PET - Oncology


A Prospective Trial Comparing Lymphangiogram, Cross-Sectional Imaging, and Positron Emission Tomography Scan in the Detection of Lymph Node Metastasis in Locally Advanced Cervical Cancer.

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PURPOSE:: This study prospectively evaluated the use of lymphangiography, computed tomography/magnetic resonance imaging, and positron emission tomography (PET) imaging of lymph node metastasis in patients receiving definitive chemoradiotherapy for cervical cancer. MATERIALS AND METHODS:: Twenty patients underwent lymphangiogram, computed tomography/magnetic resonance imaging, and PET. There was no histologic verification of metastasis. Four lymph node regions, including the internal, external, and common iliacs, and para-aortic, were scored as positive or negative for metastasis. Agreement between imaging was analyzed using multirater kappa and disease-free survival utilizing Kaplan Meier survival curves and log-rank test. RESULTS:: Agreement between imaging was most consistent in the common iliacs (P < 0.001) and least in the para-aortic region (P = 0.41). Disease-free survival (DFS) at one year was statistically associated with positive PET imaging (25%) versus negative PET imaging (86%) (P = 0.033) in the common iliac lymph node region. No other single lymph node region in any modality was statistically associated with DFS. One-year DFS in patients with any positive areas on PET imaging was 50% compared with 90% in patients with negative PET imaging (P = 0.02). Seven patients were noted to have no metastasis in any region by all 3 of the imaging modalities; the 1-year DFS in these 7 patients was 100% compared with 59% in the 13 patients with any positive nodal area (P = 0.05). CONCLUSIONS:: Positive lymphadenopathy on PET imaging was associated with reduced DFS.

Radiother Oncol. 2009 Sep 1.

Can hypoxia-PET map hypoxic cell density heterogeneity accurately in an animal tumor model at a clinically obtainable image contrast?


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BACKGROUND: PET allows non-invasive mapping of tumor hypoxia, but the combination of low resolution, slow tracer adduct-formation and slow clearance of unbound tracer remains problematic. Using a murine tumor with a hypoxic fraction within the clinical range and a tracer post-injection sampling time that results in clinically obtainable tumor-to-reference tissue activity ratios, we have analyzed to what extent inherent limitations actually compromise the validity of PET-generated hypoxia maps. MATERIALS AND METHODS: Mice bearing SCCVII tumors were injected with the PET hypoxia-marker fluoroazomycin arabinoside (FAZA), and the immunologically detectable hypoxia marker, pimonidazole. Tumors and reference tissue (muscle, blood) were harvested 0.5, 2 and 4h after FAZA administration. Tumors were analyzed for global (well counter) and regional (autoradiography) tracer distribution and compared to pimonidazole as visualized using immunofluorescence microscopy. RESULTS: Hypoxic fraction as measured by pimonidazole staining ranged from 0.09 to 0.32. FAZA tumor to reference tissue ratios were close to unity 0.5h post-injection but reached values of 2 and 6 when tracer distribution time was prolonged to 2 and 4h, respectively. A fine-scale pixel-by-pixel comparison of autoradiograms and immunofluorescence images revealed a clear spatial link between FAZA and pimonidazole-adduct signal intensities at 2h and later. Furthermore, when using a pixel size that mimics the resolution in PET, an excellent correlation between pixel FAZA mean intensity and density of hypoxic cells was observed already at 2h post-injection. CONCLUSIONS: Despite inherent weaknesses, PET-hypoxia imaging is able to generate quantitative tumor maps that accurately reflect the underlying microscopic reality (i.e., hypoxic cell density) in an animal model with a clinical realistic image contrast.


[Application of 18F-FDG PET/CT in cervical cancer with elevated levels of serum squamous cell carcinoma antigen during the follow-up.]

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Background and Objective: Lymph node metastases are commonly seen in malignant tumors of the head and neck. Detection of the primary tumors affects the quality of life and survival rates of these patients. This study was to evaluate the application of 18F-FDG PET/CT in detecting primary tumors metastasizing to lymph nodes of the neck, and to assess the positive predictive value of 18F-FDG PET/CT. METHODS: In total 93 patients with pathologically confirmed neck lymph node metastases from unknown primary tumors underwent 18F-FDG PET/CT in Sun Yat-sen University Cancer Center between June 2005 to April 2008 were entered into this study. The primary tumors of patients were initially diagnosed according to different PET/CT standards as definite diagnosis, suspicious diagnosis and no signs of primary tumors. All diagnosis based on PET/CT images were verified by pathological exams or

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additional imaging tests. Results: Forty cases made definite diagnosis by PET/CT were all confirmed by pathological or clinical exams, with a positive predictive value of 100%. Of 28 cases made suspicious diagnosis, 16 were pathologically confirmed, with a positive predictive value of 57.1%. Two patients, who were suggested lymph node metastases in mediastinum without the sign of the primary tumor by PET/CT, were clinically verified as primary mediastinal lung cancer. The primary tumors of another two patients were not detected by PET/CT, but were found under endoscopy. The total detection rate of PET/CT for the primary tumor was 60.2% (56/93). Conclusion: PET/CT is of important clinical value in detecting primary tumors metastasizing to lymph nodes of the neck.


[Effects of Qushi Huayu Decoction in prevention and treatment of fatty liver in rats based on adiponectin-free fatty acid pathway]

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OBJECTIVE: To explore the effects of Qushi Huayu Decoction (QSHYD), a compound traditional Chinese herbal medicine, in prevention and treatment of non-alcoholic fatty liver disease (NAFLD) in rats. METHODS: Forty Wistar male rats were used to establish the NAFLD model by subcutaneous injection of carbon tetrachloride (CCI(4)) for 4 weeks (twice weekly) along with high-fat and low-protein diet for 2 weeks. After two-week administration, the rats were randomly divided into four groups: untreated group, high-dose QSHYD group, medium-dose QSHYD group and low-dose QSHYD group. Another six rats were used as normal control. After 2-week treatment, the following indexes were detected: (1) liver pathology; (2) contents of serum adiponectin (ADP) and liver triglyceride (TG); (3) concentrations of liver FFA, adiponectin receptor 2 (AdipoR2), malonyl-coenzyme A (malonyl-CoA), AMP-activated protein kinase (AMPK), acetyl-CoA carboxylase (ACCase), fatty acid synthase (FAS) and carnitine palmitoyl transferase-1 (CPT-1). RESULTS: Compared with the normal group, there were physiological changes associated with hepatic steatosis and inflammation in liver tissues in the untreated group as observed by oil red O staining and HE staining. The TG, FFA, malonyl-CoA, FAS, and ACCase concentrations in liver tissues in the untreated group were elevated significantly. While the contents of ADP in serum and AdipoR2, CPT-1 and AMPK in liver tissues in the untreated group were decreased markedly. The pathological damages in each QSHYD-treated group were significantly less than those in the untreated group. The TG and FFA contents in liver tissues in each QSHYD-treated group were significantly decreased. The FAS, ACCase and malonyl-CoA concentrations in liver tissues of the high QSHYD-treated group were reduced markedly as compared with the untreated group. High- and medium-dose of QSHYD could significantly increase ADP content in serum and AMPK, CPT-1 and AdipoR2 contents in liver tissues. CONCLUSION: QSHYD can affect the ADP-FFA pathway by increasing the content of serum ADP, which may be one of its important mechanisms in preventing and treating NAFLD in rats.

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(18)F-FLT and (18)F-FDG PET to measure response to radiotherapy combined with celecoxib in two colorectal xenograft models.


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Purpose: To determine the dependence of celecoxib on the tumour micro-environment in vitro and in vivo and to compare the use of (18)F-Fluorodeoxyglucose ((18)F-FDG) and (18)F-3'-deoxy-3-fluorothymidine ((18)F-FLT) to measure tumour response. Materials and methods: In vitro, colony assays were performed on a cyclo-oxygenase 2 (COX-2) negative (HCT116) and a COX-2 positive cell line (HCA7). Xenograft models of these cell lines were treated with celecoxib and/or radiotherapy. Micro Positron Emission Tomography (microPET) scans with (18)F-FDG and (18)F-FLT were performed at different time-points. Results: In vitro, no radiosensitising effect was seen in either of the cell lines. In vivo results showed a significant effect of celecoxib in the COX-2 negative tumours (HCT116) (enhancement ratio 1.5, p = 0.02) while no significant effect was observed in the COX-2 positive model (HCA7). A good correlation between (18)F-FDG and (18)F-FLT uptake was seen in both tumour models (r = 0.48, p = 0.002; r = 0.41, p = 0.005). After irradiation, a decrease in the uptake of both tracers was observed in both tumour models, which was more pronounced in the combination group, confirming the growth delay data. Conclusions: The contradicting in vitro and in vivo results suggest a major role of the tumour micro-environment. (18)F-FLT seems a good alternative for (18)F-FDG to follow tumour growth after radiotherapy treatment.


[Clinical value of (18)F-FDG positron emission tomography-computed tomography in local liver neoplasm ablation.]

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OBJECTIVE: To assess the value of [(18)F]fluoro-2-deoxy-D-glucose positron emission tomography-computed tomography [(18)F-FDG PET-CT] in ultrasound-guided local ablation of malignant liver tumors. METHODS: Nineteen patients with 35 local residual tumor foci following previous tumor ablation underwent [(18)F-FDG PET-CT] and ultrasound-guided local ablation with intratumoral alcohol injection. RESULTS: After the second local ablation guided by [(18)F-FDG PET-CT] and ultrasound, radioactive defects were detected in the corresponding location in 31 of the 35 residual foci, and after the third local ablation, the other 4 foci also showed radioactive defects. CONCLUSION: [(18)F-FDG PET-CT] can sensitively and accurately identify tissue necrosis and residual tumors, and serves as an excellent approach for ultrasound-guided local ablation of local residual tumors.


Bastiaanmet E, Wobbes T, Hoekstra OS, van der Jagt EJ, Brouwers AH, Koolemij R, de Klerk JM, Oyen WJ, Meijer S, Hoekstra HJ.

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PURPOSE: Patients with melanoma with potentially resectable lymph node metastases require accurate staging to prevent unnecessary surgery. [(18)F]Fluorodeoxyglucose (FDG) positron emission tomography (PET) is attractive for this because melanoma typically is FDG avid. The aim of this prospective multicenter study was to perform a head-to-head comparison of FDG-PET and computed tomography (CT) in staging of patients with melanoma with palpable lymph node metastases in terms of diagnostic accuracy and impact on treatment. PATIENTS AND METHODS: All consecutive patients with palpable, proven lymph node metastases of melanoma between mid 2003 and 2007 were prospectively included. The number/site of distant metastases detected with FDG-PET and CT were recorded. Histology/cytology or 6 months follow-up were the reference standard. Intended and performed treatment was recorded. RESULTS: Distant metastases were suspected by FDG-PET in 32% of the 251 patients and by CT in 29% (P = .26). Upstaging was correct in 27% by FDG-PET and in 24% by CT (P = .18). FDG-PET detected more metastatic sites (133 v 112, P = .03), detecting significantly more bone and subcutaneous metastases. Treatment changed in 19% of patients; in 79% as a result of both scans, in 17% exclusively by FDG-PET, and in 4% exclusively by CT. In 34 patients (14%), FDG-PET had an additional value over spiral CT, and in 23 patients (9%), CT had additional value over FDG-PET. CONCLUSION: As a result of FDG-PET and CT, 27% of patients were upstaged, and treatment changed in one of five patients. FDG-PET and CT are equivalent in upstaging; however, FDG-PET detected more metastatic sites, especially bone and subcutaneous. FDG-PET and/or CT are indicated in the staging of patients with melanoma with palpable lymph node metastases.


Diagnostic evaluation of squamous cell carcinoma metastatic to cervical lymph nodes from an unknown head and neck primary site.

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OBJECTIVES/HYPOTHESIS: To discuss our experience with the diagnostic evaluation in patients with squamous cell carcinomas (SCCAs) of the head and neck metastatic to the cervical lymph nodes from an unknown primary site. METHODS:: Between June 1983 and December 2008, 236 patients were evaluated with lymph node biopsy, computed tomography (CT), and/or magnetic resonance imaging (MRI) of the head and neck, and panendoscopy with directed biopsies. Additional studies included fluorodeoxyglucose-single photon emission computed tomography (FDG-SPECT) in 26 patients and FDG-positron emission tomography (FDG-PET) or FDG-PET/CT in 21 patients. Seventy-nine patients underwent an ipsilateral (72) or bilateral (seven) tonsillectomy. RESULTS:: An occult primary site was detected in 126 patients (53.4%); six patients had twosynchronous primary cancers. The most common primary sites were in the tonsillar fossa (59 patients; 44.7%) and the base of tongue (58 patients; 43.9%). The primary site was found in 21 (29.2%) of the 72 patients with no suspicious findings on physical exam and/or radiographic evaluation compared with 105 (64.0%) of 164 remaining patients. Tonsillectomy revealed the primary cancer in 35 (44.3%) of 79 patients. FDG-SPECT and FDG-PET or FDG-PET/CT was the sole method of primary site detection in only one patient (2.1%) of 47 patients. CONCLUSIONS:: Diagnostic evaluation should include a thorough physical examination, CT and/or MRI of the head and neck, and panendoscopy with directed biopsies. Unilateral or bilateral tonsillectomy should be performed on patients with adequate lymphoid tonsillar tissue. FDG-PET or FDG-PET/CT should be considered for those with indeterminate findings on physical examination and/or head and neck CT and/or MRI if those sites are located outside of the oropharynx. Laryngoscope, 2009.
Dose-escalation using intensity-modulated radiotherapy for prostate cancer - Evaluation of the dose distribution with and without (18)F-choline PET-CT detected simultaneous integrated boost.


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BACKGROUND AND PURPOSE: The aim of the study was to evaluate the impact of a dose escalation to an (18)F-choline PET-CT defined simultaneous integrated boost (IB) on the dose distribution and changes of the equivalent uniform dose (EUD).

MATERIALS AND METHODS: PET-CT was performed in 12 consecutive patients for treatment planning. An intraprostatic lesion was defined by a tumour-to-background uptake value ratio >2 (GTV(PET)). Dose escalation was focused only on the intraprostatic lesion. Two comparisons were evaluated: whole prostate irradiation to 76Gy+/-boost to 80Gy (C1) and whole prostate irradiation to 66.6Gy+/-boost to 83.25Gy (C2). RESULTS: PTV/GTV(PET)+margins were covered by a mean EUD of 75.9/76.1Gy vs. 77.1/80.1Gy (C1) and 66.5/66.2Gy vs. 71.1/82.9Gy (C2) (p<0.01, respectively). Concerning the organs at risk, EUD increased slightly with an additional boost (mean EUD for bladder: C1 53.2Gy vs. 53.8Gy; C2 43.0Gy vs. 45.1Gy; for rectum: C1 52.0Gy vs. 52.6Gy; C2 43.0Gy vs. 45.4Gy; p<0.01, respectively). The distance to the organs at risk had a significant impact on the respective maximum doses in the treatment plans with IB. CONCLUSIONS: Treatment planning with IB allows an individually adapted dose escalation. The therapeutic ratio can be improved by a considerable dose escalation to the macroscopic tumour, but only minor EUD changes to the bladder and rectum.

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[New radiopharmaceuticals and positron-emission tomography applications at the Masaryk Memorial Cancer Institute in Brno]


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The construction and launch of the cyclotron & PET centre at the Masaryk Memorial Cancer Institute, which is run in cooperation with the Nuclear Research Institute Praha-Rez, allows the Masaryk Memorial Cancer Institute to engage in the research, development and application of new radiopharmaceuticals including compounds labelled by short-living positron emitters (especially 11C). For the immediate future, new projects are planned, e.g. using the proliferation marker 18F-fluoro-L-thymidine, or neuro-oncological studies using the proteosynthesis and amino acid transport marker 11C-methionine, and eventually also other compounds applicable outside of oncology. The existence of the PET centre at the Masaryk Memorial Cancer Institute therefore offers a wide range of possibilities to both patients and physicians in the Brno region and beyond.


Dynamic MRI and CAD vs. Choline MRS: Where is the detection level for a lesion characterisation in prostate cancer?


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Purpose: To evaluate the role of pre-interventional fused high resolution T2-weighted images with parametrically analysed dynamic contrast enhanced T1-weighted magnetic resonance (MR) images (DCE-MRI) and 1H magnetic resonance spectroscopy (MRS) for a precise biopsy for the detection of prostate cancer and for the delineation of intraprostatic subvolumes for intensity modulated radiation therapy (IMRT). Materials and methods: Inclusion criteria: Pathological prostate-specific antigen values (PSA) and/or previously negative transrectal ultrasound guided biopsy. Standardised biopsy of the prostate divided into 20 regions. Image fusion of DCE-MRI, single voxel spectroscopy, SVS; chemical shift imaging, CSI) with T2 images for morphological localisation using the MR-workstation, separate CAD-workstation (CAD: computer aided diagnosis) or a radiation treatment planning system. Correlation of these intraprostatic subvolumes with histology and cytokeratin-positive areas in prostatectomy species. Results: DCE-MRI: Sensitivity 82%, specificity 89%, accuracy 88%, positive predictive value 61%, negative predictive value 96%. SVS: Sensitivity 55%, specificity 62%. CSI: Sensitivity 68%, specificity 67%. False positive findings due to prostatitis, adenomatous hyperplasia, false negative findings due to low signal (PIN (prostatic intraepithelial neoplasia), cut-off level for DCE-MRI: lesions smaller 3 mm and less than 30% cancer cells, for SVS: lesions smaller 8 mm and less than 50% cancer cells), for CSI: lesions smaller 4 mm and less than 40% cancer cells. Conclusions: DCE-MRI and MRS are helpful for a precise biopsy of the prostate. The European Society for Therapeutic Radiology and Oncology (ESTRO) guidelines 2006 for radiation treatment planning of the prostate have to be revised, if the standardised biopsy will be replaced by a lesion-orientated biopsy. Until now it is unclear, if the parametric maps of DCE-MRI and MRS can be used for radiation treatment planning of the prostate.


