FDG-PET is very accurate for detecting active disease in children with inflammatory bowel disease.

**Background:** FDG-PET imaging has shown encouraging results in patients with inflammatory bowel disease (IBD). In adults, there is good evidence that FDG uptake levels correlate well with the degree and location of inflammation. A significant fraction of IBD cases are encountered in children or adolescents. Management of this disease depends on detection and assessment of disease relapses, which are not uncommon in children. Endoscopy is mandatory for initial disease diagnosis, but alternative noninvasive techniques would be desirable for assessing relapse or response to therapy.

**Objective:** To evaluate the utility of FDG-PET imaging in pediatric patients with IBD.

**Design:** Retrospective study.

**Participants:** 45 children with a diagnosis of IBD.

**Methods:** 21 PET/CT exams were performed, and 24 PET-only exams were performed. PET results were compared to the findings from conventional workup, including endoscopy, histology, and ultrasound. Endoscopy was performed in 35 of the 45 children. Thirty-five subjects had Crohn disease, and 10 had ulcerative colitis (UC).

**Results:** PET demonstrated 97% sensitivity and 100% specificity on a per-subject basis for active IBD. On a per-segment basis, PET demonstrated a sensitivity of 82% and a specificity of 97%. The CT component did not improve the accuracy of disease evaluation compared with PET alone.

**Conclusions:** In pediatric patients, FDG-PET reliably detects and assesses IBD with a high degree of sensitivity and specificity. The addition of CT to FDG-PET did not improve the accuracy of disease evaluation.

**Reviewer’s Comments:** This idea of using PET to assess relapsed disease or possibly response to therapy in children with IBD seems like a good one. Results from this study certainly support this notion. Whether using PET offers an improvement in outcome remains to be seen, but it is certainly less invasive than repeated endoscopy. Moreover, future studies will also need to focus on the possible differences in the performance of PET in UC versus Crohn disease. (Reviewer-David Bushnell, MD).

**Keywords:** Pediatric Inflammatory Bowel Disease, Assessing Relapse, PET
A major challenge in nuclear medicine has been to develop an infection imaging agent that does not require labeling the blood components. Tc-99m ceftriaxone and Tc-99m antigranulocyte SPECT/CT are impressive in clinical trials.

**Equivocal Bone Scans:** Han and colleagues from Glasgow, United Kingdom, found that SPECT/CT reduced the rate of equivocal bone scans from 23% to 1% in breast cancer patients, largely by localizing uptake to a location with a benign or malignant probability. Frequently, an area of arthritis or a lytic lesion would explain the abnormality. **Bone Scan Accuracy:** Gourevich and colleagues from Rambam Health Care Campus in Israel found SPECT/CT to improve diagnostic accuracy in >50% of bone scans and to guide further workup or invasive procedures in an additional 17%. Soft tissue versus osseous localization was particularly valuable.

**Localization of Infectious Foci:** Djekidel and colleagues from the University of Michigan found that hybrid SPECT/CT permitted proper localization of infectious foci in >25% of lesions found on Tc-99m and In-111 WBC scintigraphy. A major challenge has been to find an infection imaging agent that does not require labeling the blood components. **Scintibact:** Singh and colleagues from Delhi, India, reported on 99m-Tc ceftriaxone (Scintibact), a radiolabeled third-generation cephalosporin, which was able to detect hip prosthesis infections in 11 of 14 patients (sensitivity, 80%; specificity, 75%). **Localizing Joint Infections:** Graute and colleagues from Germany, using Tc-99m antigranulocyte SPECT/CT, assessed detection of low-grade joint infections in 31 patients who underwent planar scintigraphy at 5 minutes, 5 hours, and 24 hours after injection, as well as SPECT/CT at 6 hours after injection. SPECT/CT enhanced localization of infection and was useful in determining the need for surgical intervention. **Diabetic Foot Infections:** It was surprising to see an abstract on Ga-67 for infection imaging, but it merited publication due to a remarkable set of SPECT/CT images The paper was by Caillat-Vigneron from Paris reporting on diabetic foot infections. Of 51 patients, 38 had focal bone uptake adjacent to ulcers, and these patients responded to antibiotics. The authors felt that SPECT/CT was quite valuable in diagnosing osteomyelitis adjacent to foot ulcers. In the future, we may be using Ga-68 citrate, a PET agent, which was the topic of other presentations.

**Reviewer's Comments:** While PET/CT dominated oncologic nuclear medicine at the 2010 annual Society of Nuclear Medicine meeting, SPECT/CT showed continued growth in most of the other sessions, including endocrinology, GI, GU, musculoskeletal, pediatrics, pulmonary, and infectious disease. These topics accounted for approximately 200 papers which suggest that PrePET nuclear medicine procedures are maintaining a presence in the diagnostic armamentarium and are remaining a focus of substantial clinical research. (Reviewer-C. Richard Goldfarb, MD.)
Inducible Ischemia Minimally Impacts Phase Bandwidth

Impact of Ischemia on Left Ventricular Dyssynchrony by Phase Analysis of Gated Single Photon Emission Computed Tomography Myocardial Perfusion Imaging.

Aljaroudi W, Koneru J, et al:

J Nucl Cardiol 2010; November 23 (): epub ahead of print

Phase analysis in patients with a normal left ventricular ejection fraction was not significantly different in those with versus those without significant inducible ischemia.

**Background:** Phase analysis can be performed on gated SPECT myocardial perfusion images. However, the clinical impact and relevance of inducible ischemia (reversible perfusion defects) is not clearly understood.

**Objective:** To determine whether inducible ischemia on myocardial perfusion imaging (MPI) affects the phase standard deviation and phase bandwidth.

**Design:** Retrospective review.

**Participants:** 20 patients with inducible ischemia affecting >10% of the myocardium, and 20 patients without inducible ischemia.

**Methods:** A low-dose stress/high-dose rest same-day single-isotope Tc-99m sestamibi protocol was used. Imaging was started 1 hour after tracer injection.

**Results:** Phase bandwidth and phase standard deviation were similar in both groups. The change in phase bandwidth and standard deviation from stress to rest was similar in both groups. In both groups, there were no significant differences between the rest and stress phase analysis indices evaluated.

**Conclusions:** In this patient cohort in which scan acquisitions were delayed 1 hour after tracer injection, even the presence of a large reversible perfusion defect did not alter the indices of mechanical dyssynchrony by phase analysis. There was no difference in whether a low dose or a high dose of the tracer was utilized.

**Reviewer’s Comments:** The authors hypothesize that the reason there was no difference in the phase bandwidth in ischemic patients compared to non-ischemic patients was the 1-hour delay between injection time and imaging. It is interesting to note that, in this study, there were no differences between the post-stress phase indices compared to the rest phase indices. (Reviewer-Thomas F. Heston, MD).

