ± 37 mL and 117 mL ± 37 mL vs 144 mL ± 37 mL; P<0.001). Mean RVEF was higher by GBP SPECT than by cardiac MRI (32% ± 9% vs 26% ± 6%; P<0.001).

**Conclusions:** Cardiac volumes in patients with DCM determined by GBP-SPECT correlate well with those determined by cardiac MRI. LV and RV volumes are systematically lower by GBP-SPECT. RVEF by GBP-SPECT should be cautiously interpreted.

**Reviewer's Comments:** Patients who may benefit from GBP-SPECT include those with poor echocardiography windows and implantable devices or other hardware that preclude MRI. Centers with less experience using first-pass GBP imaging to determine RV function might opt to use GBP-SPECT. (Reviewer-Shayne Squires, MD).

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Keywords: Dilated Cardiomyopathy, Gated Blood Pool SPECT, Cardiac MRI, Left and Right Ventricular Indices

Print Tag: Refer to original journal article
PET Monitors Rx Response in Paget Disease of Bone

18F-Fluoride PET for Monitoring Therapeutic Response in Paget's Disease of Bone.

Installé J, Nzeusseu A, et al:


PET imaging and SUV$_{\text{max}}$ parameters must be consistent (same anatomic location and time after radiotracer injection) for reliable/meaningful comparison across time to track changes of pagetic bone remodeling/activity.

**Objective:** To evaluate semiquantitative SUV$_{\text{max}}$ values of F-18 fluoride bone incorporation as surrogate markers of bone mineralization activity patients with Paget disease of bone.

**Participants:** 14 patients with monostotic (n=9) and polyostotic (n=5) forms of Paget disease.

**Methods:** SUV$_{\text{max}}$ parameters were directly compared to empirically determined first-order kinetic influx constants characterizing F-18 plasma clearance. Baseline assessments preceded 1-month and 6-month follow-ups after the initiation of bisphosphonate therapy. Nonlinear regression (Ki-NLR) and Patlak graphical (Ki-PAT) analyses were applied to a standard 3-compartment model. Patlak analysis simplifies NLR by assuming negligible demineralization (i.e. redistribution of F-18 from bone mineral compartment).

**Results:** Both methodologies strongly correlated with one another ($r^2=0.99; P<0.05$). Both of these kinetic modeling indices also correlated with the semiquantitative SUV$_{\text{max}}$ parameter, both in assessments of bone remodeling ($0.53 < r^2 < 0.75; P<0.05$) as well as percent change from baseline as a measure of therapeutic response ($0.65 < r^2 < 0.85; P<0.05$). The two PET-based quantitative indices had weaker correlations with biochemical markers of bone resorption. Correlations of Ki-NLR and Ki-PAT to second-morning void urinary cross-linked N-terminal telopeptides (NTX) of type I collagen ($0.45 < r^2 < 0.50; P<0.05$) were only slightly better than serum cross-linked C-telopeptides (CTX) of type I collagen ($0.39 < r^2 < 0.40; P<0.05$). Both indices performed better than SUV$_{\text{max}}$. There was no correlation between PET assessment and biochemical assays of bone formation (serum total and bone-specific alkaline phosphatase).

**Conclusions:** Consistent correlations between SUV$_{\text{max}}$, Ki-PAT, and Ki-NLR throughout the study suggest that each may accurately assess the therapeutic response of pagetic bones to bisphosphonate therapy. Although easier to acquire, SUV$_{\text{max}}$ measurements must be strictly implemented to minimize potential errors, such as those associated with varying uptake periods and/or image acquisition times.

**Reviewer's Comments:** Although this is an older article, it deals with an important application of a PET radiopharmaceutical that is becoming more widely used. Reproducible correlations confirmed the accuracy of noninvasive SUV$_{\text{max}}$ measurement for tracking changes of pagetic bone remodeling/activity over time in response to bisphosphonate therapy. (Reviewer-Parren McNeely, MD).