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OBJECTIVE: To evaluate (18)FDG PET-CT for the assessment of therapy response and prediction of patient outcome after concurrent chemoradiotherapy (CCRT) for non-small cell lung cancer (NSCLC). METHODS: Forty-six patients with pathologically proven stage III NSCLC had 2 serial FDG PET-CT scans, before and during CCRT. The maximum standardized uptake value (SUV(max)) of the primary lung lesion was calculated. The value changes of SUV(max) before and during treatment were calculated according to the following equation: SUV=(SUV(before)-SUV(during))/SUV(before). The relationship between changes of the SUV(max) and the therapy response as well as long-term survival was studied in the responsive and non-responsive groups after CCRT. RESULTS: Of the 46 enrolled patients, after a medicine follow-up of 2 years, the initial SUV(max) in the responsive and non-responsive groups was 7.59+/-3.14 and 14.72+/-4.67, respectively. The SUV(max) during treatment in the two groups was 2.89+/-1.39 and 9.82+/-3.31, respectively. Significant difference (P=0.001; P=0.001) in SUV(max) was observed either before or during treatment. Furthermore, the percent change of SUV(max) before and during treatment was 61.91+/-86.69 and 33.56+/-90.37, respectively. There was significant difference between these two groups (P=0.007). In addition, the 1-year survival rate in the responsive and non-responsive group was 73% and 69%, respectively. The 2-year survival rate in the two groups was 40% and 37%, respectively. There was significant difference between these two groups (P=0.001). CONCLUSIONS: (18)FDG PET-CT is an effective method in the prediction of therapy response in patients with stage III NSCLC. The analysis of percent change of SUV(max) provides additional value in early prediction of therapy response and patient outcome.


NCCN task force: clinical utility of PET in a variety of tumor types.


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Use of PET is widespread and increasing in the United States, mainly for oncologic applications. In November 2006, the National Comprehensive Cancer Network (NCCN) gathered a panel of experts to review the literature and develop clinical recommendations for using PET scans in lymphoma and non-small cell lung, breast, and colorectal cancers. However, because its use is not restricted to these diseases, and evidence is accumulating for its application in other types of cancers, NCCN convened a second meeting in December 2008 to expand on the initial report. A multidisciplinary panel met to discuss the current data on PET application for various tumor types, including genitourinary, gynecologic, pancreatic, hepatobiliary, thyroid, brain, small cell lung, gastric, and esophageal cancers, and sarcoma and myeloma. This report summarizes the proceedings of this meeting, including discussions of the background of PET, the role of PET in oncology, principles of PET use, emerging applications, and possible future developments.

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Intensely hypermetabolic extra-axial brainstem tumor in Erdheim-chester disease.

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Erdheim-Chester disease is a rare non-Langerhans cell histiocytosis characterized by progressive histiocytic proliferation with multiorgan involvement, typically of the kidney, skin, brain, and lung, and less frequently, the heart and retro-orbital tissue. Fluorine-18 fluorodeoxyglucose positron emission tomography (F-18 FDG PET) plays an important role in the management of this disease. It has been reported that FDG PET imaging allows accurate evaluation of the extent of the disease at baseline, as well as assessment of response to any specific therapy. In this case, a 57-year-old Chinese man presented with functional decline and a urinary tract infection. He had a prior history of xanthogranulomas of bilateral canthal masses. On imaging, he was found to have left hydronephrosis, diffuse urothelial thickening, increased density of the perinephric fat, mural thickening of the descending aorta and soft tissue masses along the posterior wall of the right atrium extending into the region of the interatrial septum and involving the right atrioventricular groove. Histopathology revealed retroperitoneal fibrosis. An IV contrast-enhanced FDG PET scan showed increased activity in a previously unidentified brain stem mass and the shafts of bilateral femora. Varying levels of FDG uptake were seen in the other lesions.

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Been LB, Hoekstra HJ, Suurmeijer AJ, Jager PL, van der Laan BF, Elsinga PH.

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The evaluation of response to radiotherapy in patients with laryngeal cancer is a challenge because of the difficulty of differentiating between post-therapy changes and recurrent or residual tumor. Pet emission tomography is a non-invasive imaging tool that may be helpful in this differentiation. In this study, [18]F-fluoro-3'-deoxy-l-thymidine ([18]F[FLT]), a proliferation tracer is compared with 2-[18]F-fluoro-2-deoxy-d-glucose ([18]F[FDG]). Patients with primary laryngeal cancer, scheduled to undergo radiotherapy were included in this study. Patients underwent both [18]F[FLT-PET and [18]F[FDG-PET shortly before radiotherapy. Ten patients underwent [18]F[FLT-PET and [18]F[FDG-PET 2-3 months after radiotherapy. Scans were analyzed visually for areas of increased tracer uptake. The standardized uptake value (SUV) was measured as a semi-quantitative value of tracer uptake. Fourteen patients, all male, were included in this study. Both [18]F[FLT-PET and [18]F[FDG-PET showed increased tracer uptake in 12 out of 14 patients (86%). [18]F[FDG uptake was significantly higher than [18]F[FLT uptake (SUV(max): 4.5 vs. 2.4 (P=0.002); SUV(mean): 3.4 vs. 1.9 (P=0.002)). After radiotherapy, 3 patients had histologically proven residual or recurrent laryngeal cancer. [18]F[FDG was true positive in 2 out of 3 patients, whereas [18]F[FLT showed increased tracer uptake in only one. Of the remaining 7 patients, [18]F[FLT was true negative in all, whereas [18]F[FDG showed increased uptake in one (false positive). [18]F[FLT-PET is feasible in visualizing laryngeal cancer and its evaluation of treatment. The overall uptake of this tracer is significantly lower as compared with [18]F[FDG, but tumor to background ratios are comparable.

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Recombinant Anti-CD20 Antibody Fragments for Small-Animal PET Imaging of B-Cell Lymphomas.


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The CD20 cell surface antigen is expressed at high levels by over 90% of B-cell non-Hodgkin lymphomas (NHL) and is the target of the anti-CD20 monoclonal antibody rituximab. To provide more sensitive, tumor-specific PET imaging of NHL, we sought to develop PET agents targeting CD20. METHODS: Two recombinant anti-CD20 rituximab fragments, a minibody (scFv-C(H)3 dimer; 80 kDa) and a modified scFv-Fc fragment (105 kDa), designed to clear rapidly, were generated. Both fragments were radioiodinated with [124]I, and the minibody was additionally labeled with (64)Cu (radiometal) after conjugation to 1,4,7,10-tetraazacyclododecane-N,N',N'',N'''-tetraacetic acid (DOTA). The radioiodinated fragments and the radiometal-labeled minibody were evaluated in mice as small-animal PET imaging agents for the in vivo imaging of human CD20-expressing lymphomas. RESULTS: Rapid and specific localization to CD20-positive tumors was observed with the radioiodinated fragments. However, the tumor uptake levels and blood activities differed, resulting in different levels of contrast in the images. The better candidate was the minibody, with superior uptake (2-fold higher than that obtained with scFv-Fc) in CD20-positive tumors and low uptake in CD20-negative tumors. Ratios of CD20-positive tumors to CD20-negative tumors at 21 h were 7.0 +/- 3.1 (mean +/- SD) and 3.9 +/- 0.7 for the minibody and scFv-Fc, respectively. The ratio achieved with the (64)Cu-DOTA-minibody at 19 h was about 5-fold lower because of higher residual background activity in CD20-negative tumors. CONCLUSION: A radioiodinated minibody and a radioiodinated scFv-Fc fragment produced excellent, high-contrast images in vivo. These new immunoPET agents may prove useful for imaging CD20-positive lymphomas in preclinical models and in humans with NHL.


Initial Characterization of a Dedicated Breast PET/CT Scanner During Human Imaging.


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We have constructed a dedicated breast PET/CT scanner capable of high-resolution functional and anatomic imaging. Here, we present an initial characterization of scanner performance during patient imaging. METHODS: The system consisted of a lutetium oxyorthosilicate-based dual-planar head PET camera (crystal size, 3 x 3 x 20 mm) and 768-slice cone-beam CT. The position of the PET heads (separation and height) could be adjusted for varying breast dimensions. For scanning, the patient lay prone on a specialized bed and inserted a single pendent breast through an aperture in the table top. Compression of the breast as used in
mammography is not required. PET and CT systems rotate in the coronal plane underneath the patient sequentially to collect fully tomographic datasets. PET images were reconstructed with the fully 3-dimensional maximum a posteriori method, and CT images were reconstructed with the Feldkamp algorithm, then spatially registered and fused for display. Phantom scans were obtained to assess the registration accuracy between PET and CT images and the influence of PET electronics and activity on CT image quality. We imaged 4 women with mammographic findings highly suggestive of breast cancer (breast imaging reporting and data system, category 5) in an ongoing clinical trial. Patients were injected with (18)F-FDG and imaged for 12.5 min per breast. From patient data, noise-equivalent counting rates and the singles-to-trues ratio (a surrogate for the randoms fraction) were calculated. RESULTS: The average registration error between PET and CT images was 0.18 mm. PET electronics and activity did not significantly affect CT image quality. For the patient trial, biopsy-confirmed cancers were visualized on dedicated breast PET/CT on all patient scans, including the detection of ductal carcinoma in situ in 1 case. The singles-to-trues ratio was found to be inversely correlated with breast volume in the field of view, suggesting that larger breasts trend toward increased noise-equivalent counting rates for all other things equal. CONCLUSION: Scanning of the uncompressed breast with dedicated breast PET/CT can accurately visualize suspected lesions in 3 dimensions.

J Nucl Med. 2009 Sep;50(9):1394-400.

**Influence of Trigger PSA and PSA Kinetics on 11C-Choline PET/CT Detection Rate in Patients with Biochemical Relapse After Radical Prostatectomy.**


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The purpose of this study was to investigate the effect of total prostate-specific antigen (PSA) at the time of (11)C-choline PET/CT (trigger PSA), PSA velocity (PSAvel), and PSA doubling time (PSAdt) on (11)C-choline PET/CT detection rate in patients treated with radical prostatectomy for prostate cancer, who showed biochemical failure during follow-up. METHODS: A total of 190 patients treated with radical prostatectomy for prostate cancer who showed an increase in PSA (mean, 4.2; median, 2.1; range, 0.2-25.4 ng/mL) were retrospectively enrolled. All patients were studied with (11)C-choline PET/CT. Patients were grouped according to trigger PSA (PSA <= 1 ng/mL, 1 < PSA <= 2 ng/mL, 2 < PSA <= 5 ng/mL, and PSA > 5 ng/mL). In 106 patients, data were available for calculation of PSAvel and PSAdt. Logistic regression analysis was used to determine whether there was a relationship between PSA levels and PSA kinetics and the rate of detection of relapse using PET. RESULTS: (11)C-choline PET/CT detected disease relapse in 74 of 190 patients (38.9%). The detection rate of (11)C-choline PET/CT was 19%, 25%, 41%, and 67% in the 4 subgroups-PSA <= 1 ng/mL (51 patients), 1 < PSA <= 2 ng/mL (39 patients), 2 < PSA <= 5 ng/mL (51 patients), and PSA > 5 ng/mL (49 patients)-respectively. Trigger PSA values were statistically different between PET-positive patients (median PSA, 4.0 ng/mL) and PET-negative patients (median PSA, 1.4 ng/mL) (P = 0.0001). Receiver-operating-characteristic analysis showed an optimal cutoff point for trigger PSA of 2.43 ng/mL (area under the curve, 0.76). In 106 patients, PSAdt and PSAvel values were statistically different between patients with PET-positive and -negative scan findings (P = 0.04 and P = 0.03). The (11)C-choline PET/CT detection rate was 12%, 34%, 42%, and 70%, respectively, in patients with PSAvel < 1 ng/mL/yr (33 patients), 1 < PSAvel <= 2 ng/mL/yr (26 patients), 2 < PSAvel <= 5 ng/mL/yr (19 patients), and PSA > 5 ng/mL/yr (28 patients). The (11)C-choline PET/CT detection rate was 20%, 40%, 48%, and 60%, respectively, in patients with PSAdt > 6 mo (45 patients), 4 < PSAdt <= 6 mo (20 patients), 2 < PSAdt <= 4 mo (31 patients), and PSAdt <= 2 mo (10 patients). There was no statistical difference between PET-positive and -negative scan detection rates according to the Gleason score, pT and N status, patient age, or duration between surgery and biochemical relapse. Trigger PSA and PSAvel were found to be independent predictive factors for a PET-positive result (P = 0.002; P = 0.04) and PSAdt was found to be an independent factor only in patients with trigger PSA less than 2 ng/mL (P = 0.05) using multivariate analysis. CONCLUSION: The (11)C-choline PET/CT detection rate is influenced by trigger PSA, PSAdt, and PSAvel. This finding could be used to improve the selection of patients for scanning by reducing the number of false-negative scans and increasing the detection rate of disease in patients with early relapse and potentially curative disease.


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The magnitude of the injected activity (A(0)) has a direct impact on the statistical quality of PET images. This study aimed to develop a generalized method for maximizing the statistical quality of dynamic PET images by optimizing A(0). METHODS: Patient-specific noise-equivalent counts (PS-NECs) were used as a metric of the statistical quality of each time frame of a dynamic PET image. Previous methodology developed to extrapolate the NEC as a function of A(0) was extended to dynamic PET, enabling the NEC to be extrapolated as a function of both A(0) and the time after injection. This method allowed A(0) to be optimized after a single scan (at a single A(0)), by maximizing the NEC within the time interval for which the parameter estimation is most sensitive. The extrapolation method was validated by a series of (15)O-H2O scans of the body acquired in 3-dimensional mode. Each patient
Late relapse of a light-chain myeloma as extramedullary plasmacytoma of the thyroid gland after second allogeneic stem-cell transplantation.

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Sunitinib is an oral multitargeted tyrosine kinase inhibitor with antiangiogenic properties used for treatment of renal cell carcinoma and gastrointestinal stromal tumors at a dose of 50 mg/day consecutively for 4 weeks followed by 2 weeks off per cycle. At present, no data are available on the early prediction of sunitinib response in renal cell carcinoma. We report a clinical case of a patient with metastatic renal cell carcinoma diagnosed with 11C-acetate PET and conventional CT and treated with sunitinib. Partial and complete remission documented by CT was preceded by early functional tumor inhibition shown by 11C-acetate-PET after only 14 days of therapy. This case report highlights some interesting points related to the potential role of a novel non-FDG PET tracer, 11C-acetate, in the early prediction of the response to targeted therapies in metastatic renal cell carcinoma.


11C-acetate PET for early prediction of sunitinib response in metastatic renal cell carcinoma.


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Sunitinib is an oral multitargeted tyrosine kinase inhibitor with antiangiogenic properties used for treatment of renal cell carcinoma and gastrointestinal stromal tumors at a dose of 50 mg/day consecutively for 4 weeks followed by 2 weeks off per cycle. At present, no data are available on the early prediction of sunitinib response in renal cell carcinoma. We report a clinical case of a patient with metastatic renal cell carcinoma diagnosed with 11C-acetate PET and conventional CT and treated with sunitinib. Partial and complete remission documented by CT was preceded by early functional tumor inhibition shown by 11C-acetate-PET after only 14 days of therapy. This case report highlights some interesting points related to the potential role of a novel non-FDG PET tracer, 11C-acetate, in the early prediction of the response to targeted therapies in metastatic renal cell carcinoma.


Evaluation of 18F-FDG PET-CT for Differentiation of Pulmonary Pathology in an Approach of Outpatient Fast Track Assessment.

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INTRODUCTION: The aim of our study was to evaluate the clinical performance/implementation of integrated F-fluorodeoxyglucose positron emission tomography (PET)/computed tomography (CT) for differentiation of pulmonary pathology in an approach of outpatient fast track assessment. METHODS: A prospective study was performed in 114 consecutive patients with pulmonary symptoms and/or abnormal chest x-ray were referred for fast track assessment to the Netherlands Cancer Institute from March 2005 to September 2007. The presence of malignancy was evaluated in a multidisciplinary setting, including F-fluorodeoxyglucose-PET, diagnostic CT, and bronchoscopy (including biopsy), with histopathological evaluation as the reference standard. RESULTS: In 105 patients (92%), a final diagnosis was achieved. A malignancy was diagnosed in 84% of the patients; non-small cell lung cancer in 67%, small cell lung cancer in 7%, and metastases or other malignancies in 10%. Nonmalignant lesions
PET - Oncology

were found in 16% of the patients. Sensitivity, specificity, accuracy, positive predictive value and negative predictive value of positive PET/CT for the presence of malignancy were 97, 56, 90, 92, and 77%, respectively. PET/CT showed unexpected M1 disease (not detected on CT) in 10% of the patients. Almost half of the patients with a malignancy were scheduled for curative treatment, of whom 29 patients for surgery and 14 patients for chemoradiotherapy. CONCLUSION:: In this outpatient fast track setting, PET/CT provides valuable information for diagnosing lung cancer, with a high positive predictive value, and is useful for clinical decision making.


A Prospective Diagnostic Accuracy Study of 18F-Fluorodeoxyglucose Positron Emission Tomography/Computed Tomography, Multidetector Row Computed Tomography, and Magnetic Resonance Imaging in Primary Diagnosis and Staging of Pancreatic Cancer

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OBJECTIVE:: To prospectively compare the accuracy of combined positron emission tomography/computed tomography using F-fluorodeoxyglucose (FDG-PET/CT), multidetector row computed tomography (MDCT), and magnetic resonance imaging (MRI) in the evaluation of patients with suspected pancreatic malignancy. SUMMARY BACKGROUND DATA:: FDG-PET/CT imaging is increasingly used for staging of pancreatic cancer. Preliminary data suggest a significant influence of FDG-PET/CT on treatment planning, although its role is still evolving. METHODS:: Thirty-eight consecutive patients with suspicion of pancreatic malignancy were enrolled. Patients underwent a protocol including FDG-PET/CT, MDCT, and MRI combined with magnetic resonance cholangiopancreatography, all of which were blindly evaluated. The findings were confirmed macroscopically at operation and/or by histopathologic analysis (n = 29) or follow-up (n = 9). Results of TNM classification of different imaging methods were compared with clinical TNM classification. RESULTS:: Pancreatic adenocarcinoma was diagnosed in 17 patients, neuroendocrine tumor in 3, mass-forming pancreatitis in 4, cystic lesion in 6, and fibrosis in 2. Six patients had a finding of a normal pancreas. The diagnostic accuracy of FDG-PET/CT for pancreatic malignancy was 89%, compared with 76% and 79% for MDCT and MRI, respectively. In the differential diagnosis of suspected malignant biliary stricture at endoscopic retrograde cholangiopancreatography (n = 21), FDG-PET/CT had a positive predictive value of 92%. In 17 patients with advanced pancreatic adenocarcinoma, FDG-PET/CT had a sensitivity of 30% for N- and 88% for M-staging. Both MDCT and MRI had sensitivities of 30% for N- and 38% for M-staging. Furthermore, the clinical management of 10 patients (26%) was altered after FDG-PET/CT. CONCLUSION:: FDG-PET/CT was more sensitive than conventional imaging in the diagnosis of both primary pancreatic adenocarcinoma and associated distant metastases. In contrast, the sensitivity of FDG-PET/CT was poor in detecting local lymph node metastasis, which would have been important for an assessment of resectability. We recommend the use of FDG-PET/CT in the evaluation of diagnostically challenging cases, especially in patients with biliary strictures without evidence of malignancy in conventional imaging.