Keywords: Myocardial Perfusion, Ischemia versus Left Ventricular Dyssynchrony, Gated SPECT, Phase Analysis

Print Tag: Refer to original journal article
In-111 pentetreotide binds to somatostatin receptors, particularly subtypes 2 and 5, on many cells of neuroendocrine origin. Additionally, some common neoplasms display somatostatin receptors with various degrees of density and may be imaged. For neuroendocrine tumors (NETs), sensitivity is reported to exceed 80%, and there is a correlation between somatostatin receptor expression and prognosis: patients with a positive scan have a better treatment response to somatostatin analogues. The main limitation of somatostatin receptor scintigraphy is detection of small lesions due to suboptimal SPECT because of the relatively low dose of In-111 used for imaging. Tumors positive on somatostatin receptor scintigraphy include sympathoadrenal system tumors (pheochromocytoma, neuroblastoma, ganglioneuroma, paraganglioma); gastroenteropancreatic tumors (carcinoids, gastrinoma, insulinoma, glucagonoma, VIPoma); medullary thyroid carcinoma; pituitary adenoma; Merkel cell carcinoma; and small cell lung cancer. Common tumors that may show some positivity include breast carcinoma, melanoma, lymphomas, prostate carcinoma, non–small cell lung cancer, sarcomas, renal cell carcinoma, differentiated thyroid carcinoma, astrocytoma, and meningioma. Non-neoplastic diseases that may be visualized include autoimmune diseases, granulomas, thyroid-associated ophthalmopathy, post-radiation inflammatory disease, and bacterial infections. Clinical indications include localizing primary tumors and metastatic disease (staging), detecting recurrent disease (re-staging), monitoring therapy (surgery, radiotherapy, chemotherapy or somatostatin analogue therapy), selecting patients for radionuclide therapy, and determining prognosis. In renal failure, In-111 pentetreotide scintigraphy is not recommended because the impairment of the principal route of excretion will lead to delivery of an increased radiation dose. Interpretable scintigrams may be obtained after hemodialysis. Images obtained before dialysis are of poor diagnostic value because of circulating activity within the body. Interpretation Tips: The pituitary and thyroid are faintly visible. Intense accumulation of radioactivity is seen in the spleen, liver, and kidneys. On the 24-hour image, the gallbladder is always visible on SPECT images, even if it is not visible on the planar image. Do not confuse gallbladder uptake with liver metastases. Patients with respiratory infections often show accumulation in the nasopharynx. Diffuse lung visualization can be observed after radiation to the thorax. Patients on somatostatin analogue therapy have reduced uptake in the spleen. Liver metastases may not be seen because receptor expression by the tumor is isointense with normal liver cells.

Reviewer's Comments: This European procedure guideline is the most current word on somatostatin receptor imaging and is worth reading for more details. In the United States, the Society of Nuclear Medicine guidelines appeared almost a decade ago. Radionuclide therapy with somatostatin receptor agents seems to be fueling European interest. Hopefully, we will soon see radionuclide therapy with somatostatin receptor agents become routinely available in the United States. (Reviewer-C. Richard Goldfarb, MD).

Keywords: Neuroendocrine Tumor Imaging, Somatostatin Receptor Scintigraphy

Print Tag: Refer to original journal article
False-Positive Rate High for Mid-Therapy FDG-PET

Can 18-FDG-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 2010; October 5 (): epub ahead of print

For monitoring treatment response in head and neck cancer cases, many false positives are seen when FDG-PET is obtained during radiotherapy. The highest accuracy is achieved at 3 to 4 months after completion of radiotherapy.

**Background:** FDG-PET is widely used for the restaging of head and neck cancer patients after definitive radiation therapy. The general consensus for the timing of these scans is 3 to 4 months after completion of treatment. Few data are available on the use of PET in monitoring treatment response during radiation therapy.

**Objective:** To investigate the value of PET obtained during therapy for head and neck cancer after 47 Gy of radiation and to compare the results with the post-therapy PET scan obtained 4 months after completion of treatment.

**Methods:** 40 patients with head and neck cancer underwent 3 FDG-PET scans. The first scan was done prior to radiotherapy, the second scan was done 4 weeks into therapy after patients received approximately 47 Gy of radiation, and a third scan was done 4 months after completion of radiotherapy. PET scans were read as complete response (CR) or non-complete response (non-CR). Biopsy along with clinical and imaging follow-up was used for the gold standard.

**Results:** On the PET scans obtained during therapy, 11 patients showed CR, of which 8 represented the true outcome. Persistent hypermetabolic lesions were seen in 29 patients, but only 9 of these patients had persistent disease based on biopsy and/or follow-up. The sensitivity and specificity of the mid-therapy PET scan for detection of CR was 28.6% and 81.8%, respectively. The 2-year overall survival rates were not significantly different for patients classified as CR versus those classified as non-CR on the PET scan obtained during therapy. Post-therapy PET scans obtained 4 months after completion of therapy showed 25 CRs (accurate in 22 patients). Fifteen scans showed hypermetabolic lesions on PET, 9 of which represented residual disease. The sensitivity and specificity of 4-month post-therapy PET for the detection of CR was 78.6% and 75%, respectively. The 2-year overall survival rate of patients with a negative 4-month post-therapy PET scan was 91.8%, which was significantly higher than the 2-year overall survival rate of 49.9% found in patients with a positive post-therapy scan.

**Conclusions:** Post-therapy PET scans obtained at 4 months after completion of radiotherapy are more accurate for predicting outcome than are PET scans obtained during radiotherapy after 47 Gy of radiation in patients with head and neck cancer.

**Reviewer's Comments:** The performance of FDG-PET for the detection of residual disease in head and neck cancer is highly dependent on the timing of the study. Scans obtained during therapy show many false positives, whereas scans obtained within 1 month after completion of treatment show an unacceptable number of false negatives. The highest accuracy for FDG-PET is achieved at 3 to 4 months after completion of radiation therapy. (Reviewer-Yusuf Menda, MD).

**Keywords:** Head and Neck Cancer, Radiation Therapy, Monitoring Response With FDG-PET

**Print Tag:** Refer to original journal article
YY-90 Bremsstrahlung Feasible for Radiation Dose Estimates

90Y Bremsstrahlung Imaging for Absorbed-Dose Assessment in High-Dose Radioimmunotherapy.

Minarik D, Sjögreen-Gleisner K, et al:


In patients undergoing Zevalin® treatment for lymphoma, the large overestimation of lung dose may be due to the difficulty of scatter correction with bremsstrahlung imaging in areas of low attenuation close to hotter organs.

**Background:** Radionuclide therapy with Y-90 is available, but assessing the actual radiation dose received by normal tissues required quantitative imaging. Using the X-rays resulting from bremsstrahlung radiation appears to be practical.