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Keywords: Paget Disease of Bone, PET, Monitoring Response to Bisphosphonates With F-18 Fluoride

Print Tag: Refer to original journal article
Brain Activity Affected by Systemic Inflammation

Glucose Metabolism in the Insula and Cingulate Is Affected by Systemic Inflammation in Humans.
Hannestad J, Subramanyam K, et al:

Systemic inflammation is associated with changes in glucose metabolism in brain structures involved in the pathophysiology of depression.

**Background:** Inflammatory cytokines cause depressive symptoms in nonhuman models. Endotoxin administration in humans causes mild depressive symptoms, such as fatigue and loss of social interest. Neural correlates of depression identified by functional neuroimaging studies include the insula, cingulate, and amygdala.

**Objective:** To determine whether endotoxin administration is associated with changes in glucose metabolism in the insula, cingulate, and amygdala.

**Design:** Randomized, double-blind, placebo-controlled crossover study.

**Participants:** 9 healthy subjects (8 men, 1 woman), with an average age of 28.6 ± 8.2 years were screened to exclude psychiatric illness, illicit substance use, and antiinflammatory use.

**Methods:** Each subject received an IV dose of endotoxin and IV saline placebo 1 week apart. Each subject subsequently underwent PET and MRI on the same day as endotoxin or placebo administration. PET and MRI images of the brain were coregistered. Behavioral changes following endotoxin or placebo administration were assessed using the Montgomery-Åsberg Depression Rating Scale, and self-reported social interest was assessed using a visual analog scale. **Results:** The normalized glucose metabolism (NGM) was 3.0% ± 3.6% higher in the insula compared to placebo ($P = 0.048$) following endotoxin administration. The NGM was 2.5% ± 3.2% lower in the cingulate compared to placebo ($P = 0.06$) following endotoxin administration. No significant difference in NGM was seen in the amygdala following endotoxin administration. Decline in social interest was negatively correlated with TNF-α and IL-6 levels ($r = -0.92$, $P = 0.0005$ and $r = -0.85$, $P = 0.004$, respectively). There was a positive correlation between change in social interest and insula NGM ($r = 0.72$, $P = 0.029$).

**Conclusions:** Endotoxin administration in humans is associated with changes in NGM in 2 regions of the brain implicated in the pathophysiology of depression.

**Reviewer’s Comments:** The cingulate is one of the structures carefully scrutinized in PET scans to evaluate for Alzheimer dementia. The results of this study suggest that cingulate activity may be affected by systemic inflammation. The presence of inflammatory illness should probably be taken into account when using PET to evaluate patients for dementia. (Reviewer-Shayne Squires, MD).

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Keywords: Depression, PET, inflammation

Print Tag: Refer to original journal article
Does FDG Uptake Indicate Vulnerable CA Plaque?

Coronary Arterial 18F-FDG Uptake by Fusion of PET and Coronary CT Angiography at Sites of Percutaneous Stenting for Acute Myocardial Infarction and Stable Coronary Artery Disease.

Cheng VY, Slomka PJ, et al:


We still do not have strong evidence to support the use of PET for the a priori prediction of vulnerable coronary artery plaque.

Background: Rupture of coronary artery plaque results in acute myocardial infarction (AMI) and potentially in sudden death. Plaques vulnerable to rupture contain an elevated macrophage content. This has motivated some investigators to test whether imaging with F-18 FDG-PET can identify plaques that are prone to rupture. PET imaging of plaques is technically challenging due to small lesion size and FDG uptake in neighboring myocardium. Coronary artery lesions believed to cause symptoms in patients with stable coronary artery disease (CAD) or to cause AMI in other patients are referred to as “culprit lesions.” By definition, culprit lesions are targeted for stenting by interventional cardiologists.

Objective: To determine whether culprit lesions in AMI have elevated FDG-PET activity in comparison with culprit lesions in stable CAD.

Participants: Consecutive patients who had undergone successful percutaneous coronary intervention (PCI) for AMI or stable CAD were enrolled. Patients were excluded if they had prior coronary artery bypass grafting, multiple stents placed to treat the current lesion, or a previous stent within 10 mm of the current stent.