The higher the decrease in the standardized uptake value of positron emission tomography after chemoradiation, the better the survival of patients with gastroesophageal adenocarcinoma.


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BACKGROUND:: Postchemoradiation percentage decrease in standardized uptake value(SUV) of positron emission tomography (PET) from baseline correlates with overall survival (OS) and pathologic response. Analyses of dichotomized data are commonly reported. The authors analyzed percentage SUV decrease as both dichotomized and continuous variables. METHODS:: The authors assessed 151 consecutive patients with gastroesophageal adenocarcinoma who had chemoradiation and surgery. Baseline and postchemoradiation PET/computed tomography imaging was performed. The log-rank test and Cox proportional hazards models were used to associate percentage SUV changes and OS, and logistic regression models were used to detect the association between percentage SUV changes and pathologic response. RESULTS:: A >52% SUV decrease (dichotomized analysis) was associated with a longer OS (log-rank test, P = .023). The univariate Cox proportional hazards model indicated that greater percentage SUV decrease (as a continuous variable) was associated with a lower risk of death (hazard ratio [HR], 0.99; P = .01). Pathologic response (<50% residual cancer) was associated with longer OS (P = .003). Patients with chemoradiation resistance (>50% residual cancer) tended to have a higher risk of death than those with chemoradiation sensitivity (0-50% residual cancer; HR, 2.12; P = .099). In the multivariate model, the percentage SUV decrease (as a continuous variable) was the only prognosticator of OS (P = .01). The percentage SUV decrease was nonsignificantly associated with pathologic complete response (univariate odds ratio [OR], 1.01; P = .06 and multivariate OR, 1.03; P = .07). CONCLUSIONS:: The greater the decline in SUV after chemoradiation, the longer is the OS of gastroesophageal adenocarcinoma patients. The percentage SUV decrease as a continuous variable is a better prognosticator of OS than its dichotomized assessments.

Relationship between primary lesion FDG uptake and clinical stage at PET-CT for non-small cell lung cancer patients: An observation.


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The aim of the present study was to investigate the relationship between FDG uptake and clinical stage for non-small cell lung cancer. The patients who were histologically or cytologically proven to be adenocarcinoma (AC) or squamous cell carcinoma (SCC) lung cancer and conducted FDG PET/CT staging were retrospectively reviewed. The FDG uptake was quantified as the maximum standardized uptake value (SUVmax). And the T-N-M status was determined mainly by FDG PET-CT imaging according to the 1997 update of the international staging system for lung cancer. From December 2003 to November 2007, 266 cases (194 men and 72 women; age range 31-90 years, median 62 years) were analyzed, which included 161 AC and 105 SCC patients. The present study showed that both size (3.23+/-1.68cm vs 2.63+/-1.33cm, P=0.004) and SUVmax (9.82+/-5.08 vs 8.43+/-4.21, P=0.016) were significantly greater for SCC compared to AC. There was positive correlation between the SUVmax and size for both SCC and AC (r=0.651, 0.632, respectively; both P=0.000). Significant difference is found among different stages in SUVmax for AC (F=11.693, P=0.000) but not for SCC (F=1.514, P=0.216). After controlling the size factor, a significant correlation was found between tumor stage and FDG uptake value for AC (r=0.323, P=0.000) but not for SCC (r=0.113, P=0.252). In conclusion, this observation showed that tumor size and histologic subtype had influences upon FDG uptake in non-small cell lung cancer. It demonstrated significant correlation between clinical stage and SUVmax for AC, but not for SCC.

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GTV spatial conformity between different delineation methods by (18)FDG PET/CT and pathology in esophageal cancer.

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PURPOSE: To find optimal threshold of length and GTV delineation for esophageal cancer using (18)FDG PET/CT. MATERIALS AND METHODS: Sixteen patients with esophageal carcinoma underwent surgery. For each patient, six GTVs were defined. GTV(CT) was based on CT data alone. GTV(20%), GTV(40%), GTV(2.5) and GTV(40%M) were generated by PET/CT, using SUV(bgd)+20%(SUV(max(slice))-SUV(bgd)), SUV(bgd)+40%(SUV(max(slice))-SUV(bgd)), 2.5 and 40%SUV(max(total)) as thresholds. GTV(path) was derived from pathology. Lengths of GTVs were recorded as L(CT), L(20%), L(40%), L(2.5), L(40%M) and L(path), respectively. The former five GTVs/lengths were compared with GTV(path)/L(path) by means of a conformity index CI/CI', which is the square of intersection of two GTVs/lengths divided by their product. RESULTS: Mean L(CT), L(20%), L(40%), L(2.5), L(40%M) and L(path) were 6.30+/-2.69, 5.55+/-2.48, 6.80+/-2.92, 6.65+/-2.66, 4.88+/-1.99 and 5.90+/-2.38cm. Mean CI(CT&path)', CI(20%&path)', CI(40%&path)', CI(2.5&path)' and CI(40%M&path)' were 0.68+/-0.16, 0.84+/-0.17, 0.76+/-0.14, 0.78+/-0.15 and 0.80+/-0.11. CI(20%&path)' and CI(40%M&path)' was significantly superior to CI(CT&path)' (P<0.05). Mean GTV(CT), GTV(20%), GTV(40%), GTV(2.5), GTV(40%M) and GTV(path) were 29.16+/-18.56, 18.75+/-12.37, 12.52+/-8.08, 22.69+/-14.84, 9.18+/-5.96 and 28.16+/-17.02cm(3). Mean CIs increased significantly from CI(40%M&path)'(0.27+/-0.09) and CI(2.5&path)'(0.52+/-0.16) and CI(CT&path)'(0.77+/-0.17). CONCLUSIONS: The SUV(bgd)+20%(SUV(max(slice))-SUV(bgd)) method optimally estimated gross tumor length, but only reached an unsatisfactory CI for GTV. Due to possible motion factor enveloped in PET images and lack of histopathologic transverse reference, the information from both PET and CT should be referred to complementarily when delineating GTV.


Pitfall of (18)F-FDG-PET imaging in oncology: uterine fibromyoma.

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Activity of dasatinib against L576P KIT mutant melanoma: molecular, cellular, and clinical correlates.


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Point mutations in the KIT receptor tyrosine kinase gene have recently been identified in mucosal, acral lentiginous, and chronically sun-damaged melanomas. We have identified the first human melanoma cell line with an endogenous L576P mutation, the most common KIT mutation in melanoma (approximately 30-40%). In vitro testing showed that the cell viability of the L576P mutant cell line was not reduced by imatinib, nilotinib, or sorafenib small molecule KIT inhibitors effective in nonmelanoma cells with other KIT mutations. However, the viability of the mutant cells was reduced by dasatinib at concentrations as low as 10 nM (P = 0.004). Molecular modeling studies found that the L576P mutation induces structural changes in KIT that reduce the affinity for imatinib (ΔΔGbind = -2.52 kcal/mol) but not for dasatinib (ΔΔGbind = +0.32 kcal/mol). Two metastatic melanoma patients with the L576P KIT mutation were treated with dasatinib, including one patient previously treated with imatinib. Both patients had marked reduction (>50%) and elimination of tumor F18-fluorodeoxyglucose (FDG)-avidity by positron emission tomography (PET) imaging after dasatinib treatment. These data support the selective inhibitory effect of dasatinib against cells harboring the most common KIT mutation in melanoma, and thus has therapeutic implications for acral lentiginous, chronic sun-damaged, and mucosal melanomas.


Complete pathological response in a patient with multiple liver metastases from colon cancer treated with Folfox-6 chemotherapy plus bevacizumab: a case report.


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ABSTRACT: The complete pathological response after primary chemotherapy could represent an important prognostic factor in patients affected by colorectal liver metastases. In recent studies, increasing complete pathological response seems to be correlated with longer overall survival periods and it is recognized as an important prognostic factor in patients treated with pre-operative chemotherapy. The correlation of radiological information on residual neoplastic disease after neoadjuvant treatment, obtained with CT and PET, has to be evaluated; in fact the complete disappearance of liver metastasis on radiological imaging does not always mean a complete disappearance of tumor tissue on histological examination; when it is documented with surgical procedures and confirmed by pathologist’s examination, we can consider the complete pathological response. In recent years the addition of monoclonal antibodies to conventional chemotherapy may further increase the proportion of patients referred for surgery; bevacizumab before surgery has been shown to be feasible and safe, although concerns still exist regarding possible post-surgical and wound healing complications or bleeding. The limitation of the radiologic assessment of response as a surrogate for pathological response is even more relevant when antiangiogenic treatments are used. Excellent responses to bevacizumab-containing regimens do occur and referral to surgical oncology is a crucial step for documentation of complete pathological response.
Comparison of [(18)F]FDG uptake and distribution with hypoxia and proliferation in FaDu human squamous cell carcinoma (hSCC) xenografts after single dose irradiation.


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Purpose: This study investigated the uptake of [(18)F]2-fluoro-2-deoxy-glucose ([(18)F]FDG) in the human tumour xenograft FaDu at early time points after single dose irradiation with Positron-Emission-Tomography (PET), autoradiography and functional histology. Materials and methods: [(18)F]FDG-PET of FaDu hSCC xenografts on nude mice was performed before 25 Gy or 35 Gy single dose irradiation and one, seven or 11 days post irradiation (p.irr.). Before the second PET, mice were injected with pimonidazole (pimo) and bromodeoxyuridine (BrdU). After the PET tumours were excised, sliced and subjected to autoradiography and functional histology staining (pimo, BrdU, Ki67). [(18)F]FDG tumour uptake was quantified in the PET scans by maximal standard uptake value (SUV(max)) and in the autoradiography after co-registration to the histology slices. Results: No differences in the overall [(18)F]FDG uptake between the two dose groups and time points were found with PET or autoradiography. Comparing autoradiography and histology, the [(18)F]FDG uptake was constant in tumour necrosis over time, while it decreased in vital tumour areas and particularly in hypoxic regions. No differences in the [(18)F]FDG uptake between positive and negative areas of Ki67 and BrdU were found. Conclusions: The decline of [(18)F]FDG uptake in vital tumour and in pimonopositive areas as seen in autoradiography, was not reflected by evaluation of SUV(max) determined by PET. These findings suggest that the SUV(max) does not necessarily reflect changes in tumour biology after irradiation.


Radiolabeled 5-Iodo-3'-O-(17beta-succinyl-5alpha-androstan-3-one)-2'-deoxyuridine and Its 5'-Monophosphate for Imaging and Therapy of Androgen Receptor-Positive Cancers: Synthesis and Biological Evaluation.

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High levels of androgen receptor (AR) are often indicative of recurrent, advanced, or metastatic cancers. These conditions are also characterized by a high proliferative fraction. 5-Radioiodo-3'-O-(17beta-succinyl-5alpha-androstan-3-one)-2'-deoxyuridine 8 and 5-radioiodo-3'-O-(17beta-succinyl-5alpha-androstan-3-one)-2'-deoxyuridin-5'-yl monophosphate 13 target AR. They are also degraded intracellularly to 5-radioiodo-2'-deoxyuridine 1 and its monophosphate 20, respectively, which can participate in the DNA synthesis. Both drugs were prepared at the no-carrier-added level. Precursors and methods are readily adaptable to radiolabeling with various radiohalides suitable for SPECT and PET imaging, as well as endoradiotherapy. In vitro and in vivo studies confirm the AR-dependent interactions. Both drugs bind to sex hormone binding globulin. This binding significantly improves their stability in serum. Biodistribution and imaging studies show preferential uptake and retention of 8 and 13 in ip xenografts of human ovarian adenocarcinoma cells NIH:OVCAR-3, which overexpress AR. When these drugs are administered at therapeutic dose levels, a significant tumor growth arrest is observed.


Accurate Prediction of Pathological Rectal Tumor Response after Two Weeks of Preoperative Radiochemotherapy Using (18)F-Fluorodeoxyglucose-Positron Emission Tomography-Computed Tomography Imaging.


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PURPOSE: To determine the optimal time point for repeated (18)F-fluorodeoxyglucose-postion emission tomography (PET)-CT imaging during preoperative radiochemotherapy (RCT) and the best predictive factor for the prediction of pathological treatment response in patients with locally advanced rectal cancer. METHODS AND MATERIALS: A total of 30 patients referred for preoperative RCT treatment were included in this prospective study. All patients underwent sequential PET-CT imaging at four time points: prior to therapy, at day 8 and 15 during RCT, and shortly before surgery. Tumor metabolic treatment responses were correlated with the pathological responses by evaluation of the tumor regression grade (TRG) and the pathological TN (ypT) stage of the resected specimen. RESULTS: Based on their TRG evaluations, 13 patients were classified as pathological responders, whereas 17 patients were classified as pathological nonresponders. The response index (RI) for the maximum standardized uptake value (SUV(max)) on day 15 of RCT was found to be the best predictive factor for the pathological response (area under the curve [AUC] = 0.87) compared to the RI on day 8 (AUC = 0.78) or the RI of presurgical PET imaging (AUC = 0.66). A cutoff value of 43% for the reduction of SUV(max) resulted in a sensitivity of 77% and a specificity of 93%. CONCLUSIONS: The SUV(max)-based RI calculated after the first 2 weeks of RCT provided the best predictor of pathological treatment response, reaching AUCs of 0.87 and 0.84 for the TRG and the ypT stage, respectively. However, a few patients presented with peritumoral inflammatory reactions, which...
PET lesion segmentation using automated iso-intensity contouring in head and neck cancer.

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To improve the objectivity of the integration of positron emission tomography (PET), we used the conformity index (CI) to measure the goodness of fit of a given PET iso-SUV (standardized uptake value) level with the GTV defined on PET (GTV(PET)) and CT (GTV(CT)). Twenty-two datasets involving 20 head and neck cancer patients were identified. GTV(PET) and GTV(CT) were delineated manually. An iso-intensity method was developed to automatically segment GTV(PET-ISO) using (a) SUV and (b) maximum intensity thresholding (% Max), over a range of intensities. For each intensity, GTV(PET-ISO) was compared to GTV(PET) using the conformity index CI(PET) (and, similarly, to GTV(PET) using CICT). Comparing GTV(PET) to GTV(PET-Io) vs comparing GTV(CT) to GTV(PET-ISO), the average peak CI was 0.68 +/- 0.09 vs 0.49 +/- 0.12 (p < 0.001), the optimum GTV(PET) using the conformity index CI(PET) (and, similarly, to GTV(CT) using CICT). Comparing GTV(PET) to GTV(PET-Io) vs comparing GTV(CT) to GTV(PET-ISO), the average peak CI was 0.68 +/- 0.09 vs 0.49 +/- 0.12 (p < 0.001), the optimum iso-SUV was 2.7 +/- 0.7 vs 2.9 +/- 1.0 (p=0.253), and the % Max SUV was 21.8% +/- 7.6% vs 23.8% +/- 8.6% (p=0.310), respectively. The radiation oncologist's volumes corresponded to a lower iso-SUV (3.02 +/- 0.58 vs 4.36 +/- 0.77, p<0.001) and lower % Max SUV (24.1 +/- 9.1% vs 34.3 +/- 11.2%, p<0.001) than those drawn by the nuclear medicine physician. Though manual editing may still be necessary, PET iso-contouring is one method to improve the objectivity of GTV definition in head and neck cancer patients. Iso-SUV's can also be used to study the differences between PET's role as a nuclear medicine diagnostic test versus a radiation oncology treatment planning tool.


Positron emission tomography for the detection of colorectal adenomas.


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BACKGROUND: (18)F-fluorodeoxyglucose ((18)F-FDG) positron emission tomography (PET) has been reported to detect colorectal adenomas. AIMS: This study aimed to evaluate the sensitivity of (18)F-FDG PET with computed tomography image fusion (PET/CT) for detecting colorectal adenomas. METHODS: We retrospectively compared the results of 92 (18)F-FDG PET/CT studies followed by colonoscopy. Colonoscopy and histology were considered as the gold standard. RESULTS: One hundred fifty-seven lesions were observed. All the 12 malignancies were identified by (18)F-FDG PET/CT but only 27 out of 119 resected adenomas (sensitivity 22.7%) and none of the hyperplastic polyps were detected. At the univariate and multivariate analyses there was a significant statistical association between adenomas sized more than 10 mm, presence of villous component and high-grade dysplasia and the ability of (18)F-FDG PET/CT to detect adenomas. (18)F-FDG PET/CT showed an overall sensitivity of 29.8%, a specificity of 81.1%, a positive predictive value (PPV) of 84.8% and a negative predictive value (NPV) of 24.6% for the neoplastic colorectal lesions globally considered. CONCLUSION: (18)F-FDG PET/CT has a low sensitivity to detect adenomas. However, because of the specificity and PPV of the technique for neoplastic colorectal lesions, the presence of a focal colorectal FDG uptake justifies the patient undergoing colonoscopy.


S-100B Concentrations Predict Disease-Free Survival in Stage III Melanoma Patients.

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BACKGROUND: Elevation of the tumor marker S-100B in melanoma patients is a highly specific indicator of recurrence. MATERIALS AND METHODS: The role of S-100B in disease-free survival (DFS) was evaluated in stage III melanoma patients (staged with fluorodeoxyglucose positron emission tomography [FDG-PET] and computed tomography [CT]) with palpable lymph node metastases who underwent therapeutic lymph node dissection. S-100B and LDH were measured on the day before surgery (d = -1) and on days 1, 2, and 7 postoperatively. Multivariate logistic regression was used to study factors associated with preoperative elevation of S-100B. Univariate (log-rank test) and multivariate (Cox regression) survival analyses were performed to identify factors associated with DFS. RESULTS: Between 2004 and 2008, 56 patients (median age 57, range 24-93) years, 27 males (48%) and 29 females (52%) entered the study. Preoperative S-100B elevation was found in 27 patients (48%) and elevated LDH in 20 patients (36%). No association was found between these two markers at any time. Multivariate analysis showed that elevated S-100B preoperatively (hazard ratio [HR] 2.7, P = .03) was associated with DFS. S-100B elevation was associated with increased tumor size (odds ratio [OR] 3.40; P = .03). CONCLUSION: Elevated S-100B preoperatively in patients with optimally staged clinical stage III melanoma is associated with decreased disease-free survival. S100-B could be used as a prognostic marker in the stratification of new adjuvant trials to select stage III melanoma patients for adjuvant systematic treatment.
Practice patterns and guideline adherence of medical oncologists in managing patients with early breast cancer.