**Objective:** To evaluate the feasibility of using bremsstrahlung radiation from Y-90 beta decay to quantify radiation dose in patients undergoing Zevalin® treatment for lymphoma. Comparisons were made with prior In-111 Zevalin studies.

**Methods:** A total of 3 patients were referred for Y-90 Zevalin treatment. Each subject had bone marrow stem cell support so that the critical organ was the liver. The pre-therapy In-111 Zevalin scan was performed to estimate the amount of administered Y-90 Zevalin activity to yield a 12-Gray liver dose. SPECT/CT images were acquired at 1, 24, 48, 120, 144, and 166 hours after injection to obtain organ residence times for both the In-111 pretherapy scans and the Y-90 bremsstrahlung therapy scans. Whole body imaging was also performed at the 1-hour point to confirm the SPECT dosimetric results. The SPECT images were reconstructed iteratively with accurate correction for attenuation and scatter radiation, and absolute activity was inferred from calibration sources. The whole body images were analyzed with the pixel-based conjugate view approach to determine activity levels.

**Results:** The time activity curves generated for the liver and kidneys were very similar for both the In-111 pretherapy scans and the Y-90 therapy scans, with good agreement in the estimated radiation dose for these 2 organs. The results for the spleen were more variable but were still within 30% between the pretherapy and therapy estimates. The dose estimated for the lungs was about 65% higher for the Y-90 scans compared to the In-111 results.

**Conclusions:** Y-90 bremsstrahlung imaging for radiation dose estimates is feasible and may play a role in future treatment planning regimens for radionuclide therapy.

**Reviewer's Comments:** The authors make the case that there is good agreement between the dose estimates from In-111 and Y-90 Zevalin. Quantifying how much radiation is actually delivered to the tumor and normal tissues is important. Being able to potentially rely on bremsstrahlung imaging gives an additional tool. However, the results of this study also imply that In-111 Zevalin is a reliable surrogate, and it is certainly a better imaging agent. Therefore, In-111 Zevalin could be administered along with the Y-90 Zevalin to provide a potentially better way to obtain dose information than is seen with bremsstrahlung imaging. (Reviewer-Mark T. Madsen, MD).

**Keywords:** Lymphoma, Zevalin Treatment, Quantifying Radiation Dose, Bremsstrahlung Radiation

Print Tag: Refer to original journal article
Radioiodine Imaging Not Needed in High-Risk WDTC

The Role of Routine Diagnostic Radioiodine Whole-Body Scintigraphy in Patients With High-Risk Differentiated Thyroid Cancer.

de Meer SG, Vriens MR, et al:

J Nucl Med 2011; January (): epub ahead of print

It is important to consider age when determining risk categories for patients with well-differentiated thyroid cancer (WDTC). Radioiodine imaging does not appear to be indicated in the follow-up of high-risk WDTC.

Background: The value of radioiodine imaging for follow-up in patients who have well-differentiated thyroid cancer (WDTC) and low-risk disease is very limited. In contrast, the value of radioiodine imaging in patients with high-risk disease is still debated.

Objective: To assess the utility of follow-up imaging with I-131 after thyroidectomy and adjuvant radioiodine ablation.

Design: Retrospective study.

Participants: Patients with WDTC who received radioiodine ablation following thyroidectomy.

Methods: All patients underwent follow-up radioiodine imaging 1 year after thyroidectomy and ablation. Imaging was performed 1 week after administration of 1.0 mCi of I-131. Some patients were prepared using recombinant thyroid-stimulating hormone (rTSH) as opposed to hormone withdrawal. Stimulated thyroglobulin (Tg) levels with a normal/abnormal cutoff of 0.2 ng/mL were obtained at the same time. High-risk disease was defined as T3/T4 tumor status and/or nodal involvement.

Results: The study included 112 subjects. The serum stimulated Tg was negative in 32 subjects, who also were negative for Tg antibodies. Radioiodine images were negative in all of these cases but one. This single case was later determined to be a false-positive result. Serum Tg was positive in 65 cases (with negative Tg antibodies), and radioiodine imaging was positive in only 8 of these patients.

Conclusions: Radioiodine imaging is not indicated in the follow-up of patients with high-risk WDTC.

Reviewer’s Comments: The subject of this article is important. I would like to embrace these results because my sense is that diagnostic I-131 imaging has limited value even in higher risk patients with WDTC. However, I am concerned about several aspects of the protocol. The diagnostic yield when imaging 1 week following administration of 1 mCi of I-131 is very likely to not be optimal. My feeling is that it is best to image 5 days following 2-3 mCi of I-131. And when rTSH is used instead of hormone withdrawal, the optimal protocol, in my opinion, is 3 mCi of I-123 imaged 1-2 days following administration. These protocols are based on best estimates for optimizing target/background ratios. The authors also did not use age as a factor in determining high versus low risk disease, which is a notable design flaw. Regarding the many potential false-negative results from I-131 images, it is important to point out that a stimulated Tg level cutoff of 0.2 ng/mL is rather low: at this level false-positive results are known to occur. In fact, it is almost certainly more reliable to use a rising Tg level as an indicator of disease presence when actual levels are <1.0 (Reviewer-David Bushnell, MD).

Keywords: High-Risk Differentiated Thyroid Cancer, Diagnosis, I-131 Whole Body Scans

Print Tag: Refer to original journal article
When using Tc-99m tetrofosmin gated SPECT, early imaging after stress testing did not reduce imaging quality and, it also resulted in a more pronounced defect size compared to imaging at 30 and 60 minutes post-stress.

**Background:** The standard recommendation for cardiac-gated SPECT imaging using Tc-99m agents is to delay acquisitions after stress testing for approximately 30 minutes to allow for hepatic and bowel clearance, making interpretation of the myocardium more accurate. However, this delay may cause the scan to miss ventricular stunning and possibly result in some mild yet significant decrease in the perfusion defect seen. Because of minimal redistribution by Tc-99m tetrofosmin, perfusion images 30 minutes after stress reflect stress perfusion. However, ventricular size and function at 30 minutes post-stress primarily reflects resting conditions.

**Objective:** To evaluate the feasibility, image quality, and clinical impact of early imaging post-stress when using Tc-99m tetrofosmin gated SPECT.

**Design:** Prospective cohort study.

**Participants:** 194 patients were prospectively included and analyzed. Patients were regular patients referred for clinical reasons to gated SPECT myocardial perfusion imaging (MPI). The study cohort consisted of 69% males, 41% of patients with a BMI >27, 20% of patients who were diabetic, 52% of patients had a negative history for coronary artery disease (CAD), 73% of patients who underwent exercise stress, and 27% of patients who underwent dipyridamole stress.

**Methods:** Three gated-SPECT Tc-99m tetrofosmin studies were performed on each patient at 30 minutes after injection at rest, at 30 minutes post-stress, and immediately post-stress. The gated SPECT protocol used a weight-based dosing of Tc-99m tetrofosmin. Semiquantitative scoring of scan quality was performed. Cedars-Sinai QGS and QPS software was utilized.