Methods: Each patient underwent CT coronary angiography (CTA) and cardiac FDG-PET within the same session at ≤7 days after PCI (median, 2 days). Images were coregistered to determine FDG uptake in the coronary artery at the site of stent placement. Using FDG activity in the left atrial cavity as background and maximum FDG activity at the site of the culprit lesion, a maximum target-to-background ratio (maxTBR) was calculated.

Results: The study included 7 patients with stable CAD and 20 patients with AMI. The frequency of maxTBR >2.0 was 12/20 in the AMI group versus 1/7 in the stable CAD group (P = 0.04). In multivariate analysis adjusting for active smoking, pre-PCI aspirin use, time between PCI and FDG injection, myocardial FDG uptake, and stent-myocardium distance, the presentation with AMI was positively associated with maxTBR >2.0 at the site of PCI (odds ratio 31.6; 95% confidence interval, 1.1 to 905.7, P = 0.044). The maxTBR of the ascending aorta was not significantly different between AMI and stable coronary artery disease groups. C-reactive protein was significantly higher in the AMI group (3.8 ± 4.4 vs. 0.4 ± 0.2, P = 0.02). However, no biomarker was significantly correlated with maxTBR of the culprit lesion.

Conclusions: Increased FDG uptake is more likely to occur in culprit coronary artery lesions of patients with AMI than in patients with stable CAD.

Reviewer’s Comments: PET cannot be used to predict a priori which coronary artery lesions are vulnerable to plaque rupture, but it does support the hypothesis that rupture is related to lesion inflammation. (Reviewer-Shayne Squires, MD).

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Keywords: Ruptured Coronary Artery Plaque, Identifying Plaques Vulnerable to Rupture, FDG-PET

Print Tag: Refer to original journal article
PET Highly Accurate for Primary Adrenal Carcinoma

Preoperative 18F-FDG Uptake Is Strongly Correlated With Malignancy, Weiss Score, and Molecular Markers of Aggressiveness in Adrenal Cortical Tumors.

Gust L, Taieb D, et al:

World J Surg 2011; November 30 (): epub ahead of print

FDG-PET has an accuracy of >95% for diagnosing adrenal carcinoma.

Background: Adrenal tumors have become more common as CT exams have detected these lesions incidentally. Most of these lesions are benign, especially in patients without an underlying known malignancy. Overall, only about 10% of these tumors are actually malignant.

Objective: To evaluate the accuracy of FDG-PET/CT for diagnosing primary adrenal carcinoma.

Design: Retrospective study.

Participants: 51 patients with adrenal tumors who were referred for surgical resection.

Methods: Both CT and PET/CT had been performed in all subjects. PET/CT images were reviewed by 2 experienced reviewers who were blinded to all other diagnostic results for the patients. SUV\textsubscript{max} was determined for adrenal lesions along with the ratio of adrenal to liver SUV\textsubscript{max}. Final tumor diagnosis was established histologically and/or with clinical imaging follow-up.

Results: The mean tumor diameter was 63 mm (range, 15 to 210 mm). Overall, 21 tumors were functional and 30 were nonfunctioning. In addition, 22 tumors were malignant, and 29 were benign. In 21 of the 22 adrenal carcinomas, the SUV\textsubscript{max} adrenal/liver ratio was >1.7 and the mean tumor SUV\textsubscript{max} for the malignancies was 7.3 (range, 4.0 to 21.8). In 28 of the 29 benign tumors, the SUV\textsubscript{max} adrenal/liver ratio was <1.7. Using this ratio of 1.7 as the cutoff, the authors reported a sensitivity and specificity of 95% and 97%, respectively, for the diagnosis of adrenal carcinoma with FDG-PET.

Conclusions: PET is a useful diagnostic tool for preoperative evaluation of primary adrenal tumors.

Reviewer's Comments: If you’re interested, the authors also report correlations between various molecular tumor markers and FDG uptake in this study. The adrenal-to-liver SUV ratio has been used by other authors with success to distinguish between adrenal adenomas and adrenal metastases from a known primary tumor. In my own practice, if this ratio is <1, I report the adrenal mass as benign, and if it is >2, I report it as malignant. (Reviewer-David Bushnell, MD).

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Keywords: Primary Adrenal Carcinoma, Diagnosis, PET/CT

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