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BACKGROUND: Studies of adherence to breast cancer guidelines have often focused on primary therapies, but concordance with other guideline recommendations has not been examined as extensively. This study assesses the knowledge and practice patterns of medical oncologists in the United States to inform education and quality improvement initiatives that can improve breast cancer care. METHODS: A survey containing case vignettes and related questions was developed to examine oncologists' clinical decision-making in evaluating and treating women with early breast cancer. The instrument was distributed to a random sample of 742 oncologists in the United States and yielded 205 responses (27.6% response rate). Responses from 184 practicing medical oncologists were analyzed relative to the 2007 NCCN Clinical Practice Guidelines in Oncology: Breast Cancer. RESULTS: Most oncologists made guideline-consistent choices in clarifying indeterminate human epidermal growth factor 2 (HER2) status (85%), initial treatment for early breast cancer (95%), and postsurgical management of locally advanced breast cancer (82%). Guideline-discordant choices were seen in the lack of clip placement before neoadjuvant chemotherapy (36%), unnecessary use of PET scanning for initial assessment (34%), inappropriate assessment of menopausal status (33%), inappropriate use of tumor markers (22%), and use of chest imaging (16%) during posttherapeutic surveillance. CONCLUSIONS: Oncologists often make guideline-consistent choices, but discordant clinical decisions may occur in important aspects of care for early breast cancer. Broadening the diffusion and adoption of guideline recommendations is an important mechanism for addressing these gaps and may substantially improve the quality of breast cancer care.


A bone marrow F-18 FDG uptake exceeding the liver uptake may indicate bone marrow hyperactivity.


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OBJECTIVE: In clinical positron emission tomography (PET) studies for oncology, it is occasionally required to differentiate a diffuse increase in bone marrow (BM) F-18 fluoro-2-deoxyglucose (FDG) uptake due to the involvement of malignancy or hematopoietic disease and that due to the administration of hematopoietic cytokines, an inflammation reaction, or stimulation by some types of malignancy. The objectives of this study were to clarify the relationships between BM F-18 FDG uptake and blood parameters as well as age, and also to determine the degree of F-18 FDG accumulation that constitutes an abnormal level referring to blood parameters. METHODS: Records of 65 patients, 32 with benign diseases and 33 with malignancies without metastasis in bone and liver until a half year after the PET examination, were analyzed retrospectively. Regions of interest were placed on the liver and the lower thoracic and lumbar vertebrae to measure the standardized uptake value (SUV), and vertebral SUVs were averaged as the BM SUV(mean). The BM SUV(mean) was divided by the liver SUV to calculate the BM/liver ratio. The relationships among the BM SUV(mean), or BM/liver ratio, and blood parameters and age were tested using multiple regression analysis. RESULTS: In both patients with and without malignancy, a multiple regression model using the BM/liver ratio showed a higher coefficient of determination value than that using the BM SUV(mean), indicating that the correction by the liver SUV reduced the interindividual variation in the BM SUV(mean). The BM/liver ratio was negatively correlated with age (beta = -0.41 and -0.43, respectively) and positively correlated with serum C-reactive protein (CRP) level (beta = 0.39 and 0.46, respectively) in both groups of patients. Every patient with benign disease who had a ratio greater than or equal to 1 had an increased CRP level. CONCLUSIONS: The BM F-18 FDG uptake depends on the patient's age and serum CRP level, both with and without malignancy. A BM F-18 FDG uptake greater than or equal to that of the liver may indicate BM activation.

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18F-DOPA PET is superior to conventional imaging with 123I-metaiodobenzylguanidine scintigraphy, CT, and MRI in localizing tumors causing catecholamine excess.


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Context: Catecholamine excess is rare, but symptoms may be life-threatening. Objective: To investigate the sensitivity of 6-[F-18]fluoro-L-dihydroxyphenylalanine positron emission tomography ((18)F-DOPA PET), compared to (123)I-
PET - Oncology

metaiodobenzylguanidine ((123)I-MIBG) scintigraphy and CT/MRI for tumor localization in patients with catecholamine excess. Design and Setting: All consecutive patients with catecholamine excess visiting the UMCG, Groningen, between March 2003 and January 2008 were eligible. Patients: 48 patients were included. The final diagnosis was pheochromocytoma in 40, adrenal hyperplasia in 2, paraganglioma in 2, ganglioneuroma in 1, unknown in 3. Main Outcome Measures: Sensitivities and discordancy between (18)F-DOPA PET, (123)I-MIBG and CT or MRI, were analyzed for individual patients and lesions. Metanephrines and 3-methoxytyramine in plasma and urine, uptake of (18)F-DOPA with PET were measured to determine the whole-body metabolic burden and correlated with biochemical tumor activity. Gold standard was a composite reference standard. Results: (18)F-DOPA PET showed lesions in 43 patients, (123)I-MIBG in 31 and CT/MRI in 32. Patient-based sensitivity for (18)F-DOPA PET, (123)I-MIBG and CT/MRI was 90, 65 and 67% (P<.01 for (18)F-DOPA PET vs. both (123)I-MIBG and CT/MRI, P=1.0 (123)I-MIBG vs. CT/MRI). Lesion-based sensitivities were 73, 48 and 44% (P<.001 for (18)F-DOPA PET vs. both (123)I-MIBG and CT/MRI, P=.51 (123)I-MIBG vs. CT/MRI). The combination of (18)F-DOPA PET with CT/MRI was superior to (123)I-MIBG with CT/MRI (93 vs. 76%, P<.001). Whole-body metabolic burden measured with (18)F-DOPA PET correlated with plasma normetanephrine (r=0.82), and urinary normetanephrine (r=0.84), and metanephrine (r=0.57). Conclusion: To localize tumors causing catecholamine excess (18)F-DOPA PET is superior to (123)I-MIBG scintigraphy and CT/MRI.


[18F-FDG uptake of lymphoma lesions of various histological subtypes.]

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Background and Objective: Malignant lymphoma has high 2-fluorine-18-fluoro-2-deoxy-D-glucose (18F-FDG) uptake. This study was to analyze 18F-FDG uptake of lymphoma lesions of various histological subtypes. Methods: FDG PET/CT images of 102 naive lymphoma patients were analyzed. The maximal standardized uptake value (SUVMax) of every single lesion and the SUVMax of mediastinal blood pool were measured and used to calculate the mean T/MB value (tumor SUVMax/mediastinal SUVMax) of every patient. The mean T/MB value of the patients with the same subtype of lymphoma was calculated. The differences in T/MB value between Hodgkin's lymphoma (HL) and non-Hodgkin's lymphoma (NHL) patients, between HL and indolent NHL, invasive NHL patients, between B-cell NHL and NK/T-cell NHL patients, and between diffuse large B-cell lymphoma (DLBCL) patients of different stages were analyzed. The expression of Ki-67 in lymph nodes from four patients with relative low T/MB value was detected. Results: The T/MB values were 4.50+/−1.54 in HL patients and 5.21+/−2.86 in NHL patients (P=0.154). The T/MB value was significantly higher in invasive NHL patients than in HL and indolent NHL patients (P<0.001). The T/MB values were 5.29+/−3.00 in B-cell NHL patients and 4.91+/−2.30 in NK/T-cell NHL patients (P=0.57). There was also no significant difference between DLBCL patients of different stages. The positive rate of Ki-67 was lower in the four patients with relative low T/MB value than in positive control group. Conclusions: 18F-FDG uptake of lymphoma lesions is related to lymphoma invasion, but not related to cell origin and clinical stage. The low 18F-FDG uptake in four patients may be related to low expression of Ki-67.

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Intradiploic Meningioma Mimicking Calvarial Metastasis: Case Report.

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Meningiomas are the most common benign intracranial neoplasms. Nearly 20% of all primary intracranial tumors are meningiomas. Primary intraosseous meningiomas are a subtype of the meningiomas that represents the most uncommon manifestation of meningiomas. Although rare, these tumors can be found to occur in unexpected areas of the head and neck. The patient was a 78-year-old male who was operated two times for urinary bladder cancer. During his routine oncology follow-ups, the PET scan revealed an osteolytic interosseous meningioma. The possibility of an intraosseous meningioma mimicking a metastatic tumor should be kept in mind.


[18F-FDG PET/CT for the detection of primary tumors metastasizing to lymph nodes of the neck.]

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Background and Objective: Lymph node metastases are commonly seen in malignant tumors of the head and neck. Detection of the primary tumors affects the quality of life and survival rates of these patients. This study was to evaluate the application of 18F-FDG PET/CT in detecting primary tumors metastasizing to lymph nodes of the neck, and to assess the positive predictive value of 18F-FDG PET/CT. Methods: In total 93 patients with pathologically confirmed neck lymph node metastases from unknown primary tumors underwent 18F-FDG PET/CT in Sun Yat-sen University Cancer Center between June 2005 to April 2008 were entered into this study. The primary tumors of patients were initially diagnosed according to different PET/CT standards as definite diagnosis,
suspicious diagnosis and no signs of primary tumors. All diagnosis based on PET/CT images were verified by pathological exams or additional imaging tests. Results: Forty cases made definite diagnosis by PET/CT were all confirmed by pathological or clinical exams, with a positive predictive value of 100%. Of 28 cases made suspicious diagnosis, 16 were pathologically confirmed, with a positive predictive value of 57.1%. Two patients, who were suggested lymph node metastases in mediastinum without the sign of the primary tumor by PET/CT, were clinically verified as primary mediastinal lung cancer. The primary tumors of another two patients were not detected by PET/CT, but were found under endoscopy. The total detection rate of PET/CT for the primary tumor was 60.2% (56/93). Conclusion: PET/CT is of important clinical value in detecting primary tumors metastasizing to lymph nodes of the neck.


Application of 18F-fluorodeoxyglucose positron emission tomography in diagnosis of malignant diseases.

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OBJECTIVE: To testify the efficacy of 18F-fluorodeoxyglucose (18F-DG) positron emission tomography (PET) in the diagnosis of cancer. METHODS: A total of 170 patients with diagnosed cancer or suspicious cancer were enrolled in this study, and underwent 18F-DG PET. The standard uptake value (SUV) and diameter for each abnormal region in PET images were analyzed. All data were analyzed by SPSS 11.5. RESULTS: PET scan identified a primary cancer in 45.8% (11/24) patients. The sensitivity and specificity of PET scan in differentiating malignant lesions from benign ones were 78.8% (52/66) and 77.1% (27/35) respectively. Twenty-nine out of 68 (42.6%) lesions were detected earlier by PET than by computed tomography. The SUV of primary cancer was significantly higher than that of metastatic lymph nodes (5.84 +/- 3.12 vs. 3.14 +/- 2.24, P<0.001). And SUV of primary lung cancer was also significantly higher than that of metastatic lung cancer (6.30 +/- 3.01 vs. 2.86 +/- 2.37, P<0.01). CONCLUSION: 18F-DG PET plays a very important role in cancer diagnosis.


Circulating tumor cells and bone metastases as detected by FDG-PET/CT in patients with metastatic breast cancer.

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BACKGROUND: We evaluated the relationship between the detection and prognostic significance of circulating tumor cells (CTCs) and sites of metastases detected by 2-[fluorine-18]fluoro-2-deoxy-D-glucose-positron emission tomography/computed tomography (FDG-PET/CT) in patients with metastatic breast cancer (MBC). PATIENTS AND METHODS: From May 2004 to January 2008, 195 patients with relapsed/progressive MBC underwent whole-body FDG-PET/CT and provided blood samples for assessment of CTC count. RESULTS: Higher CTC numbers were detected in patients with bone metastases relative to those with no bone lesions (mean 65.7 versus 3.3, P = 0.0122) and in patients with multiple bone metastases relative to those with one or two bone lesions (mean 77.7 versus 2.6, P < 0.001). CTCs predicted overall survival (OS) in 108 patients with multiple sites of metastases including bone (P = 0.0008) but not in 58 without bone metastases (P = 0.4111) and in 29 with bone involvement only (P = 0.3552). All 15 patients but one with human epidermal growth factor receptor 2 (HER-2) positive tumors who were treated with trastuzumab-based regimens had <5 CTCs at progression. In multivariate analysis, CTCs, but not bone metastases, remained a significant predictor of OS. CONCLUSION: Presence of extensive bone metastases as detected by FDG-PET/CT is associated with increased CTC numbers in MBC.

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PET-CT imaging in pediatric oncology.

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Positron emission tomography (PET)-computed tomography (CT) is emerging as a valuable tool for assessing a wide variety of pediatric malignancies, including lymphomas, soft-tissue tumors, and bone sarcomas. PET-CT may provide information that is not apparent on conventional imaging performed to stage these diseases and monitor their response to treatment. The use of PET-CT in children requires an awareness of the technical and logistical issues unique to this patient population. In addition, interpretation of pediatric PET-CT imaging requires familiarity with aspects of pediatric anatomy and physiology that differ from those of adults. In this article, the technical considerations in performing pediatric PET-CT, pitfalls in the diagnostic use of PET-CT in children, and current and emerging applications of PET-CT in pediatric oncology are reviewed.
PET - Oncology


(18)F-FDG uptake and its clinical relevance in primary gastric lymphoma.


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We studied the clinical relevance of (18)F-fluorodeoxyglucose ((18)F-FDG) uptake in patients with primary gastric lymphoma underwent positron emission tomography (PET)/computed tomography (CT) scan. Forty-two patients with primary gastric lymphoma were analysed: 32 diffuse large B-cell lymphomas (DLBCL) and 10 extranodal marginal zone B-cell lymphomas of mucosa-associated lymphoid tissue (MALT lymphomas). The PET/CT scans were compared with clinical and pathologic features, and the results of CT and endoscopy. Nine patients were up-staged based on the results of their PET/CT scan compared to CT (seven DLBCLs, two MALT lymphomas) while six patients were down-staged by the PET/CT scan. The standard uptake value (SUV) was used as an indicator of a lesion with a high metabolic rate. The high SUVmax group, defined as an SUVmax >/= median value, was significantly associated with an advanced Lugano stage (p < 0.001). Three patients with DLBCL, who showed an initially high SUVmax, died of disease progression. Among 24 patients for whom follow-up PET/CT scan with endoscopy was performed, 11 patients with ulcerative or mucosal lesions showed residual (18)F-FDG uptake. All of these gastric lesions were grossly and pathologically benign lesions without evidence of lymphoma cells. In conclusion, PET/CT scan can be used in staging patients with primary gastric lymphoma; however, the residual (18)F-FDG uptake observed during follow-up should be interpreted cautiously and should be combined with endoscopy and multiple biopsies of the stomach.

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Localized large cell lymphoma: is there any need for radiation therapy?

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PURPOSE OF REVIEW: Diffuse large B-cell lymphoma is the most common lymphoma diagnosed in the United States and presents as localized disease in about 25% of the patients. The standard of care was established by Southwest Oncology Group trial 8736, which showed the superiority of a short course of chemotherapy followed by radiation over a longer course of chemotherapy alone. This review discusses the studies that followed with the intent to establish whether the standard of care has changed. RECENT FINDINGS: Subsequent studies examined the role of radiation therapy, the number of cycles and intensity of chemotherapy, and addition of rituximab. Interpretation of results has been confounded by patient selection, especially by including patients with bulky stage II disease. Quality of radiation therapy may have diminished its efficacy in some of the studies. Concurrent administration of rituximab provided a more modest improvement as compared with advanced disease setting. Attempts are now made to use PET scans to eliminate the need for radiation therapy in some patients. SUMMARY: Radiation therapy remains useful when administered expeditiously and as initially described, but PET scans successfully define a subset of patients who do not benefit from radiation. Using a longer or more intensive course of rituximab-containing chemotherapy without radiation has never been compared to combined modality treatment and remains investigational.

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Targeting the Warburg effect in hematological malignancies: from PET to therapy.

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PURPOSE OF REVIEW: To highlight key studies providing rationale for and utility in targeting glycolysis for the treatment of hematological malignancies. RECENT FINDINGS: Several therapeutic strategies are capitalizing on the diagnostic utility of fluoro-deoxyglucose positron emission tomography that relies on increased glycolysis and glucose utilization in tumor cells. Although aerobic glycolysis was initially proposed by Warburg to be due to mitochondrial impairment, recent studies have shown a preferential switch to glycolysis in tumor cells with functional mitochondria. Increased glucose consumption can be advantageous for a tumor cell through stimulation of cellular biosynthetic, energetic, and pro-survival pathways. We now have a greater appreciation for the utilization of glucose in specific metabolic pathways that in some aspects can be complemented with other nutrients such as glutamine. Targeting glucose consumption for the treatment of hematological malignancies seems to be a promising field that will require characterization of tumor cell specific targets to inhibit glucose uptake and/or glycolysis. It is imperative to further our understanding of the tumor cell metabolome to target cellular bioenergetics in the treatment of cancer. SUMMARY: Targeting the glycolytic pathway for the treatment of hematological malignancies has sufficient rationale given the utility of fluoro-deoxyglucose positron emission tomography in diagnostic imaging. Further research is required in developing tumor cell specific therapeutics.
PET - Oncology


**PF-00477736 mediates checkpoint kinase 1 signaling pathway and potentiates docetaxel-induced efficacy in xenografts.**


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**PURPOSE:** Checkpoint kinase 1 (Chk1) plays a critical role in the activation of mitotic spindle checkpoint and DNA damage checkpoint. We examined the preclinical use of the Chk1 inhibitor PF-00477736 as a docetaxel-sensitizing agent. Specifically, we investigated the correlation between PF-00477736-mediated modulation of biomarkers and the sensitization of docetaxel efficacy.

**EXPERIMENTAL DESIGN:** In vitro and in vivo studies using COLO205 and other cell lines were done to assess PF-00477736-induced enhancement of docetaxel efficacy and effects on associated biomarkers. RESULTS: PF-00477736 significantly enhanced the docetaxel-induced efficacy in tumor cells and xenografts. Docetaxel induced dose- and time-dependent increase in the levels of phosphorylated Chk1 (Ser(345)), phosphorylated histone H3 (Ser(10)), and gammaH2AX foci and promoted the cytoplasmic localization of phosphorylated Cdc25C (Ser(216)). PF-00477736 cotreatment suppressed docetaxel-induced changes in phosphorylated histone H3 and cytoplasmic phosphorylated Cdc25C (Ser(216)) levels and concurrently sensitized the docetaxel-induced apoptosis. Docetaxel alone or in combination with PF-00477736 induced significant antiproliferative activity in xenografts, shown via [18F]FLT-PET imaging. However, changes in [18F]FLT uptake did not reflect the potentiation of docetaxel efficacy. In contrast, bioluminescence imaging showed that PF-00477736 sensitized docetaxel-induced suppression of tumor survival. CONCLUSIONS: Docetaxel triggers mitotic spindle checkpoint activation at low concentrations and activates both the DNA damage checkpoint and the spindle checkpoint at high concentrations. In combination with docetaxel, PF-00477736 abrogates the mitotic checkpoint, as well as the DNA damage checkpoint, and results in sensitization to docetaxel. Chk1 inhibitor PF-00477736 offers a therapeutic potential for the enhancement of taxane therapy.