**Results:** Quality of the immediate post-stress images was as good as the 30-minute post-stress images. Perfusion, thickening, and motion were similar with no significant difference between early and 30-minute post-stress images. The left ventricular ejection fraction was statistically lower in the 30-minute post-stress acquisitions compared to immediate images, although this difference was clinically insignificant (65% versus 63%, respectively). Perfusion defect scores were also higher in ischemic patients on the immediate acquisition images (14.2) compared to 30-minute post-stress images (12.4).

**Conclusions:** Early imaging post-stress when using Tc-99m tetrofosmin is feasible and results in scans of a quality similar to the 30-minute delayed images. Perfusion defect size and left ventricular ejection fraction were, on average, lower in the delayed compared to the early images.

**Reviewer’s Comments:** The differences seen in perfusion defect size and ejection fraction, when taken as a whole, are statistically significant but clinically insignificant. However, in individual patients, this difference may be more pronounced. Early imaging post-stress when using Tc-99m tetrofosmin appears both reasonable clinically and of benefit to patient flow. (Reviewer-Thomas F. Heston, MD).

Keywords: Myocardial Perfusion Imaging, Tetrofosmin, Gated SPECT, Early Imaging
A decline in ejection fraction on gated SPECT following stress may indicate an increased risk for cardiovascular events.

**Background:** Stress/Rest ejection fraction (EF) changes with Rb-82 PET have been shown to be useful for predicting obstructive coronary artery disease (CAD). Presumably, ischemia developing during stress leads to myocardial dysfunction and a reduction in EF.

**Objective:** To examine the significance of a decline in EF following stress SPECT imaging.

**Participants/Methods:** Patients with reversible defects were excluded from the study group. Inclusion criteria consisted of a decrease in EF ≥5% following stress compared with rest. The control group consisted of patients with no reversible defects and either an increase in EF with stress or a decrease of ≤4%. Gated sestamibi SPECT imaging was performed in all individuals. The stress protocol was either symptom-limited treadmill or dipyridamole 0.56 mg/kg. Patients were followed up for a mean of 22 months for cardiac-related events.

**Results:** There were 57 subjects in both the study group and the control group. The control group was well matched for age, gender, and cardiac risk factors. The number of individuals who underwent pharmacologic stress was the same for the 2 groups. During follow-up, a total of 13 cardiac events were recorded in the study group, and 6 occurred in the control group. Event-free survival was significantly better in the control group compared to the study group.

**Conclusions:** An EF decrease >5% with stress was an important finding.

**Reviewer's Comments:** In patients receiving dipyridamole, the "stress" remains in place during imaging as long as aminophylline has not been given to the patient. This is somewhat different than in patients who undergo treadmill exercise, in which case the stress truly has been stopped prior to SPECT imaging. Therefore, it would have been useful for the authors to tell us how many of the 13 events occurred in subjects who underwent pharmacologic versus exercise stress imaging. In any case, it seems that these data support the notion that a drop in EF with a stress SPECT protocol may be an important risk factor for future cardiac events. (Reviewer-David Bushnell, MD).

**Keywords:** Obstructive Coronary Artery Disease, Stress Ejection Fraction, SPECT
Improved compensation for spatial resolution losses allows cardiac SPECT studies to be acquired with fewer events without sacrificing image quality.

**Background:** Reconstruction algorithms that provide resolution restoration are now commercially available for myocardial perfusion SPECT imaging that allow either reduced radiation dose or faster imaging.

**Objective:** To compare the UltraSPECT Wide Beam Reconstruction (WBR™) approach on cardiac SPECT studies with reduced number of collected events with conventionally acquired studies reconstructed with filtered backprojection.

**Methods:** Line source and contrast phantom studies were performed to assess spatial resolution and contrast recovery with WBR and conventional reconstruction algorithms. These algorithms were also applied to 2-day stress-rest cardiac SPECT studies performed on 92 patients. Forty of these were administered half the conventional activity and had both standard and double-time acquisitions. Fifty-two had the standard activity administered with half- and full-time acquisitions. Studies with the conventional number of collected events were reconstructed with filtered backprojection, while the studies that had half the events were reconstructed with the WBR algorithm. Summed stress and rest scores along with left ventricular ejection fraction (LVEF) were compared between the 2 approaches.

**Results:** Overall, the contrast recovery in the phantom studies was better with WBR, but for the smallest spheres (<15 mm), filtered backprojection was the best of the reconstruction methods. The spatial resolution was substantially better with WBR for the line source phantom. The image quality assessment for the WBR studies with half the events (either half-time or half-activity) was judged similar to that of the filtered backprojection images with the standard number of events. There was no statistical difference in the summed scores or LVEF found from the standard and half-event number comparison, and the correlation coefficients were all >0.9. No significant difference was found in the clinical outcomes among the groups.

**Conclusions:** Applying the WBR technique to cardiac SPECT studies with half the conventional number of events yields results that are comparable to standard cardiac SPECT with filtered backprojection. Using the WBR approach allows either half-time imaging with the standard activity or full-time imaging with half the amount of radioactivity.

**Reviewer’s Comments:** This study and its results are similar to others that have been published recently, except that the authors specifically examined imaging with half the administered activity. Because of the relatively high patient radiation dose associated with cardiac SPECT, this is certainly germane. However, performing the studies in half the time is likely to create fewer problems with patient motion. As I have noted in the past, cardiac SPECT studies with Tc-99m do not suffer from lack of counts, so there is probably room for activity reduction even without the application of resolution recovery algorithms. (Reviewer-Mark T. Madsen, MD).

**Keywords:** Myocardial Perfusion Scintigraphy, Reconstruction Algorithms, Filtered Backprojection, Wide Beam Reconstruction
FDOPA Uptake Significant in Newly Diagnosed Brain Tumors

Correlation of 6-18F-Fluoro-L-Dopa PET Uptake With Proliferation and Tumor Grade in Newly Diagnosed and Recurrent Gliomas.

Fueger BJ, Czernin J, et al:

J Nucl Med 2010; 51 (October): 1532-1538

F-18 DOPA-PET/CT uptake correlates with glioma tumor grade and proliferative activity in newly diagnosed brain tumors.

**Background:** Tumor grade and proliferative activity are known predictors of outcome in patients with brain gliomas. However, due to the heterogeneity of these tumors, invasive biopsy techniques often yield samples that underestimate the true malignant potential. As such, disease is not accurately graded. The uptake of other PET tracers as noninvasive alternatives for this purpose has been demonstrated. However, the data are either scarce or conflicting regarding the ability of FDOPA-PET/CT to do the same.

**Objective:** To determine if a correlation exists between FDOPA uptake and glioma tumor grade and proliferative activity (as measured by the Ki-67 index), and to determine if FDOPA-PET/CT can differentiate low-grade versus high-grade tumors.

**Methods:** 59 patients with various brain tumors (newly diagnosed, n=22; recurrent, n=37) were evaluated. All had tissue sampling performed for Ki-67 analysis and to determine tumor grade. All patients underwent FDOPA-PET/CT. Patients with recurrent tumors underwent scanning at a mean of 51 weeks after last chemoradiation therapy.

**Results:** The Ki-67 index was significantly higher with higher tumor grades (P=0.0001). However, no significant difference (P=0.20) was noted between patients with newly diagnosed versus those with recurrent disease. FDOPA uptake was significantly higher in grade III versus grade II tumors and in grade IV versus grade II disease (but not between grade II and grade III; there were no grade I patients in this study). Also, there was a significant correlation between SUV$_{\text{max}}$ and the Ki-67 index in patients with newly diagnosed disease but not in patients with recurrent disease. In the newly diagnosed group, the ROC showed the optimal SUV$_{\text{max}}$ cutoff to be 2.72 in differentiating high-grade from low-grade disease.

**Conclusions:** FDOPA uptake may be a reflection of proliferative activity and tumor grade in newly diagnosed brain tumors, but not in recurrent brain tumors.

**Reviewer’s Comments:** This interesting study shows the potential of FDOPA-PET/CT in the management of newly diagnosed brain tumors. These findings suggest that FDOPA uptake is predictive of tumor grade and aggressiveness. Because this finding has potentially important treatment and prognostic implications, larger prospective studies are needed to further investigate this. As for the lack of correlation seen between FDOPA uptake and tumor grade/Ki-67 index, the authors postulate that the post-therapeutic changes to the blood-brain barrier may account for this. (Reviewer-Damita Thomas, MD).

Keywords: Glioma, Tumor Grade vs FDOPA Activity, Proliferation Index

Print Tag: Refer to original journal article
In patients with advanced local esophageal cancers, those with complete response to definitive chemoradiotherapy by FDG-PET have similar outcomes those who go on to have esophagectomy.

**Background:** For treatment of esophageal cancer, chemoradiotherapy (CRT) followed by surgery (trimodality therapy) has been shown, in most trials, to be better than surgery alone. The literature is less clear about whether the addition of surgery to definitive CRT is advantageous to all patients.

**Objectives:** To determine whether FDG-PET staging predicts outcomes in patients with locally advanced esophageal cancer undergoing CRT alone or trimodality therapy and to determine whether FDG-PET can identify patients who may not benefit from esophagectomy after receiving definitive CRT.

**Design:** Retrospective study.

**Participants:** 163 patients with stage I through IVA esophageal cancer who underwent CRT with or without resection with curative intent.

**Methods:** 90% of patients received fluorouracil and platinum. The median radiation dose was 54 Gy. All patients underwent evaluation for surgery. Resection was performed 4 to 6 weeks after CRT. Pretreatment FDG-PET scans were performed before CRT. Post-therapy scans were performed after CRT and before surgery. FDG-PET complete response after CRT (PET-CR) was defined as SUV ≤3. Local failure was defined as failure within the radiation portals.

**Results:** 105 patients (trimodality, n=55; CRT alone, n=50) were evaluable for post-therapy FDG-PET response. Median follow-up was 30 months for living patients. For patients treated with CRT only, the median survival was 38 months in those who achieved PET-CR (38%) and 11 months in those without PET-CR. For patients treated with CRT only, the 2-year survival rate was 71% in those who achieved PET-CR and was 11% in those without PET-CR. Freedom from local failure was also better in patients achieving PET-CR (75%) than in those without (28%). Patients who achieved PET-CR after definitive CRT had overall survival and freedom from local failure rates equivalent to patients who underwent trimodality therapy (P=0.92 and 0.15, respectively). There were fewer adenocarcinomas among patients who achieved PET-CR (37%) than among those without PET-CR (71%, P=0.02), and histology (squamous versus adenocarcinoma) was the only significant predictor for achieving PET-CR. On multivariate analysis, PET-CR correlated significantly with survival and freedom from local failure. Among patients who received trimodality therapy, those with PET-CR achieved pathologic response in 53% of esophagectomy specimens while those without PET-CR achieved pathologic response in 33% of esophagectomy specimens (P=0.18).

**Conclusions:** In patients treated with CRT alone who achieved PET-CR, the survival and local control rates are not significantly different from patients who go on to surgical resection.

**Reviewer's Comments:** The authors are clear that this study is not sufficient to change clinical practice, but the findings could lead to prospective studies in which post-CRT staging with FDG-PET is used to assign patients to CRT only versus CRT plus surgery. (Reviewer-Shayne Squires, MD).
Avoid Strenuous Activity Prior to FCH-PET/CT

The Effects of Muscle Exercise and Bed Rest on [18F]Methylcholine PET/CT.

Roef M, Vogel WV:

Eur J Nucl Med Mol Imaging 2010; October 22 (): epub ahead of print

Strenuous activity prior to FCH-PET/CT may result in significant FCH uptake that could potentially make interpretation difficult.

Background: Fluoromethyl choline (FCH) has received growing interest as alternatives to FDG are being sought. As with any new tracer, it is important to properly characterize its physiologic uptake and the circumstances under which uptake may be altered to ensure accurate interpretation of the images.

Objective: To evaluate the effect of strenuous exercise on muscular uptake of FCH.

Methods: 10 patients undergoing FCH imaging for evaluation of recurrent prostate cancer were subdivided into 3 groups: no exercise (n=3), light exercise (n=3), and strenuous exercise (n=4). Light exercise was defined as a 50-m walk, and strenuous exercise was defined as holding a 15-lb weight while in an upright sitting position. All underwent FCH PET/CT imaging 5 minutes after injection. Using the “no exercise” patients for comparison, FCH uptake in arm and gluteal muscles (those thought to be directly affected in the strenuous group) underwent intra- and inter-patient comparison.

Results: Compared to the no exercise group, the bicep/gluteal uptakes of FCH were increased 45%/74% in the light exercise group and were increased 202%/112% in the strenuous exercise group. The authors found no visual differences between left and right sides in patients who underwent light exercise. However, there was a significant visual difference between left and right sides in the patients holding the weights, with the weight-bearing side demonstrating markedly increased activity. FCH uptake was also seen in other muscles in the strenuous activity group but not in the light activity group.

Conclusions: FCH uptake by the bicep and gluteal muscles is increased following strenuous activity. Therefore, strenuous activity should be avoided prior to imaging because image interpretation could potentially be affected.