**Positron emission tomography in staging early lung cancer: a randomized trial.**

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**BACKGROUND:** Among patients with early-stage non-small cell lung cancer (NSCLC), preoperative imaging tests are important in defining surgical candidates. **OBJECTIVE:** To assess whether whole-body positron emission tomography and computed tomography (PET-CT) plus cranial imaging correctly upstages cancer in more patients with NSCLC than does conventional staging plus cranial imaging. **DESIGN:** Randomized clinical trial with recruitment from June 2004 to August 2007. The centralized, computer-generated, variable block size randomization scheme was stratified by treatment center and cancer stage. Participants, health care providers, and outcome assessors were not blinded to imaging modality assignment. **SETTING:** 8 hospitals and 5 PET-CT centers in academic institutions. **PATIENTS:** Eligible patients were older than 18 years; had histologic or cytologic proof of stage I, II, or IIIA NSCLC on the basis of chest radiography and thoracic CT; and had a tumor considered to be resectable. **INTERVENTION:** PET-CT or conventional staging (abdominal CT and bone scan). All patients also had cranial imaging using CT or magnetic resonance imaging. **MEASUREMENTS:** The primary outcome was correct upstaging, thereby avoiding stage-inappropriate surgery. Secondary outcomes were incorrect upstaging and incorrect understaging. **RESULTS:** 170 patients were assigned to PET-CT and 167 to conventional staging. Eight patients (3 who had PET-CT and 5 who had conventional staging) did not have planned surgery. Disease was correctly upstaged in 23 of 167 PET-CT recipients and 11 of 162 conventional staging recipients (13.8% vs. 6.8%; difference, 7.0 percentage points [95% CI, 0.3 to 13.7 percentage points]), thereby sparing these patients from surgery. Disease was incorrectly upstaged in 8 PET-CT recipients and 1 conventional staging recipient (4.8% vs. 0.6%; difference, 4.2 percentage points [CI, 0.5 to 8.6 percentage points]), and it was incorrectly understaged in 25 and 48 patients, respectively (14.9% vs. 29.6%; difference, 14.7 percentage points [CI, 5.7 to 23.4 percentage points]). At 3 years, 52 patients who had PET-CT and 57 patients who had conventional staging had died. Limitation: The relatively small sample and the fact that some patients did not have planned surgery limited the ability to determine precise differences in clinical outcomes that were attributable to testing strategies. **CONCLUSION:** Preoperative staging with PET-CT and cranial imaging identifies more patients with mediastinal and extrathoracic disease than conventional staging, thereby sparing more patients from stage-inappropriate surgery, but the strategy also incorrectly upstaged disease in more patients.


**The value of perioperative imaging in patients with uterine sarcomas**

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OBJECTIVE: To explore the yield and impact of pretreatment imaging on management among patients undergoing surgical resection and treatment of uterine sarcomas. METHODS: A retrospective chart review was done for women with histologically confirmed uterine sarcomas treated at Barnes Jewish Hospital/Washington University from 2001 to 2007. Descriptive statistics, Cox multivariate models, and Kaplan-Meier plots were used to evaluate associations and survival. RESULTS: A total of 92 patients were identified and 55 (60%) were diagnosed with stage I-IV disease. Perioperative imaging was obtained in 84 (91%) cases, including chest X-ray in 66 (72%), computerized tomography (CT) of the abdomen and pelvis in 59 (64%), chest CT in 33 (36%), positron emission tomography (PET) in 8 (9%), and CT of the head, pelvic magnetic resonance imaging (MRI), or bone scan in a total of 2 (2.2%). Imaging identified abnormalities concerning for metastases in 30 (32%) studies. Thirty-four recurrences have been documented, and 21 (62%) of these treatment failures were extrapelvic. Multivariate analysis of this series noted that tomographic evidence of extraperitoneal disease predicted recurrence (p=0.028) and incomplete surgical resection (p=0.003, HR 6.095% CI 1.9-19.9) predicted disease-free survival. Imaging contributed to change in surgical and post-surgical treatment decisions in 8 (9%) patients. CONCLUSION: Pretreatment imaging studies change management in a minority of patients with newly diagnosed uterine sarcomas.


Patterns of failure and prognostic factor analyses in locally advanced cervical cancer patients staged by positron emission tomography and treated with curative intent.

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PURPOSE: The aim of this retrospective analysis was to assess whether parameters derived from magnetic resonance imaging (MRI) and positron emission tomography (PET) provide incremental prognostic value compared with International Federation of Gynecology and Obstetrics (FIGO) stage in cervix cancer patients treated with curative intent using concurrent chemoradiotherapy. MATERIALS AND METHODS: This was a retrospective study of patients with locoregionally advanced cervical cancer staged by examination under anesthesia and pretreatment MRI and PET. Potential prognostic factors examined were derived from either clinical evaluation (age, FIGO stage, clinical diameter, histology), MRI (corpus invasion, tumor volume), or PET (lymph node metastasis). Outcome measures examined were overall survival, relapse-free survival, time to failure, local failure, nodal failure, and distant failure. RESULTS: There were 206 eligible patients. The mean potential follow-up was 4.4 years. At 5 years, for all patients, overall survival rate was 59%. For all outcome measures apart from local failure, for which adenocarcinoma histology was the most powerful adverse prognostic factor (HR, 4.29; P < 0.0001), lymph node status on PET was the dominant unifactor and multifactor prognostic factor. Corpus involvement on MRI was significantly associated with nodal involvement on PET but of MRI-derived parameters only tumor volume has prognostic value, limited to time to failure and nodal failure. CONCLUSIONS: Nodal status on PET was the major predictor of outcome in locally advanced cervix cancer treated with chemoradiation and was superior to FIGO staging. Tumor volume measured from MRI appears to be an important predictor of loco-regional relapse.

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Positron emission tomography / computerized tomography evaluation of primary Hodgkin's disease of liver.

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Occurrence of primary Hodgkin's lymphoma (PHL) of the liver is extremely rare. We report on a case of a 60-year-old male who presented with liver mass and B-symptomatology. Hepatoma or hepatic metastasis from a gastrointestinal primary was initially suspected. Tumor markers like AFP, CEA, Total PSA, and CA-19.9 were within normal limits. Positron Emission Tomography / Computerized Tomography (PET/CT) revealed a large hepatic lesion and a nodal mass in the porta hepatis. A liver biopsy was consistent with Hodgkin's lymphoma. There was complete regression of the hepatic lesion and evidence of shrinkage of the nodal mass following four cycles of chemotherapy. 18F Fluoro -de-oxy Glucose (FDG) PET / CT in this case helped in establishing a primary hepatic lymphoma by demonstrating the absence of pathologically hypermetabolic foci in any other nodes or organs. PET / CT scan is a useful adjunct to conventional imaging and histopathology, not only to establish the initial diagnosis, but also to monitor treatment response in PHL.

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OBJECTIVES: We choose to review current knowledge focused on pretreatment evaluation and prognostic markers in cervical cancer and make recommendations for future research. METHODS: We convened representatives from 10 of the member groups belonging to the Gynecologic Cancer Intergroup, members of the NCI’s Gynecologic Cancer Steering Committee and its Cervical Cancer Task Force, investigators in the fields of imaging, translational research, gynecologic, radiation and medical oncology, patient advocates and NCI program staff for a two-day retreat. RESULTS: Clinical examination must remain mandatory for staging and evaluation. Measurements of tumor volume should also be mandatory. Magnetic resonance imaging provides the most accurate imaging measure of tumor volume. Identification of lymph node (LN) metastasis needs to remain a high priority. Promising data in FDG-PET warrants multicenter validation. Validated prognostic markers include tumor volume, uterine corpus extension, cervical lymph-vascular space invasion, extent of LN metastasis, current tobacco smoking, hemoglobin levels at time of diagnosis, and HPV-16 associated cancer. No ‘high-technology’ biomarkers are ready for validation in multicenter trials. DISCUSSION: Our current specimen collections are inadequate for discovery and validation of biomarkers. Current and future trials should mandate collection of fixed tissues as well as DNA/RNA. Effective crossgroup collaboration is necessary to permit timely completion of phase III trials. Centers with appropriate expertise and resources in the developing world should be encouraged to participate in the current clinical trial networks.

Usefulness of FDG-PET/CT for the diagnosis of intravascular large B-cell lymphoma presenting with fever of unknown origin and renal dysfunction.

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A 76-year-old man presented with fever of unknown origin and renal dysfunction. Laboratory examination revealed anemia, thrombocytopenia, hypoalbuminemia, proteinuria, and elevations of C-reactive protein, lactate dehydrogenase, creatinine and ferritin. (18)F-fluorodeoxyglucose positron emission tomography/computed tomography (FDG-PET/CT) imaging showed FDG accumulation in the renal cortex and spleen. Based on the imaging study, renal biopsy was performed and histological diagnosis of intravascular large B-cell lymphoma (IVLBCL) was made. Renal impairment due to IVLBCL is uncommon and is often difficult to diagnose early. FDG-PET/CT may be a useful tool for the early diagnosis of IVLBCL.

[18F]2-fluoro-2-deoxyglucose positron emission tomography/computed tomography in predicting radiation pneumonitis.

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BACKGROUND: Prevention is presently the only available method to limit radiation-induced lung morbidity. A good predictor is the key point of prevention. This study aimed to investigate if [(18)F]2-fluoro-2-deoxyglucose (FDG) uptake changes in the lung after radiotherapy could be used as a new predictor for acute radiation pneumonitis (RP). METHODS: Forty-one patients with lung cancer underwent FDG positron emission tomography/computed tomography (FDG-PET/CT) imaging before and after radiotherapy. The mean standardized uptake value (SUV) was measured for the isodose regions of 0 - 9 Gy, 10 - 19 Gy, 20 - 29 Gy, 30 - 39 Gy, 40 - 49 Gy. The mean SUV of these regions after radiotherapy was compared with baseline. The mean SUV in patients who developed RP was also compared with that in those who did not. The statistical difference was determined by matched pair t test. The Radiation Therapy Oncology Group (RTOG) criteria were used for diagnosis and grading of RP. RESULTS: With a median follow-up of 12 months, 11 (26.8%) of the 41 patients developed grade 2 and above acute RP. The mean SUV of regions (10 - 19 Gy, 20 - 29 Gy, 30 - 39 Gy, 40 - 49 Gy) increased after radiation therapy in all 41 patients. The mean SUVs after radiation therapy were 0.54, 0.68, 1.31, 1.74 and 2.27 for 0 - 9 Gy, 10 - 19 Gy, 20 - 29 Gy, 30 - 39 Gy and 40 - 49 Gy, respectively. Before the radiation therapy, the mean SUV of these regions after radiotherapy was compared with baseline. The mean SUV in patients who developed RP subsequently. CONCLUSION: The mean SUV of the lung tissue may be a useful predictor for the acute RP. FDG-PET/CT may play a new role in the study of the radiation damage of the lung.

Imaging of peritoneal carcinomatosis.

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Imaging studies are crucial in the evaluation of patients with suspected or known peritoneal cancerous dissemination. Despite the major progress that has occurred in radiological technology in the last few years, adequate and early detection of peritoneal surface disease remains a challenge. Improvements in spatial resolution are still insufficient to detect small volume peritoneal implants, often resulting in an underestimation of peritoneal disease burden, as assessed at subsequent surgical exploration. Cytoreductive surgery
combined with perioperative intraperitoneal chemotherapy has provided unprecedented results in the management of peritoneal-based neoplasms, provided that a complete (adequate) cytoreduction is achieved. Diagnostic imaging tests are used to select patients who may benefit from this combined treatment by ruling out extraperitoneal involvement and signs of unresectable peritoneal disease. Furthermore, a careful assessment of the disease distribution within the peritoneal cavity, guided by a deep knowledge of the disease's clinical and biological behavior helps in planning the surgical procedure. Close interaction and cooperation between surgeons and radiologists is of utmost importance in this regard, and dedicated, motivated radiologists are required. Contrast-enhanced, multidetector computed tomography scan remains the standard imaging modality in the assessment of peritoneal carcinomatosis. Magnetic resonance imaging may offer complementary valuable data. Positron emission tomography (PET) has a more limited role, its main indication being the detection of unsuspected extraperitoneal involvement in nonmucinous neoplasms.


Cardiac positron emission tomography.

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Positron emission tomography (PET) is a powerful, quantitative imaging modality that has been used for decades to noninvasively investigate cardiovascular biology and physiology. Due to limited availability, methodologic complexity, and high costs, it has long been seen as a research tool and as a reference method for validation of other diagnostic approaches. This perception, fortunately, has changed significantly within recent years. Increasing diversity of therapeutic options for coronary artery disease, and increasing specificity of novel therapies for certain biologic pathways, has resulted in a clinical need for more accurate and specific diagnostic techniques. At the same time, the number of PET centers continues to grow, stimulated by PET's success in oncology. Methodologic advances as well as improved radiotracer availability have further contributed to more widespread use. Evidence for diagnostic and prognostic usefulness of myocardial perfusion and viability assessment by PET is increasing. Some studies suggest overall cost-effectiveness of the technique despite higher costs of a single study, because unnecessary follow-up procedures can be avoided. The advent of hybrid PET-computed tomography (CT), which enables integration of PET-derived biologic information with multislice CT-derived morphologic information, and the key role of PET in the development and translation of novel molecular-targeted imaging compounds, have further contributed to more widespread acceptance. Today, PET promises to play a leading diagnostic role on the pathway toward a future of high-powered, comprehensive, personalized, cardiovascular medicine. This review summarizes the state-of-the-art in current imaging methodology and clinical application, and outlines novel developments and future directions.
A false positive for metastatic lymph nodes in the axillary region of a breast cancer patient following mastectomy.


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Recent advanced imaging modalities such as positron emission tomography (PET) detect malignancies using 2-[18F]-fluoro-2-deoxy-D-glucose (18-FDG) with high accuracy, and they contribute to decisions regarding diagnosis, staging, recurrence, and treatment response. Here, we report a case of false-positive metastatic lymph nodes that were diagnosed by PET/CT and ultrasonography in a 48-year-old breast cancer patient who had undergone mastectomy. The tumors, which were oval shaped and resembled lymph nodes, were detected by ultrasonography. PET/CT revealed high uptake of 18-FDG in the tumors. To investigate the proposed recurrence and to re-evaluate the biology of the recurrent tumors, a tumor was removed from the brachial plexus of the patient. Histological findings revealed it to be a schwannoma. All imaging modalities including PET/CT failed to distinguish benign tumors from metastatic lymph nodes in the brachial plexus. After resection of the schwannomas, the patient complained of a slight motor disorder of the second finger on the right hand. Hence, it is important to consider a false-positive case of lymph node metastasis in a breast cancer patient following mastectomy.

Role of PET in gynecologic malignancy.

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PURPOSE OF REVIEW: The purpose of this review is to outline the current state-of-the-art use of PET imaging for patients with gynecologic malignancies. RECENT FINDINGS: Recent findings with clinical impact when PET is utilized in patients with gynecologic cancer are primarily limited to patients with cancer of the uterine cervix and for patients with ovarian cancer. PET is used in patients with other gynecologic cancers such as endometrial cancer, uterine sarcomas, vulvar cancer, and vaginal carcinoma but with less well defined clinical impact than cervical and ovarian cancers. SUMMARY: PET is utilized in patients with cervical cancer for initial staging, guiding therapy, evaluating response to therapy, and for long-term follow-up. The primary uses of PET in patients with ovarian cancer are for the evaluation of adnexal masses and for the diagnosis and evaluation of recurrent disease.

Quantitative imaging biomarkers in neuro-oncology


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Conventional structural imaging provides limited information on tumor characterization and prognosis. Advances in neurosurgical techniques, radiotherapy planning and novel drug treatments for brain tumors have generated increasing need for reproducible, noninvasive, quantitative imaging biomarkers. This Review considers the role of physiological MRI and PET molecular imaging in understanding metabolic processes associated with tumor growth, blood flow and ultrastructure. We address the utility of various techniques in distinguishing between tumors and non-neoplastic processes, in tumor grading, in defining anatomical relationships between tumor and eloquent brain regions and in determining the biological substrates of treatment response. Much of the evidence is derived from limited case series in individual centers. Despite their ‘added value’, the effect of these techniques as an adjunct to structural imaging in clinical research and practice remains limited.

Monitoring predominantly cytostatic treatment response with 18F-FDG PET.

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(18)F-FDG PET and, more recently, PET/CT have been established as response biomarkers for monitoring cytotoxic or cytoreductive cancer therapies. With the advent of targeted cancer therapies, which are predominantly cytostatic, (18)F-FDG PET is increasingly being used to monitor the therapeutic response to these agents as well. The impressive outcome of (18)F-FDG PET
studies in patients with gastrointestinal stromal tumors treated with imatinib mesylate brought to the forefront the use of this biomarker for assessing the response to targeted therapies. The use of (18)F-FDG PET for this purpose has practical challenges, including quantitative analysis and timing of scans. This review provides a summary of clinical studies of targeted therapies done to date with (18)F-FDG PET and provides guidance on practical issues to ensure the optimal interpretation of imaging data in drug development and for patient care.

Cancer. 2009 Jun 19

The diagnostic and prognostic utility of positron emission tomography/computed tomography-based follow-up after radiotherapy for head and neck cancer.

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BACKGROUND: The detection of subclinical head and neck cancer recurrence or a second primary tumor may improve survival. In the current study, the authors investigated the clinical value of a follow-up program incorporating serial (18)F-fluorodeoxyglucose-

PET/CT in the detection of recurrent disease in patients with head and neck cancer. METHODS: A total of 240 PET/CT scans were reviewed in 80 patients with head and neck cancer who were treated with radiotherapy (RT) from July, 2005 through August, 2007. All patients were followed with clinical examination, PET/CT, and correlative imaging for a minimum of 11 months (median follow-up, 21 months). RESULTS: The sensitivity, specificity, and positive and negative predictive values of PET/CT-based follow-up for detecting locoregional recurrence were 92%, 82%, 42%, and 98%, respectively. Corresponding values for distant metastases or second primary tumors were 93%, 96%, 81%, and 98%, respectively. Eight patients (10%) developed disease recurrences or second primary tumors that were amenable to salvage surgery with negative surgical margins. The 2-year progression-free survival and 2-year overall survival rates were significantly different between patients who had a negative and those with a positive PET/CT result within 6 months of the completion of RT (93% vs 30% [P<.001] and 100% vs 32% [P=.001], respectively). CONCLUSIONS: Although post-therapy follow-up using PET/CT is reported to be a highly sensitive technique for the detection of recurrent disease. Furthermore, negative PET/CT results within 6 months of the completion of RT offer significant prognostic value. Cancer 2009. (c) 2009 American Cancer Society.