Reviewer's Comments: This interesting study evaluates the physiologic behavior of FCH following exercise. Studies of this type are particularly important when evaluating novel tracers for imaging because they help better characterize tracer kinetics under various physiologic and/or pathologic conditions, thus identifying the pitfalls of imaging with specific tracers. The authors hypothesize that increased muscular uptake likely reflects increased delivery of the tracer due to increased muscular perfusion following increasing levels of exercise. They point out that, although the observed increased activity did not obscure evaluation of recurrent prostate cancer, it may preclude accurate interpretation of soft tissue tumors if FCH is to be used for that purpose. As such, the authors recommend that patients avoid strenuous activity prior to FCH-PET/CT imaging. (Reviewer-Damita Thomas, MD).

Keywords: Fluoromethyl Choline, FCH Muscle Uptake, Effect of Exercise

Print Tag: Refer to original journal article
Breast Cancer Prognostic Markers Correlate With FDG Uptake

Correlation of High 18F-FDG Uptake to Clinical, Pathological and Biological Prognostic Factors in Breast Cancer.

Groheux D, Giacchetti S, et al:

Eur J Nucl Med Mol Imaging 2010; November 6 (): epub ahead of print

Several poor prognostic markers of breast cancer are associated with increased uptake on FDG-PET/CT which may be helpful when using FDG-PET/CT as a staging tool.

**Background:** Breast cancer is second only to lung cancer as the cause of female cancer mortality. As such, tremendous efforts have been and are currently being made to better characterize the disease. Given its proven efficacy in the diagnostic and therapeutic monitoring of other cancers, the use of FDG-PET/CT in breast cancer has been less well defined. Several studies have suggested that FDG uptake may correlate with certain prognostic markers of breast cancer. Further evaluation of this relationship may help better define the use of FDG-PET/CT in the workup of this disease.

**Objective:** To assess how several prognostic markers of breast cancer affect uptake on FDG-PET/CT.

**Methods:** FDG-PET/CT was prospectively done in 131 patients with T2 to T4 breast cancers prior to neoadjuvant therapy. All patients had histological, immunohistochemical staining, and functional assays done to determine histological grade, ER/PR status, and HER2 neu status, as well as p53 gene mutational status. Clinical lymph node status was also assessed.

**Results:** FDG uptake was significantly higher in higher grade tumors (grades 3 and 4 versus grade 2) and in patients with invasive ductal carcinoma versus lobular carcinoma. Uptake was also significantly higher in patients who were ER- and PR-negative and in those with triple negative tumors and with p53 gene mutation, while uptake was not significantly changed with HER2 neu status. No significant correlation was found between FDG uptake and tumor size or clinical lymph node status. **Conclusion:** Some, but not all, poor prognostic markers of breast cancer are associated with significantly higher FDG uptake on FDG-PET/CT.

**Reviewer’s Comments:** This intriguing study demonstrates some interesting correlations between FDG uptake and several breast cancer prognostic markers. Because the role of FDG-PET/CT is not well defined in breast cancer, this study may potentially shed light on how this modality can best be used in the workup of this disease. The authors suggest that, due to the current findings, FDG-PET/CT may be useful in select patients in the baseline staging of the disease. Because FDG uptake is lower among lobular receptor-positive cancers, the authors warn that these particular tumors may yield false-negative results on FDG-PET/CT imaging. (Reviewer-Damita Thomas, MD).

**Keywords:** Breast Cancer, Prognosis, FDG-PET/CT, Molecular Biomarkers vs FDG Uptake

**Print Tag:** Refer to original journal article
Dual Imaging Improves Diagnostic Accuracy for Lung Lesions

Can Multimodality Imaging Using 18F-FDG/18F-FLT PET/CT Benefit the Diagnosis and Management of Patients With Pulmonary Lesions?

Xu B, Guan Z, et al:

Eur J Nucl Med Mol Imaging 2010; October 9 (): epub ahead of print

Imaging with both FDG and FLT may be useful in better characterizing equivocal pulmonary lesions.

**Background:** FDG-PET/CT has proven to be a useful diagnostic tool in the evaluation of several cancers. However, when evaluating pulmonary lesions, FDG is not without its pitfalls due to the enhanced glucose metabolism exhibited by benign entities. As such, multiple imaging modalities are often used. Also, other tracers detecting other pathways characterized by tumor biology are being evaluated in oncologic imaging.

**Objective:** To determine if dual PET/CT imaging with FDG and FLT can improve diagnostic accuracy of indeterminate pulmonary lesions.

**Participants:** 73 patients with no prior lung pathology and an indeterminate pulmonary lesion detected on either x-ray or CT were evaluated.

**Methods:** All patients had FDG and FLT scans with 7 days of each other. SUV\textsubscript{max} from each scan type and an FLT:FDG SUV ratio were measured. The gold standard was follow-up for 22 months to determine what was ultimately done about the lesion in question.

**Results:** Of the 73 patients, 42 had solitary nodules and 31 had ≥2 lesions. At the 22-month follow-up, diagnosis was confirmed by surgery in 42 and by clinical evidence in 31 (lung cancer, n=28; TB, n=18; benign inflammatory/pseudotumor lesions, n=27). In all lesions, FDG SUVs were higher than FLT SUVs. However, both FLT and FDG SUVs were significantly higher in the cancer lesions versus the TB and inflammatory lesions. Sensitivity, specificity, and accuracy (sens/spec/acc) were best when all modalities (FDG-PET/CT and FLT-PET/CT) were used. The sens/spec/acc was 100%/91%/95% when all modalities were used, was 82%/68%/73% for FDG-PET/CT alone, and was 82%/71%/75% for FLT-PET/CT alone. Also, the FLT:FDG SUV ratio was able to distinguish between cancer, TB, and inflammatory patient groups. The authors also found that dual imaging impacted patient management in almost 32% of the patients.

**Conclusions:** Dual imaging with FDG-PET/CT and FLT-PET/CT improves diagnostic accuracy of equivocal lung lesions and also impacts the subsequent management of the patient.

**Reviewer’s Comments:** This interesting study shows the synergistic potential of using FDG- and FLT-PET/CT in the evaluation of equivocal pulmonary lesions. As the authors point out, enhanced glucose metabolism is just one aspect of tumor biology that can be detected. As such, detecting thymidine metabolism with FLT may provide another aspect of tumorogenicity that may aid in the evaluation of indeterminate pulmonary lesions. This, in turn, may potentially decrease the overall number of studies (particularly invasive procedures) required to accurately characterize a lesion. This study shows promise in the dual use of FDG and FLT for this purpose. (Reviewer-Damita Thomas, MD).

Keywords: Indeterminate Pulmonary Lesions, PET/CT, Diagnostic Accuracy, FDG, FLT

Print Tag: Refer to original journal article
Use of FMISO-PET and MET-PET with Gd-enhanced MRI may lead to better delineation of glioblastomas, which could improve treatment targeting.

Background: Glioblastomas (GBMs) are challenging tumors because they are highly infiltrative and portend a poor prognosis. As such, considerable efforts are underway to better characterize this malignancy and improve on the current management strategy. Studies have shown that GBM tissue hypoxia can be detected by FMISO-PET and is associated with tumor angiogenesis as imaged by Gd-enhanced MRI. This, in turn, is associated with tumor aggressiveness which can be detected by MET-PET.

Objective: To characterize the relationship between tumor hypoxia, aggressiveness, and neovascularization in GBM as detected by FMISO-PET, MET-PET, and Gd-enhanced MRI, respectively.

Methods: 10 patients with newly diagnosed GBM were evaluated. All patients underwent FMISO- and MET-PET as well as Gd-enhanced MRI. Tumor volumes were measured on MRI and MET-PET images, using indices of ≥1.3 and ≥1.5 to evaluate degree of increased MET uptake compared to MRI in a given tumor volume (1.5 index represented stricter threshold of identifying increased MET uptake in a tumor volume compared to enhancement seen on MRI). All resection specimens underwent immunohistochemical staining for the proliferative marker Ki-67.

Results: MET-PET uptake did not significantly correlate with the Ki-67 index. However, the tumor uptake of MET with an index of ≥1.3 was greater than (but did not reach significance) and independent of enhancement seen on MRI, but it was similar when an index of 1.5 was used. The region of FMISO uptake was not significantly different from tumor volumes as measured by MRI. There was also a significant correlation between FMISO and MET-PET uptake.

Conclusions: GBM hypoxia is closely linked with neovascularization as detected by FMISO-PET and MRI, respectively. The increased MET-PET uptake seen outside of tumor volumes measured by MRI may reflect detection by MET-PET of an infiltrative malignant process that is independent of tumor volume as detected by MRI.

Reviewer's Comments: The study findings demonstrate interesting relationships between various factors of GBM tumor biology: neovascularization, hypoxia, and aggressiveness. It is intuitive that there were correlations between MET, FMISO, and MRI findings suggesting that tumor metabolism, hypoxia, and neovascularization are related. However, it is interesting that Ki-67 did not correlate with the tumor’s metabolic activity as detected by MET-PET in this study, which is different from the findings shown in other investigations. In addition, MRI enhancement represented only 77% of MET uptake, which the authors believe reflects the ability of MET-PET to detect an infiltrative process that MRI fails to detect. This finding, if confirmed with larger studies, may improve tumor delineation, which may impact surgical resection and outcomes. (Reviewer-Damita Thomas, MD).

Keywords: Glioblastoma, Tumor Hypoxia, Tumor Aggressiveness, Neovascularization

Print Tag: Refer to original journal article
Gated SPECT Ventricular Dyssynchrony Is Common

**Prevalence and Predictors of Mechanical Dyssynchrony as Defined by Phase Analysis in Patients With Left Ventricular Dysfunction Undergoing Gated SPECT Myocardial Perfusion Imaging.**

Samad Z, Atchley AE, et al:

J Nucl Cardiol 2010; November 17 (): epub ahead of print

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Gated SPECT ventricular dyssynchrony is common among patients with a reduced ejection fraction, increased QRS duration, and perfusion defects.

**Background.** Cardiac resynchronization therapy (CRT) is being increasingly utilized in the treatment of patients with heart failure. Gated SPECT imaging has the potential to help identify patients most likely to benefit from CRT through the use of phase analysis of the gated acquisitions.

**Objective:** To identify the prevalence of SPECT-derived mechanical dyssynchrony and report the clinical variables that predict mechanical dyssynchrony in patients with a reduced left ventricular ejection fraction (LVEF).

**Design:** Retrospective review.

**Participants:** Patients referred for clinical reasons to gated SPECT imaging. All patients were aged >18 years, weighed <440 lbs, had LVEFs <35%, and had an interpretable scan. There were 260 patients evaluated.

**Methods:** Gated SPECT acquisition sets were analyzed using a count-based Fourier analysis method. This converted regional myocardial counts into a continuous thickening function, which allowed resolution of the phase of the onset of myocardial contraction. Significant left ventricular dyssynchrony was defined as a phase standard deviation of >42°.

**Results:** In the entire cohort of patients studied, gated SPECT-derived mechanical dyssynchrony was 52%. Using a multivariate analysis, the predictors of dyssynchrony were black race, male gender, QRS duration, LVEF, and summed rest score.

**Conclusions:** Significant SPECT-based mechanical dyssynchrony, as determined by an elevated phase standard deviation, is common among patients with left ventricular dysfunction. Gated SPECT-derived phase analysis may be useful in the identification of appropriate patients for cardiac resynchronization therapy.

**Reviewer's Comments:** The clinical benefit of phase analysis using gated SPECT still is not well defined. These authors use phase standard deviation to define dyssynchrony, whereas others have found the phase bandwidth to be more predictive of clinical ventricular dyssynchrony. (Reviewer-Thomas F. Heston, MD).

**Keywords:** Heart Failure, Myocardial Perfusion Imaging, Gated SPECT, Phase Analysis, Mechanical Dyssynchrony

Print Tag: Refer to original journal article
Positron emission mammography may be an accurate alternative for patients with newly diagnosed breast cancer who cannot undergo MRI for presurgical planning.

**Background:** During the last 2 decades, breast cancer morbidity has decreased due to screening mammography and self breast exams. However, breast cancer imaging still has limitations. Breast density, the impact of hormonal replacement therapy (HRT), lesions size, and heterogeneous FDG avidity are factors that confound MRI and FDG-PET breast imaging results. As such, interest has grown in the use of positron emission mammography (PEM) as a higher-spatial-resolution and breast-specific alternative to whole body FDG-PET (WBPET) that allows detection of smaller lesions.

**Objective:** To compare the utility of PEM with MRI and WBPET in the presurgical planning of patients with newly diagnosed breast cancer.

**Design:** Prospective study.

**Participants:** 182 women with biopsy-proven breast cancer who were of varying menopausal statuses (26% premenopausal; 7% perimenopausal; 66% postmenopausal).

**Methods:** All patients underwent WBPET, MRI, and PEM, and all had previously undergone mammography. All biopsies were performed approximately 12 days before imaging. Results were compared to histopathological analysis of resection specimens.

**Results:** PEM and MRI were equally sensitive (93%) in the detection of index lesions, and the sensitivities of both were significantly better than that for WBPET (68%). Also, in terms of size, both PEM and MRI showed good correlation with the actual specimen, demonstrating a Spearman correlation coefficient of 0.61 (with PEM slightly underestimating the size of lesions compared to histology and MRI).

**Conclusions:** PEM is an accurate alternative to MRI in the preoperative planning of patients with newly diagnosed breast cancer.