Prognostic significance of mid- and post-ABVD PET imaging in Hodgkin's lymphoma: the importance of involved-field radiotherapy.

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BACKGROUND: Although positron emission tomography (PET) response to chemotherapy (CT) has prognostic significance in Hodgkin's lymphoma (HL), it is unclear whether patients with 2-[fluorine-18]fluoro-2-deoxy-D-glucose (FDG)-PET positivity during and/or after CT can be rendered disease free with consolidative involved-field radiotherapy (IFRT). METHODS: Patients with HL treated with adriamycin, bleomycin, vinblastine and dacarbazine (ABVD)-based CT and radiotherapy (RT) at our institution from January 2000 to March 2007 were eligible. All patients had either a post-treatment PET or PET-CT before initiation of RT or a negative midtreatment PET or PET-CT. The primary end point was failure-free survival (FFS) for patients with and without residual FDG avidity after ABVD. The treatment outcome of patients with interim PET positivity during CT was also reported. RESULTS: Seventy-three patients were included in this study. Twenty patients (out of 46) were PET positive on interim PET, and 13 patients (out of 73) were PET positive at the conclusion of CT. At a median follow-up of 3.4 years for surviving patients, the 2-year FFSs for patients PET-negative versus PET-positive disease after ABVD were 95% and 69%, respectively (P < 0.01). On bivariable Cox regression, post-ABVD positivity (hazard ratio 4.8, P = 0.05) was predictive of disease recurrence after controlling for bulky disease. Of the 20 patients with interim PET positivity, three recurred, with a 2-year FFS of 85%. Among the 13 patients with interim PET positivity, but became PET negative at the completion of CT, the 2-year FFS was 92%. CONCLUSION: Sixty-nine per cent of patients with residual FDG avidity after ABVD were free of disease after consolidative RT, indicating a majority of patients with persistent lymphoma can be cured by sterilizing this PET-positive disease.

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AIM: The aim of this study was to investigate early changes in uptake of 2-deoxy-2-[18F]fluoro-D-glucose (FDG) in vivo and in vitro in a squamous-cell carcinoma (SCC) cell line originating from a human head and neck SCC during cytotoxic therapy with
PET - Oncology

respect to metabolism in tumor cells and in surrounding stromal tissue. MATERIALS AND METHODS: In 60 nude mice with xenografted SCC, 50 animals were treated with cisplatin. Early changes in the tumor FDG uptake following therapy were evaluated sequentially with phosphor imaging. Using this technique, areas with focal hypermetabolism were detected. The cells creating the focal hypermetabolism were then identified histopathologically on the corresponding sections. In addition, early FDG uptake versus the number of viable tumor cells was measured in vitro following cisplatin treatment. RESULTS: An early transient increase in FDG uptake in tumor cells was seen on day 1 in treated tumors, followed by a rapid decrease confirmed by subsequent tumor regression. This metabolic flare was present in all treated tumors but not in the controls. In vitro, an increase in FDG uptake per cell was observed. CONCLUSIONS: Our results provide new insights into the early metabolic changes in squamous-cell carcinomas subjected to cytotoxic therapy and thus contribute to the discussion on the feasibility of early predictive PET studies.


Biochemotherapy in the treatment of metastatic melanoma in selected patients.


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INTRODUCTION: Bioimmunochemotherapy (BCT) is a combination of biological agents and cytostatics that has shown an increase in response rate (RR) in metastatic melanoma patients. The aim of the study is to evaluate RR, progression- free survival (PFS), overall survival (OS) and treatment toxicity. MATERIALS AND METHODS: Retrospective analysis of 11 metastatic melanoma patients treated from January 2002 to June 2008 with cisplatin 20 mg/m(2) i.v. days 1-4, dacarbazine 800 mg/m(2) i.v. day 1, vinblastine 1.5 mg/m(2) i.v. days 1-4, interleukin (IL)-2 29 MIU/m(2) s.c. 5.8 days and interferon (IFN)-alpha-2b 5 MIU/m(2) s.c. days 5.9, 11, 13 and 15, with the support of granulocyte colony-stimulating factor (G-CSF) and antibiotics. Patients with ECOG 0, age < or = 65 years and with measurable disease were included. The planned number of courses was 4. RR was measured by Revised Evaluation Criteria in Solid Tumour (RECIST) criteria (computed tomography [CT] +/- proton emission tomography [PET]). Toxicity was measured according to the National Cancer Institute (NCI) common toxicity criteria. RESULTS: Observed RRs were 18% complete response (CR), 27% partial response (PR), 9% stable disease (SD) and 46% disease progression. The median PFS was 4 months (95% CI, 0.10 m), with a 23% one-year PFS. Median OS was 4.6 months (95% CI, 0.9, 19 m), with a 29% one-year OS. Eighty-three percent of patients experienced grade 3-4 toxicity, mainly due to neutropenia, thrombocytopenia and flu-like syndrome. CONCLUSIONS: Treatment with BCT shows an increase in RR, some achieving durable CR; nevertheless it cannot be considered a standard treatment and should be employed only in selected patients.


Dose painting in radiotherapy for head and neck squamous cell carcinoma: value of repeated functional imaging with (18)F-FDG PET, (18)F-fluoromisonidazole PET, diffusion-weighted MRI, and dynamic contrast-enhanced MRI.


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The purpose of this work was to evaluate the potential of functional imaging with (18)F-FDG PET, (18)F-fluoromisonidazole PET, diffusion-weighted MRI, and dynamic contrast-enhanced MRI to provide an appropriate and reliable biologic target for dose painting in radiotherapy for head and neck squamous cell carcinoma (HNSCC). METHODS: Fifteen patients with locally advanced HNSCC, treated with concomitant chemoradiotherapy, were prospectively enrolled in a bioimaging protocol. Sequential PET ((18)F-FDG and (18)F-fluoromisonidazole) and MRI (T1, T2, dynamic enhanced, and diffusion-weighted sequences) were performed before, during, and after radiotherapy. RESULTS: Median follow-up was 30.7 mo (range, 6.3-56.3 mo); in 7 patients, disease recurred. Disease-free survival correlated negatively with the maximum tissue-to-blood (18)F-fluoromisonidazole ratio (T/B(max)) on the baseline (18)F-fluoromisonidazole scan (P = 0.04), with the size of the initial hypoxic volume (P = 0.04), and with T/B(max) on the (18)F-fluoromisonidazole scan during treatment (P = 0.02). All locoregional recurrences were within the (18)F-FDG-avid regions on baseline (18)F-FDG PET; 3 recurrences mapped outside the hypoxic volume on baseline (18)F-fluoromisonidazole PET. Lesions (primary tumor and lymph nodes) where a locoregional recurrence developed during follow-up had significantly lower apparent diffusion coefficients on diffusion-weighted MRI during week 4 of radiotherapy (0.0013 vs. 0.0018 mm(2)/s, P = 0.01) and at 3 wk after treatment (0.0014 vs. 0.0018 mm(2)/s, P = 0.01) and a significantly higher initial slope on baseline dynamic enhanced MRI (26.2 vs. 17.5/s, P = 0.03) than did lesions that remained controlled. CONCLUSION: These results confirm the added value of (18)F-PDG PET and (18)F-fluoromisonidazole PET for radiotherapy planning of HNSCC and suggest the potential of diffusion-weighted and dynamic enhanced MRI for dose painting and early response assessment.
Quantification of Local Tumor Response to Fractionated Radiation Therapy for non-Hodgkin Lymphoma using Weekly (18)F-FDG PET/CT Imaging.

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PURPOSE: To quantify, in a feasibility study, metabolic and volumetric response to fractionated radiation therapy (RT) using weekly (18)F fluoro-deoxyglucose positron emission tomography (PET) imaging for 10 non-Hodgkin lymphoma (NHL) patients, and to correlate them to clinical outcome. METHODS AND MATERIALS: Ten patients with chemotherapy-refractory NHL planned for radical RT were prospectively entered into a research study. PET/computed tomography (CT) scans were acquired before RT, and repeated weekly during the 3- to 4-week course of RT, and at 1 and 3 months after therapy. Gross tumor volumes were contoured on CT scans and the corresponding maximum standardized uptake values (SUV(max)) determined in the coregistered PET images. The clinical outcomes of interest were local tumor response at 3 months post-RT and local tumor status at last follow-up or time of death. RESULTS: (18)F fluoro-deoxyglucose uptake from inflammation was rarely observed. The responses showed a large variability between patients. SUV(max) decreased consistently with a median of -2.1% per Gy (range, -3.3 to -0.7) and the median of the volumetric response was -2.2% per Gy (range, -2.8 to +0.5). Initial SUV(max) was not correlated with local control, whereas smaller initial tumor volume was, with smaller tumors more likely to achieve local control. The responses after treatment were also correlated to local control, but not the responses during treatment. CONCLUSIONS: Radiation does not confound the FDG uptake in the NHL tumor and normal tissues. Only smaller initial tumor volume and metabolic and volumetric response after completion of radiation therapy significantly correlated with eventual local control.

Influence of 2-(18F) fluoro-2-deoxy-D-glucose positron emission tomography/computed tomography on recurrent ovarian cancer diagnosis and on selection of patients for secondary cytoreductive surgery.


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The objective of this prospective study was to compare the sensitivities and the specificities of combined 2-(F) fluoro-2-deoxy-D-glucose positron emission tomography/computed tomography (PET/CT), abdominal/transvaginal ultrasound (US), and CT for diagnosing recurrent ovarian cancer (OC) and to evaluate the influence of PET/CT on referral of patients with solitary recurrence to secondary cytoreductive surgery. From April 2005 to November 2007, 60 patients were consecutively included to PET/CT 68 times. The inclusion criteria were remission of 3 months or longer and recurrent OC suspected from physical examination, US, or CT scans and the corresponding maximum standardized uptake values (SUVMax(max)) determined in the coregistered PET images. The clinical outcomes of interest were local tumor response at 3 months post-RT and local tumor status at last follow-up or time of death. RESULTS: (18)F fluoro-deoxyglucose uptake from inflammation was rarely observed. The responses showed a large variability between patients. SUVMax(max) decreased consistently with a median of -2.1% per Gy (range, -3.3 to -0.7) and the median of the volumetric response was -2.2% per Gy (range, -2.8 to +0.5). Initial SUVMax(max) was not correlated with local control, whereas smaller initial tumor volume was, with smaller tumors more likely to achieve local control. The responses after treatment were also correlated to local control, but not the responses during treatment. CONCLUSIONS: Radiation does not confound the FDG uptake in the NHL tumor and normal tissues. Only smaller initial tumor volume and metabolic and volumetric response after completion of radiation therapy significantly correlated with eventual local control.

In Vivo Measurements of Tumor Metabolism and Growth after Administration of Enzastaurin Using Small Animal FDG Positron Emission Tomography.


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Background. The use of 2-[18F]fluoro-2-deoxy-D-glucose ([18F]FDG) may help to establish the antitumor activity of enzastaurin, a novel protein kinase C-beta II (PKC-betaII) inhibitor, in mouse xenografts. Methods. The hematologic cell line RAJI and the solid tumor cell line U87MG were each implanted in NOD/SCID mice. Standard tumor growth measurements and [18F]FDG PET imaging were performed weekly for up to three weeks after tumor implantation and growth. Results. Concomitant with caliper measurements, [(18)F]FDG PET imaging was performed to monitor glucose metabolism. Heterogeneity of glucose uptake in various areas of the tumors was observed after vehicle or enzastaurin treatment. This heterogeneity may limit the use of [(18)F]FDG PET imaging to measure enzastaurin-associated changes in xenograft tumors. Conclusion. [(18)F]FDG PET imaging technique does not correlate with standard caliper assessments in xenografts to assess the antitumor activity of enzastaurin. Future studies are needed to determine the use of [(18)F]FDG PET imaging in preclinical models.
Modification of glucose metabolism in radiation-induced brain injury areas using cervical spinal cord stimulation.

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PURPOSE: Radiation-induced brain injury (RBI) is an insidious side-effect of radiotherapy mediated by vascular alterations, inflammation and ischaemia. In previous studies we had shown potential increases in loco-regional blood flow and glucose metabolism in brain tumours by using electrical cervical spinal cord stimulation (SCS). In this preliminary report we demonstrate the effect of cervical SCS on RBI-tissue metabolism, as assessed using [(18)F]fluorodeoxyglucose-positron emission tomography (FDG-PET).

METHODS: SCS devices were inserted in eight patients with diagnosis of potential RBI in previously irradiated areas. While the SCS device was deactivated, each patient underwent an initial FDG-PET study to evaluate the clinical status. A second FDG-PET study was performed later the same day while the SCS device was activated in order to evaluate the effect of cervical SCS on glucose metabolism.

RESULTS: Basal glucose metabolism in RBI areas was 31% lower than peri-RBI areas (p = 0.009) and 32% lower than healthy contra-lateral areas (p = 0.020). There was a significant increase in glucose uptake during SCS in both the RBI (p = 0.005) and the peri-RBI (p = 0.004) areas, with measured increases of 38 and 42%, respectively. The estimated potential maximal residual activity of the first FDG dose’s contribution to the activity on the second scan was ≤14.3 +/- 4.6%.

CONCLUSIONS: In this study using PET, SCS increased glucose metabolism in RBI and peri-RBI areas. These results warrant further clinical investigation to elucidate more fully the clinical usefulness of SCS in these patients.

Genomic biomarkers for molecular imaging: predicting the future.

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Over the past few decades, great strides have been made in anatomical imaging of disease that has led to their diagnosis with minimal invasion. Despite these advances, diseases such as cancer continue to take one human life every minute in the United States. Complimentary approaches that pertain directly to the genesis of the disease might contribute to its early diagnosis and subsequent management. In cancer, an array of molecular abnormalities leading to the modulations in expression of key proteins important in the cellular signaling pathways and cell proliferation has been identified. These specific disease fingerprints, biomarkers, are overexpressed on malignant cell surfaces or within the cytoplasm, and they provide unique targets that are promising for improving cancer diagnosis and therapy. We and others have designed, synthesized, and evaluated some novel probes specific for those oncogenes and oncogene product biomarkers for PET and SPECT molecular imaging of certain types of cancers. This article briefly describes this approach and gives specific examples that depict the ability of molecular imaging to detect occult lesions not detectable by current scintigraphic approaches. The article also outlines a few examples predicting other possible applications of targeting such specific probes not yet used.

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Mutational profile of advanced primary and metastatic radioactive iodine-refractory thyroid cancers reveals distinct pathogenic roles for BRAF, PIK3CA, and AKT1.


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Patients with poorly differentiated thyroid cancers (PDTC), anaplastic thyroid cancers (ATC), and radioactive iodine-refractory (RAIR) differentiated thyroid cancers have a high mortality, particularly if positive on [(18)F]fluorodeoxyglucose (FDG)-positron emission tomography (PET). To obtain comprehensive genetic information on advanced thyroid cancers, we designed an assay panel for mass spectrometry genotyping encompassing the most significant oncogenes in this disease: 111 mutations in RET, BRAF, NRAS, HRAS, KRAS, PIK3CA, AKT1, and other related genes were surveyed in 31 cell lines, 52 primary tumors (34 PDTC and 18 ATC), and 55 RAIR, FDG-PET-positive recurrences and metastases (nodal and distant) from 42 patients. RAS mutations were more prevalent than BRAF (44 versus 12%; P = 0.002) in primary PDTC, whereas BRAF was more common than RAS (39 versus 13%; P = 0.04) in PET-positive metastatic PDTC. BRAF mutations were highly prevalent in ATC (44%) and in metastatic tumors from RAIR PTC patients (95%). Among patients with multiple metastases, 9 of 10 showed between-sample concordance for BRAF or RAS mutations. By contrast, 5 of 6 patients were discordant for mutations of PIK3CA or AKT1. AKT1_G49A was found in 9 specimens, exclusively in metastases. This is the first documentation of AKT1 mutation in thyroid cancer. Thus, RAIR, FDG-PET-positive metastases are enriched for BRAF mutations. If BRAF is mutated in the primary, it is likely that the metastases will harbor
the defect. By contrast, absence of PIK3CA/AKT1 mutations in one specimen may not reflect the status at other sites because these mutations arise during progression, an important consideration for therapies directed at phosphoinositide 3-kinase effectors.


Imaging bone metastases in breast cancer: techniques and recommendations for diagnosis.

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Bone is the most common site of distant metastases from breast carcinoma. The presence of bone metastases affects a patient's prognosis, quality of life, and the planning of their treatment. We discuss recent innovations in bone imaging and present algorithms, based on the strengths and weaknesses of each technique, to facilitate the most successful and cost-effective choice of imaging studies for the detection of osseous metastases. Skeletal scintigraphy (bone scan) is very sensitive in the detection of osseous metastases and is recommended as the first imaging study in patients who are asymptomatic. Radiographs are recommended for the assessment of abnormal radionuclide uptake or the risk of pathological fracture and as initial imaging studies in patients with bone pain. MRI or PET-CT can be considered for cases of abnormal radionuclide uptake that are not addressed by radiography. Osseous metastases can lead to emergent situations, such as spinal-cord compression or impending fracture of a weight-bearing bone, and imaging guidelines are essential for early detection and initiation of appropriate therapy. The imaging method used in non-emergent situations, such as assessment of the ribs, sternum, pelvis, hips, and joints, should be guided by the strengths and limitations of each technique.


Imaging tumour-bearing animals using clinical scanners.