**Reviewer's Comments:** This interesting study demonstrates the efficacy of PEM in the preoperative characterization of breast cancer lesions. In addition to the similar sensitivity of PEM to MRI, the authors also point out that breast density, HRT status, and menopausal status did not affect the ability of PEM to detect cancer lesions. Although these factors did not hamper detection of cancer on MRI, this finding with PEM is an important one in that PEM imaging may be a better alternative for women who cannot undergo MRI due to claustrophobia or hormonal/menstrual status, both of which are known to alter regional blood flow and thus, potentially cause artifacts that can result in lower specificity of the modality. This prospective study is a good start. However, further multicenter trials are warranted to confirm these findings. (Reviewer-Damita Thomas, MD).

**Keywords:** Breast Cancer, Presurgical Planning, Positron Emission Mammography, PET, MRI

**Print Tag:** Refer to original journal article
Use Hepatic SUV as a Reference Background in Lymphoma

Improvement of Early 18F-FDG PET Interpretation in Diffuse Large B-Cell Lymphoma: Importance of the Reference Background.

Itti E, Juweid ME, et al:

J Nucl Med 2010; 51 (December): 1857-1862

As a reference background, $SUV_{\text{max}}$ of the liver is superior to the $SUV_{\text{max}}$ of the mediastinal blood pool in assessing early response to therapy for diffuse large B-cell lymphoma.

**Background:** FDG PET/CT imaging is useful in the identification of patients with diffuse large B-cell lymphoma who respond to chemotherapy. The International Harmonization Project (IHP) interpretation criteria include a reference background criterion above which a residual mass is considered positive. Whether these IHP criteria should be adapted to end-of-treatment evaluations remains unknown.

**Objective:** To determine if the IHP criteria can be used for mid-treatment evaluation of residual masses in patients with diffuse large B-cell lymphoma.

**Design:** Prospective trial.

**Participants:** 92 patients with newly diagnosed diffuse large B-cell lymphoma.

**Methods:** Patients underwent FDG-PET before and after 2 cycles of chemotherapy. Two reference backgrounds were used: (1) the mediastinal blood pool (MBP) at the level of the aortic arch, and (2) the liver. Both $SUV_{\text{mean}}$ and $SUV_{\text{max}}$ for the reference background were used. SUV values were corrected for body weight. When the residual mass on the second PET scan (obtained after 2 cycles of chemotherapy) was at least 125% as hot as the reference background, the mass was considered positive. Chemotherapy was not changed or modified based on PET results.

**Results:** With MBP as a reference, PET was unable to distinguish early responders from nonresponders when using the cutoff of 1.25 for the ratio $SUV_{\text{max}}$(lesion):$SUV_{\text{max}}$(MBP). When the $SUV_{\text{mean}}$ of the MBP was used, accuracy was worse. With $SUV_{\text{max}}$ of liver as a reference, the 2-year progression-free survival rate was significantly different between patients with PET-negative findings (81.8% [95% confidence interval, 71%-93%]) and patients with PET-positive findings (51.8% [95% confidence interval, 35%-69%], $P=0.003$). Accuracy was increased when a cutoff threshold of 1.4 was utilized: a lesion was considered positive when the $SUV_{\text{max}}$(lesion) was at least 140% of the $SUV_{\text{max}}$ of the sample liver. Accuracy was 73% for progression-free survival and 70% for overall survival when using this criterion.

**Conclusions:** Using liver $SUV_{\text{max}}$ as a reference background is preferable to using mediastinal blood pool $SUV_{\text{max}}$ when assessing the early response to chemotherapy in diffuse B-cell lymphoma. A cutoff threshold for defining response as $SUV_{\text{max}}$(lesion) of <140% above reference background is more accurate in predicting survival, compared to a threshold of 125%.

**Reviewer's Comments:** The authors do not state precisely how they determined their volume of interest when calculating the liver $SUV_{\text{max}}$. However, it is common to use a 3-cc sphere in the mid-liver. Selecting a region too high could result in underestimating SUV values due to respiratory motion. The LLR (lesion to liver ratio) was found to be more accurate than the LBR (lesion to mediastinal blood pool ratio) in predicting overall survival in the lymphoma patients in this study. (Reviewer-Thomas F. Heston, MD).

**Keywords:** Large B-Cell Lymphoma, Monitoring Mid-Therapy Response, PET, Reference Backgrounds

**Print Tag:** Refer to original journal article
Radiosensitizing Chemotherapy May Aid in NET Treatment

Phase II Study of Radiopeptide 177Lu-Octreotate and Capecitabine Therapy of Progressive Disseminated Neuroendocrine Tumours.

Claringbold PG, Brayshaw PA, et al:

Eur J Nucl Med Mol Imaging 2010; October 30 (): epub ahead of print

In patients undergoing treatment of advanced-stage neuroendocrine tumors, combination therapy with the radiopeptide Lu-177 octreotate and capecitabine appears to be quite safe.

**Background:** Lutetium-177 DOTATATE (Lu-177 octreotate) has proven effective in treating patients with advanced-stage neuroendocrine tumors (NETs). However, while survival is prolonged in many individuals, complete remissions are rare. One possible way to improve response to this treatment is to use it in conjunction with a radiosensitizing agent. Radiotherapy with the radiosensitizing chemotherapy agent 5-FU has been shown to be very effective.

**Objective:** To conduct a phase II clinical trial with capecitabine (the 5-FU prodrug) combined with Lu-177 octreotate in patients with progressive NETs.

**Participants:** 33 subject with well-differentiated progressive NETs. The primary tumor site was small bowel in 13 patients and pancreas in 10.

**Methods:** Patients received treatment with Lu-177 octreotate, 7.8 GBq per cycle. Amino acid infusion was given at the time of Lu-177 octreotate therapy. Oral capecitabine was given for 2 weeks at the time of each Lu-177 octreotate cycle.

**Results/Conclusions:** Of the 33 subjects, 25 completed 4 cycles of radiopeptide therapy and associated capecitabine treatment. The cumulative radiation dose for kidneys for the group at completion of all therapy was 9.6 Gy (4.5-14.6 Gy). Overall toxicity was considered minimal. Only 1 individual experienced grade 3 thrombocytopenia. There were no resulting cases of neutropenia, and there were no resulting cases of significant renal toxicity. A partial remission was achieved in 24% of patients, and no complete remissions were achieved. A stable disease status was achieved in 70% of subjects. Biochemical response based on serum chromagranin A levels was seen in all subjects. Of 24 symptomatic patients at the start of the study, 10 demonstrated complete amelioration of their symptoms.

**Reviewer’s Comments:** Achievement of disease stabilization in patients with progressive disease is sometimes overlooked in importance. The 94% combination of disease response plus disease stabilization in this series is very impressive and somewhat higher than that seen in other studies in which radiopetitie therapy has been used alone. It appears that the addition of capecitabine to Lu-177 octreotate therapy is very safe and may improve efficacy. (Reviewer-David Bushnell, MD).

Keywords: Neuroendocrine Tumors, Treatment, Lu-177 Octreotate Plus Capecitabine

Print Tag: Refer to original journal article