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Purpose: We investigated the capability of small animal imaging in clinical scanners for cancer research focusing on positron emission tomography (PET), computed tomography (CT) and magnetic resonance imaging (MRI). Methods and materials: We summarise basic principles, benefits and drawbacks of imaging modalities and discuss issues associated with animal welfare during imaging and its related effects on imaging results based on data from literature supplemented by own experiences. Results: MRI of tumour-bearing mice and rats in the clinical scanner is well-established for morphological and functional imaging in oncology. Clinical PET/CT did not yet establish as a research tool due to limited resolution and sensitivity, but its feasibility for tumour imaging has been demonstrated in mice. Anesthesia, animal handling and application of substances (e.g., contrast media) may alter animal physiology and, thus, also influence imaging results. Conclusions: Small animal imaging in clinical scanners offers good image quality and presents an alternative to dedicated small animal scanners for numerous applications in cancer research. Successful and meaningful small animal imaging in clinical as well as dedicated scanners prerequisites a thorough knowledge of animal morphology and physiology, a deep understanding of likely influences of animal manipulation on imaging and an adequate care for animal welfare.

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Combining 6-fluoro-[18F]-dihydroxyphenylalanine and [18F]fluoro-2-deoxy-d-glucose positron emission tomography for distinction of non-carcinoid malignancies in carcinoid patients.

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AIM: Carcinoid patients frequently develop a second primary malignancy (SPM), which can deserve full treatment. Distinguishing a SPM from carcinoid lesions is therefore important. Differentiation can be achieved using the difference in uptake between different positron emission tomography (PET) tracers. METHODS AND RESULTS: Between January 2005 and August 2008, 105 carcinoid patients were seen at the Department of Medical Oncology for treatment and follow-up. We identified 3 patients who presented with a new SPM in whom differentiation between carcinoid lesions and the SPM was guided by functional imaging of the catecholamine pathway with 6-fluoro-[18F]-dihydroxyphenylalanine ([18F]-DOPA) PET and [18F]fluoro-2-deoxy-d-glucose ([18F]-FDG) PET as radiotracer for the glucose metabolism. All 3 patients had metastatic carcinoid disease and localised adenocarcinoma based on the PET-scans. For the adenocarcinoma they received curative treatment. CONCLUSION: The difference in uptake between these PET techniques can be used for decision making when a primary or metastatic SPM is suspected.
To summarize, this patient is a relatively young, otherwise healthy female who is status post lobectomy. She has been diagnosed with stage IIIA NSCLC that is EGFR-positive by IHC and FISH, but EGFR and KRAS wild type. Optimal MLNS or MLND is ideally performed in the pre- and/or perioperative setting, but this did not happen in this case. While more extensive examination of the mediastinum after the primary operation could be undertaken—removing some of the unknowns about this patient’s true stage and prognosis—the relative risks and benefits of such an additional procedure in the setting of PET-negative microscopic level 7 and 9 disease probably do not justify such an approach. Assuming the absence of additional information, the recommendation of the University of Colorado Clinical Thoracic Oncology program is to commence a course of four cycles of adjuvant cisplatin-based chemotherapy. The pros and cons of postoperative radiotherapy will be discussed with the patient. If she wishes to proceed with PORT, this will commence following the adjuvant chemotherapy. Due to the inadequate lymph node sampling, she would not be eligible for adjuvant therapy as part of the ECOG 1505 trial of cisplatin chemotherapy with or without bevacizumab, but if she declines PORT, she may be eligible for the RADIANT trial of erlotinib vs placebo following her adjuvant cisplatin-based therapy.

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and 3.58, respectively. Patients with low pre-SBRT SUV were more likely to experience initial 2-week rises in SUV, whereas patients with high pre-SBRT SUV commonly had SUV declines 2 weeks after treatment (p = 0.036). Six of 13 patients had primary tumor SUV(max) >3.5 at 12 months after SBRT but remained without evidence of local disease failure on further follow-up. CONCLUSIONS: A substantial proportion of patients may have moderately elevated FDG-PET SUV(max) at 12 months without evidence of local failure on further follow-up. Thus, slightly elevated PET SUV(max) should not be considered a surrogate for local treatment failure. Our data do not support routine serial FDG-PET/computed tomography for follow-up of patients receiving SBRT for Stage I NSCLC.

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Cervical cancer histology and tumor differentiation affect 18F-fluorodeoxyglucose uptake.

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BACKGROUND: This study aimed to evaluate the variation in cervical cancer glucose metabolism for different tumor histologies and levels of differentiation, as measured by the uptake of 18F-fluorodeoxyglucose (FDG) by positron emission tomography (PET).

METHODS: The study population consisted of 240 patients with International Federation of Gynecology and Obstetrics stages Ib1 through IVb cervical cancer, who underwent a pretreatment FDG-PET. Tumor histology included 221 squamous cell (SC), 4 adenosquamous (AS), and 15 adenocarcinoma (AC) tumors. There were 14 well, 145 moderately, and 81 poorly differentiated tumors. The stage distribution was as follows: 70 stage I tumors (9 AC, 2 AS, and 59 SC), 102 stage II tumors (3 AC, 1 AS, and 98 SC), 64 stage III tumors (3 AC, 1 AS, and 60 SC), and 4 stage IV tumors (4 SC). From the FDG-PET, maximal standardized uptake value (SUVmax) was determined. The variation in SUVmax was analyzed for differences based on tumor histology and differentiation. RESULTS: For all patients, the mean SUVmax was 11.62 (range, 2.50-50.39). The mean SUVmax by histology was as follows: SC, 11.91 (range, 2.50-50.39); AS, 8.85 (range, 6.53-11.26); and AC, 8.05 (range, 2.83-13.92). Squamous versus nonsquamous tumors demonstrated a significant difference in SUVmax (P=0.0153). SUVmax and tumor volume were not found to be correlated (R2=0.013). The mean SUVmax was 8.58 for well-differentiated, 11.56 for moderately differentiated, and 12.23 for poorly differentiated tumors. The mean SUVmax was significantly different for well-differentiated versus poorly differentiated cervical tumors (P=0.0474). CONCLUSIONS: Cervical tumor FDG uptake varied by histology and differentiation. SC tumors demonstrated a significantly higher SUVmax compared with nonsquamous cell tumors, and poorly differentiated tumors also had a higher SUVmax.

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In this issue of Clinical Cancer Research, London and colleagues evaluate a small molecule multiple-targeted tyrosine kinase inhibitor in dogs with c-kit driven skin cancer. The study represents another example of opportunities to include pet dogs in studies that improve our understanding of human cancer biology and therapy.


A Prospective Randomized Trial to Study the Impact of Pretreatment FDG-PET for Cervical Cancer Patients with MRI-Detected Positive Pelvic but Negative Para-Aortic Lymphadenopathy.

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PURPOSE: This prospective randomized study was undertaken to determine the possible impact of 18F-fluorodeoxyglucose positron emission tomography (FDG-PET) on extrapelvic metastasis detection, radiation field design, and survival outcome for cervical cancer patients with enlarged pelvic nodes on MRI image. METHODS AND MATERIALS: Inclusion criteria were patients with newly diagnosed Stage I-IVA cervical cancer and with positive pelvic but negative para-aortic lymph nodes (PALN) as detected by magnetic resonance image and good performance status for concurrent chemoradiotherapy. Eligible patients were randomized to receive either pretreatment FDG-PET (study group) or not (control group). Whole pelvis was the standard irradiation field for the control group and those with no extrapelvic findings on PET. The radiation fields for the rest of the study group were extended to include the PALN region or were modified according to the extrapelvic PET finding. RESULTS: From January 2002 to April 2006, 129 patients were included, and 66 of them were randomized to receive FDG-PET. PET detected seven extrapelvic metastases (11%, 6 PALN and 1 omental node), and four of them remained disease-free after treatment modification. For patients who underwent PET compared with those who did not, there were no differences in the 4-year rates of overall survival (79% vs. 85%, p = 0.65), disease-free survival (75% vs. 77%, p = 0.64), and distant metastasis-free survival (82% vs. 78%, p = 0.83). CONCLUSIONS: Pretreatment FDG-PET in conjunction with magnetic resonance imaging can improve the detection of extrapelvic metastasis, mainly PALN, and
help select patients for extended-field radiotherapy. However, the addition of FDG-PET may not translate into survival benefit, even though PALN relapses are reduced.

Int J Radiat Oncol Biol Phys. 2009 May 21

Comparison of Tumor Volumes as Determined by Pathologic Examination and FDG-PET/CT Images of Non-Small-Cell Lung Cancer: A Pilot Study.


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PURPOSE: To determine the cut-off standardized uptake value (SUV) on (18)F fluoro-2-deoxy-glucose (FDG) positron emission tomography/computed tomography (FDG-PET/CT) images that generates the best volumetric match to pathologic gross tumor volume (GTV(path)) for non-small-cell lung cancer (NSCLC). METHODS AND MATERIALS: Fifteen patients with NSCLC who underwent FDG-PET/CT scans followed by lobectomy were enrolled. The surgical specimen was dissected into 5-7-mum sections at approximately 4-mm intervals and stained with hematoxylin and eosin. The tumor-containing area was outlined slice by slice and the GTV(path) determined by summing over all the slices, taking into account the interslice thickness and fixation-induced volume reduction. The gross tumor volume from the PET images, GTV(PET), was determined as a function of cut-off SUV. The optimal threshold or optimal absolute SUV was defined as the value at which the GTV(PET) was the same as the GTV(path). RESULTS: The fixation process induced a volumetric reduction to 82% +/- 10% (range, 62-100%) of the original. The maximal SUV was 10.1 +/- 3.6 (range, 4.2-18.7). The optimal threshold and absolute SUV were 31% +/- 11% and 3.0 +/- 1.6, respectively. The optimal threshold was inversely correlated with GTV(path) and tumor diameter (p < 0.05), but the optimal absolute SUV had no significant correlation with GTV(path) or tumor diameter (p > 0.05). CONCLUSION: This study evaluated the use of GTV(path) as a criterion for determining the optimal cut-off SUV for NSCLC target volume delineation. Confirmatory studies including more cases are being performed.


Stereotactic Body Radiotherapy for Recurrent Squamous Cell Carcinoma of the Head and Neck: Results of a Phase I Dose-Escalation Trial.


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PURPOSE: To evaluate the safety and efficacy of stereotactic body radiotherapy (SBRT) in previously irradiated patients with squamous cell carcinoma of the head and neck (SCCHN). PATIENTS AND METHODS: In this Phase I dose-escalation clinical trial, 25 patients were treated in five dose tiers up to 44 Gy, administered in 5 fractions over a 2-week course. Response was assessed according to the Response Evaluation Criteria in Solid Tumors and [(18)F]-fluorodeoxyglucose standardized uptake value change on positron emission tomography-computed tomography (PET-CT). RESULTS: No Grade 3/4 or dose-limiting toxicities occurred. Four patients had Grade 1/2 acute toxicities. Four objective responses were observed, for a response rate of 17% (95% confidence interval 2%-33%). The maximum duration of response was 4 months. Twelve patients had stable disease. Median time to disease progression was 4 months, and median overall survival was 6 months. Self-reported quality of life was not significantly affected by treatment. Fluorodeoxyglucose PET was a more sensitive early-measure response to treatment than CT volume changes. CONCLUSION: Retreatment up to 44 Gy using SBRT is well tolerated in the acute setting and warrants further evaluation in combination with conventional and targeted therapies.


[A recurrent gastric cancer patient with multiple organ metastasis who achieved partial remission by multidisciplinary therapy (radiochemotherapy plus hyperthermia)]

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A 77-year-old male patient visited our hospital for postoperative gastric cancer in September of 2007. He suffered from serious appetite loss, general fatigue, nausea and some other side effects since he was taking S-1(100 mg/day) for the postoperative adjuvant therapy. Chest enhanced CT (as of September, 2007) revealed right mediastinum lymph node metastases and multiple liver metastases that had been diagnosed at the operation were evaluated as remission. He re-started S-1 with a lower dose(80 mg/day) soon after he visited our hospital as an outpatient. That side-effect was slightly improved. However, PET-CT (as of May, 2008) showed another metastasis of left supraclavicular lymph nodes (Virchow lymph nodes). Multidisciplinary therapy, chemotherapy(docetaxel 60 mg/m2, every 3 weeks), radiotherapy and hyperthermia were performed and PET-CT (as of July, 2008) showed left supraclavicular lymph node metastases were evaluated as complete remission, and as to right mediastinum lymph node metastases, we achieved partial remission. Thus, overall partial remission was achieved with the RECIST guideline.
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A phase 0 trial of riluzole in patients with resectable stage III and IV melanoma.


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PURPOSE: Ectopic expression of GRM1 in murine melanocytes results in transformation into a form of melanoma, and more than 60% of human melanoma samples tested ectopically express GRM1. Stimulation of this receptor in vitro results in up-regulation of activated extracellular signal-regulated kinase (ERK). Furthermore, a xenograft model of melanoma treated with riluzole, an oral GRM1 blocking agent, showed decreased tumor growth compared with the untreated controls. We have now completed a phase 0 trial of riluzole in patients with melanoma. EXPERIMENTAL DESIGN: Patients enrolled on this trial underwent a pretreatment biopsy, took 200 mg of oral riluzole per day for 14 days, and then underwent resection of their remaining tumor. We compared the levels of pERK and pAKT in the pretreatment and post-treatment samples and assessed the metabolic activity of pretreatment and post-treatment tumors using fluorodeoxyglucose positron emission tomography (FDG-PET) scanning. RESULTS: We accrued 12 patients and all expressed GRM1. We found a significant decrease in pAKT and/or pERK in post-treatment tumor samples as compared with pretreatment samples in 4 (34%) patients. These four patients had a significant decrease in FDG-PET intensity post-treatment as well. Two other patients had a clinical response with no corresponding metabolic response; five patients had similar pretreatment and post-treatment FDG-PET scan findings; and one patient had progressive disease. CONCLUSIONS: Our data show that glutamate blockade with riluzole can inhibit signaling through the mitogen-activated protein kinase and phosphatidylinositol 3-kinase/AKT pathways and suppress the metabolic activity of melanoma. The ectopic expression of metabotropic glutamate receptors may be important in the pathogenesis of human melanoma, and targeting this pathway may be an effective therapy.


Regulation of glucose metabolism by 6-phosphofructo-2-kinase/fructose-2,6-bisphosphatases in cancer.

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A high rate of glycolytic flux, even in the presence of oxygen, is a central metabolic hallmark of neoplastic tumors. Cancer cells preferentially utilize glycolysis in order to satisfy their increased energetic and biosynthetic requirements. This metabolic phenotype has been confirmed in human studies using positron emission tomography (PET) with (18)F-2-fluoro-deoxy-glucose which have demonstrated that tumors take up 10-fold more glucose than adjacent normal tissues in vivo. The high glucose metabolism of cancer cells is caused by a combination of hypoxia-responsive transcription factors, activation of oncogenic proteins and the loss of tumor suppressor function. Over-expression of HIF-1alpha and myc, activation of ras and loss of p53 function each have been found to stimulate glycolysis in part by activating a family of regulatory bifunctional 6-phosphofructo-2-kinase/fructose-2,6-bisphosphatases (PFKFB). The PFKFB enzymes synthesize fructose-2,6-bisphosphate (F2,6BP) which allosterically activates 6-phosphofructo-1-kinase (PFK-1), a rate-limiting enzyme and essential control point in the glycolytic pathway. PFK-1 is inhibited by ATP when energy stores are abundant and F2,6BP can override this inhibition and enhance glucose uptake and glycolytic flux. It is therefore not surprising that F2,6BP synthesis is stimulated by several oncogenic alterations which simultaneously cause both enhanced consumption of glucose and growth. Importantly, these studies suggest that selective depletion of intracellular F2,6BP in cancer cells may suppress glycolytic flux and decrease their survival, growth and invasiveness. This review will summarize the requirement of the 6-phosphofructo-2-kinase/fructose-2,6-bisphosphatases for the regulation of glycolysis in tumor cells and their potential utility as targets for the development of antineoplastic agents.


Incidental focal F-18 FDG accumulation in lung parenchyma without abnormal CT findings.

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F-18 fluorodeoxyglucose (FDG) PET/CT that simultaneously offers anatomic and metabolic information is widely used and has become an effective modality in many clinical fields, especially oncology. For accurate interpretation, it is necessary to understand false-positive findings in the F-18 FDG PET image, such as physiologic conditions, findings related to patients' medical and surgical histories, normal variants, and artificial conditions. We report three cases of incidental focal F-18 FDG accumulation in lung parenchyma without abnormal CT findings in the PET/CT images. In the primary PET/CT studies, two cases showed single and one case showed multiple FDG foci in the lung without any CT abnormalities. All FDG accumulations disappeared in PET/CT studies repeated 1-3 days after the primary scannings. These artifacts are probably related to microembolisms attributable to the intravenous injection of F-18 FDG. Therefore, a cautious interpretation of the correspondence between anatomic and metabolic images is required and repeated PET/CT is helpful.
Automated synthesis of an 18F-labelled pyridine-based alkylating agent for high yield oligonucleotide conjugation.


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Alkylating agents have been shown to be very promising for the radiolabelling of oligonucleotides with fluorine-18. In this report we describe the fully automated synthesis of 2-bromo-N-[3-(2-[[18]F]fluoropyridin-3-yl)oxy]propylacetamide ([[18]F]FPyBrA) utilizing a modular synthesis unit. Reaction conditions for the coupling of this pyridine-based alkylating agent at the 5’ end of a fully phosphorothioated random 20-mer DNA sequence were optimized to achieve very high radiochemical yields (>90%) and a maximum specific activity of 5-6 GBq/micromol. The potential for rapid purification by solid phase extraction without need of chromatographic isolation of the radiolabelled oligonucleotide presents an overall benefit for the application of oligonucleotides in preclinical studies and potential clinical applications.

Gynecol Oncol. 2009 Aug;114(2):310-4

The role of PET/CT in the management of patients with cervical cancer: practice patterns of the members of the Society of Gynecologic Oncologists.

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OBJECTIVES: Recent data has highlighted the role of PET/CT in the pretreatment evaluation and follow-up of patients with cervical cancer. The objective of our study was to assess the acceptance of PET/CT into the management of patients with cervical cancer. We also explored potential barriers to the use of these imaging modalities in patients with cervical cancer. METHODS: A 14-item electronic questionnaire was initially sent to all working addresses of members of the SGO (n=1048). An opt-out option was offered. For members who did not respond within 3 weeks, a second electronic invitation was sent. A third request was finally sent to further improve response rates. Data were collected and analyzed using a commercially available on-line survey database. RESULTS: A total of 305 responses were collected for an overall 30% response rate. PET/CT appears to be widely available (99%) and accessible (75%) in most practices. Although 83% of members order routine CT imaging for all newly diagnosed cervical cancer cases, only 28% routinely order a PET/CT. Conversely, 64% would order a PET/CT for newly diagnosed patients with advanced disease or those at high risk for distant metastatic disease. Most members (82%) do not routinely use PET/CT to assess response to treatment. Twenty percent of members believe that no useful prognostic information can be obtained from routine use of molecular imaging in patients with cervical cancer. The most common barriers for use of PET/CT cited by members were perceived lack of third-party payer coverage and lack of scientific evidence. CONCLUSIONS: Despite clear scientific data supporting the use of PET/CT in patients with cervical cancer and apparent widespread availability, this imaging modality remains highly underutilized in clinical practice. Clarifying insurance coverage early in the evaluation process and replicating studies that have shown effectiveness of PET/CT in multiple roles may improve adoption of this potentially useful imaging modality.


PET/CT in paediatric oncology: indications and pitfalls.

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Influence of N-butylscopolamine on SUV in FDG PET of the bowel.

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OBJECTIVES: Peristalsis can lead to confusing FDG PET bowel uptake artefacts and potential for recording inaccurate mean standardised uptake value (SUV) measurements in PET-CT scans. Accordingly, we investigate the influence of different SUV normalisation methods on the FDG PET uptake of the bowel and assess which one(s) have least dependence on body size factors in patients with and without the introduction of the anti-peristalsis agent N-butylscopolamine (Buscopan). METHODS: This study consisted of 92 prospective oncology patients, each having a whole body (18)F-FDG PET scan. Correlations were investigated between height, weight, glucose, body mass index (bmi), lean body mass (ibm) and body surface area (bsa) with maximum and mean SUV recorded for bowel normalised to weight (SUV(w)), ibm (SUV(ibm)), bsa (SUV(bsa)) and blood glucose corrected versions (SUV(wg), SUV(ibmg), SUV(bsag)). RESULTS: Standardised uptake value normalisations were significantly different between control and Buscopan groups with less variability experienced within individual SUV normalisations by the administration of Buscopan. Mean
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SUVR normalisations accounted for 80% of correlations in the control group and 100% in the Buscopan group. Further, >86% of all correlations across both groups were dominated by mean SUVR normalisations of which, about 69% were accounted for by SUVR(bsa) and SUVR(bsag). CONCLUSIONS: We recommend avoiding mean SUVR(bsa) and individual glucose normalisations especially, mean SUVR(bsag) as these dominated albeit relatively weak correlations with body size factors in control and Buscopan groups. Mean and maximum SUVR(w) and SUVR(lbm) were shown to be independent of any body size parameters investigated in both groups and therefore considered suitable for monitoring FDG PET uptake in the normal bowel for our patient cohort.


Variation in FDG uptake on PET in patients with radiation-induced pelvic insufficiency fractures: a review of 10 cases.

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INTRODUCTION: The information available on (18)F-fluorodeoxyglucose (FDG) uptake on PET in radiation-induced pelvic insufficiency fracture (PIF) is limited. In this study, we reviewed the findings of FDG-PET in 10 cases with PIF. MATERIALS AND METHODS: We diagnosed 83 cases of PIF in patients who received pelvic radiotherapy between Jan 1995 and Aug 2005. Among these patients, we selected 10 patients who performed FDG-PET and reviewed the FDG uptake. RESULTS: Mild FDG uptake was still present at 6-months after the diagnosis of PIF in two patients. Eight patients had mild and diffuse FDG uptake and two patients had intense and heterogeneous uptake. All patients had vertical uptake parallel to the sacroiliac joints and one patient had the typical ‘H’ sign associated with PIF. The maximum of standardized uptake values was variable and ranged from 2.4 to 7.2. In three patients, follow-up PET images were obtained. All patients had FDG uptake that decreased with time. CONCLUSION: The FDG-PET demonstrated a variable degree of uptake in patients with a PIF. The pattern of uptake was diffuse and vertical, parallel to the sacroiliac joints. Therefore, clinicians should be careful with the interpretation of FDG uptake around the sacroiliac joints, and keep in mind false-positive lesions such as PIFs.


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INTRODUCTION: The aim of this pilot study was to determine heparanase plasma levels (HP) at diagnosis and at restaging in children diagnosed with Hodgkin lymphoma and to investigate whether this parameter provides prognostic information for response to treatment after induction therapy. PATIENTS AND METHODS: HP levels of 19 pediatric patients (mean age: 10.3 years (y) (range, 4-18 y), 9 girls, 10 boys) with Hodgkin lymphoma were assayed at diagnosis and at restaging. HP levels were determined using an ELISA anti-human heparanase immunoassay kit. According to diagnosis, CAT scan and/or FDG/ PET-CT fusion were performed to assess response to treatment after 2-3 courses of chemotherapy. Two patients received VAMP protocol (1 stage IIA, 1 stage IIA), 1 received AV-PC (nonbulky stage IIA), 4 received COPP/ABV (3 stage IIA bulky, 1 stage IIIA nonbulky), 4 received ABVE-PC (2 stage IIB, 1 stage IIA bulky, 1 stage IIIA bulky), 2 received ABVD (1 stage IIA bulky, 1 stage IIIA), and 6 received escalated BEACOPP (1 stage IIIA, 3 stage IVA, 2 stage IVB). RESULTS: Changes in HP levels were found to correlate with response to treatment for most of the children. At diagnosis, average HP level was 1019 pg/mL (range, 141-5733 pg/mL), decreasing at restaging to 598 pg/mL (range, 62-3267 pg/mL) (p = .034). At diagnosis, the average HP of the 16 patients in CR or VGPR was 1104 pg/mL; it had decreased at restaging to 586 pg/mL (p = .032). At diagnosis, the average HP level for the 3 patients with TP or PR was 1704 pg/mL; it had increased to 1938 pg/mL at restaging (p = .166). Due to the small number of patients, no correlation was observed between HP levels at diagnosis, staging, or any other clinical prognostic factor. CONCLUSIONS: Changes in plasma HP levels correlated with response to treatment for children diagnosed with Hodgkin lymphoma. This provides a rationale for exploring clinical interest in plasma heparanase measurements of a larger group, using the test for clinical trials of antiangiogenic therapies.


Dose, timing, schedule, and the choice of targeted epitope alter the efficacy of anti-CD22 immunotherapy in mice bearing human lymphoma xenografts.

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CD22 is a cell-surface adhesion molecule on most B-cell NHL, so it is a promising target for immunotherapy. HB22.7 is an anti-CD22 mAb that binds the two NH(2)-terminal immunoglobulin domains and specifically blocks the interaction of CD22 with its ligand. CD22-blocking mAbs induce apoptosis in neoplastic B-cells and are functionally distinguishable from other anti-CD22 mAbs. This study assessed the optimal dose, route, schedule, and the targeted CD22 epitope. Raji NHL-bearing nude mice were studied. A non-blocking anti-CD22 mAb (HB22.27) was used as a control. HB22.27 had minimal effect, whereas HB22.7 improved survival and shrank tumors substantially. HB22.7 doses greater than 1.4 mg/week did not further increase efficacy (or toxicity). Tumors less than 200 mm(3) had a higher response rate than did larger tumors. Various schedules of HB22.7 administration were tested; one dose every other week was more effective than more or less frequent dosing. Pharmacokinetic studies revealed that the half-life of HB22.7 was 28 days; this correlated with the time needed to re-populate cell-surface CD22 after treatment with HB22.7. ImmunotoPET showed that NHL was rapidly and specifically targeted by copper-64-labeled-HB22.7. This study provided data as to the targeted CD22 epitope.


Clinical management of borderline tumours of the ovary: results of a multicentre survey of 323 clinics in Germany.

The aim of this survey was to analyse the standard of care in diagnostic, surgery, chemotherapy and aftercare management for patients with borderline tumours of the ovary (BOTs) in Germany. A structured questionnaire comprising different dimensions was sent to all 1114 gynaecological departments. The questionnaire could be returned anonymously. The overall response rate was 29.0% (323 departments). Most departments were on secondary care (71.8%), tertiary care (23.2%) or university hospital (5.0%) level. Most clinicians performed not more than five BOT operations (89.2%) per year. Most departments (93.2%) used in addition to classical bimanual examination and vaginal ultrasound, tumour marker CA-125 detection, CT scan, MRI or PET-CT techniques. Departments in university and tertiary care hospitals performed more often a fresh frozen section (87 vs 64%). In young women, clinicians performed much seldom unilateral salpingo-oophorectomy (92%) and only in 53% biopsies of the contralateral ovary. Generally, biopsies of the contralateral ovary were performed in 4-53% of the patients. Chemotherapy was mostly favoured in high-risk patients with tumour residual, microinvasion or invasive implants. Thus, a high grade of insecurity in diagnostic and therapy of BOT exists in some gynaecological departments and underlines the need for more educational and study activities.


Absolute dose reconstruction in proton therapy using PET imaging modality: feasibility study.

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A simple analytical model is developed that allows efficient absolute dose reconstruction in patients undergoing radiation treatments using proton beams. The model is based on the solution of the inverse problem of dose recovery from the 3D information contained in the PET signal, obtained immediately after the treatment. The core of the proposed model lies in the analytical calculation of the introduced positron emitters' species matrix (PESM) or kernel, facilitated by previously developed theoretical calculations of the proton energy fluence distribution. Once the PESM is known, the absolute dose distribution in a patient can be found from the deconvolution of the 3D activity distribution obtained from the PET scanner with the calculated species matrix. As an example, we have used FLUKA Monte Carlo code to simulate the delivery of the radiation dose to a tissue phantom irradiated by a parallel-opposed beam arrangement and calculated the resultant total activity. Deconvolution of the calculated activity with the PESM leads to the reconstructed dose being within 2% of that delivered.


Initial results of hypoxia imaging using 1-alpha-D: - (5-deoxy-5-[(18)F]-fluoroarabinofuranosyl)-2- nitroimidazole ( (18)F-FAZA).


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PURPOSE: Tumour hypoxia is thought to play a significant role in the outcome of solid tumour therapy. Positron emission tomography (PET) is the best-validated noninvasive technique able to demonstrate the presence of hypoxia in vivo. The locally developed PET tracer for imaging hypoxia, 1-alpha-D: - (5-deoxy-5-[(18)F]-fluoroarabinofuranosyl)-2-nitroimidazole ((18)F-FAZA), has been shown to accumulate in experimental models of tumour hypoxia and to clear rapidly from the circulation and nonhypoxic tissues. The safety and general biodistribution patterns of this radiopharmaceutical in patients with squamous cell carcinoma of the head and neck (HNSSC), small-cell lung cancer (SCLC) or non-small-cell lung cancer (NSCLC), malignant lymphoma, and high-grade gliomas, were demonstrated in this study. METHODS: Patients with known primary or suspected metastatic HNSSC, SCLC or NSCLC, malignant lymphoma or high-grade gliomas were dosed with 5.2 MBq/kg of (18)F-FAZA, then scanned 2-3 h after injection using a PET or PET/CT scanner. Images were interpreted by three experienced nuclear medicine physicians. The location and relative uptake scores (graded 0 to 4) of normal and abnormal (18)F-FAZA biodistribution patterns, the calculated tumour-to-background (T/B) ratio, and the maximum standardized uptake value were recorded. RESULTS: Included in the study were 50 patients (32 men, 18 women). All seven patients with high-grade gliomas showed very high uptake of (18)F-FAZA in the primary
tumour. In six out of nine patients with HNSCC, clear uptake of (18)F-FAZA was observed in the primary tumour and/or the lymph nodes in the neck. Of the 21 lymphoma patients (15 with non-Hodgkin’s lymphoma and 6 with Hodgkin’s disease), 3 demonstrated moderate lymphoma-related uptake. Of the 13 lung cancer patients (12 NSCLC, 1 SCLC), 7 had increased (18)F-FAZA uptake in the primary lung tumour. No side effects of the administration of (18)F-FAZA were observed. CONCLUSION: This study suggests that (18)F-FAZA may be a very useful radiopharmaceutical to image hypoxia in the tumour types selected. Especially the high uptake by gliomas was encouraging. Given the good imaging properties, including acceptable T/B ratios in the tumour categories studied, (18)F-FAZA could be considered as a very promising agent for assessing the hypoxic fraction of these tumour types.


Perception of burden experienced during diagnostic tests by melanoma patients with lymph node metastases.

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Melanoma patients with lymph node metastases have to deal with diagnostic tests to exclude the presence of distant metastases; results of the tests could have major implications for their prognosis and treatment. There are, however, few studies concerning the patients’ psychological issues and perception of diagnostic tests. The aim of this study was to describe the burden of diagnostic tests [radiograph, computed tomography (CT) and positron emission tomography (PET)] experienced by melanoma patients with lymph node metastases. Patients were asked to complete a questionnaire concerning satisfaction and burden experienced during the diagnostic tests. The levels of embarrassment, discomfort and anxiety for the different tests, as well as total scores for each burden were calculated. Logistic regression was used to examine factors associated with the degree of experienced burden. Fifty-nine of the 68 patients completed the questionnaire and the response rate was 87%. The overall mean scores on satisfaction and quality of life were high. More than half of the patients experienced no burden during PET, 65% no burden during computed tomography and 80% no burden during chest radiograph. Patients experienced significantly more discomfort during the PET scan than during the CT (P<0.003). Less burden was experienced (in univariate analysis) by patients who were more satisfied. The overall experienced burden by patients is low and should therefore not interfere with primary choice for a diagnostic test based on accuracy, costs and percentage of patients upstaged. Attention should be paid in explaining the procedure and answering questions of the patients to reduce burden.


Cesarean section scar mimicking uterine malignant neoplasm at positron emission tomography/computed tomography.

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Positron emission tomography/computed tomography (PET/CT) is a functional imaging method of metabolic processes and is being used extensively in gynecologic oncology for treatment planning. However, some hypermetabolic conditions may mimic malignant neoplasms. We report a case with a positive finding at PET/CT examination of the uterus that proved to be a cesarean section scar with high expression of glucose transporter-1 and glucose transporter-4. This case report emphasizes the value of the knowledge of patient history and awareness of the limitations of PET/CT to enable a correct diagnosis in patients with positive findings at PET/CT examination.

Respiration. 2009 May.

Impact of FDG-PET-Induced Treatment Choices on Long-Term Outcome in Non-Small Cell Lung Cancer.


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Background: The TNM staging reflects the anatomic extent of lung cancer and estimates the survival expectation. Addition of FDG-PET to conventional staging (CS) improves accuracy, but few data have described the impact of this on long-term survival in relation to treatment. Objectives: To study the influence of FDG-PET on long-term outcome. Methods: Long-term outcome data of patients were retrieved out of previously published PET studies of the Leuven Lung Cancer Group. All patients had a potential for radical treatment, and at least 5-year follow-up data. Patients were dichotomized in early (I-IIIA) versus late (IIB-IV) stages. Results: A first analysis - comparison of the 2 staging algorithms, CS alone versus CS+PET - confirmed the better staging capabilities of the latter. A second analysis, focusing on discordant findings and interaction of both staging algorithms, demonstrated that patients with early stage on PET did well, while those with late stage on PET did poorly, irrespective of findings on CS. The third analysis focused on the relation between treatment choices at the multidisciplinary board and outcome, which is especially relevant in patients with discordant finding on CS and CS+PET. From all radically treated patients, only those with early stage on CS+PET had a good outcome, but not those with early stage on CS and an unexplained late stage finding on PET. Conclusion: This long-term follow-up
analysis confirms that addition of PET to CS results in better stage designation and prognosis. Additionally, discordant findings between CS and CS+PET should be considered relevant, with need for cytological/histological examination.

**Oncology (Williston Park).** 2009 Mar;23(3):269-70

**Nuclear medicine imaging in breast cancer: current strategies and future directions.**

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**Oncology (Williston Park).** 2009 Mar;23(3):255-61

**Role of positron-emission tomography scan in the diagnosis and management of breast cancer.**

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Positron-emission tomography (PET) scan is a widely used imaging modality in the management of various malignancies. There is considerable controversy regarding its use in breast cancer diagnosis and treatment. In this review, we discuss published data on the use of 2-[18F]-fluoro-2-deoxy-D-glucose (FDG-PET) in the staging workup of locally advanced breast cancer, and management of locally recurrent and metastatic breast cancer. FDG-PET is a useful tool in staging advanced breast cancer and assessing the extent of disease involvement when metastasis is suspected. It might also aid in assessing early response to therapy. Future goals of improving PET scan accuracy in the management of breast cancer will be achieved through utilizing radiotracers, based on a better understanding of tumor biology and improvement in breast-specific PET scans.


**Whole-body 18FDG PET-CT imaging of systemic sarcoidosis: ophthalmic oncology and uveitis.**

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PURPOSE: To describe whole-body 18-fluorodeoxyglucose (FDG) positron emission tomography/computed radiographic tomography (PET-CT) imaging of ophthalmic patients with systemic sarcoidosis. METHODS: Four systemic sarcoidosis patients were evaluated with PET-CT for staging. Two had been treated for conjunctival melanoma and two had been referred for atypical choroidal tumors. PET-CT images were studied for presence of tumor or tissue with increased standardized uptake values, indicating increased metabolic activity. RESULTS: In all cases, PET-CT revealed focal systemic lesions with increased uptake (SUV range 1.7-5.9 kg/mL). Cases 1 and 2 had a previous diagnosis of sarcoidosis (without ocular involvement), while cases 3 and 4 were diagnosed during their work-up. PET-CT revealed the presence and distribution of systemic sarcoid granulomas. CONCLUSIONS: In this series, PET-CT staged patients with eye cancer and systemic sarcoidosis and aided in differentiating between a metastatic choroidal tumor and uveal sarcoid granuloma. PET-CT offers a method to assess the presence and distribution of systemic sarcoidosis.

**Appl Radiat Isot.** 2009 Jul;67(7-8 Suppl):S351-4

**Positron emission tomography and [18F]BPA: a perspective application to assess tumour extraction of boron in BNCT.**


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Positron emission tomography (PET) has become a key imaging tool in clinical practice and biomedical research to quantify and study biochemical processes in vivo. Physiologically active compounds are tagged with positron emitters (e.g. (18)F, (11)C, (124)I) while maintaining their biological properties, and are administered intravenously in tracer amounts (10(-9)-10(-12)M quantities). The recent physical integration of PET and computed tomography (CT) in hybrid PET/CT scanners allows a combined anatomical and functional imaging: nowadays PET molecular imaging is emerging as powerful pharmacological tool in oncology, neurology and for treatment planning as guidance for radiation therapy. The in vivo pharmacokinetics of boron carrier for BNCT and the quantification of (10)B in living tissue were performed by PET in the late nineties using compartmental models based on PET data. Nowadays PET and PET/CT have been used to address the issue of pharmacokinetic, metabolism and accumulation of BPA in target tissue. The added value of the use of L-[(18)F]FBPA and PET/CT in BNCT is to provide key data on the tumour extraction of (10)B-BPA versus normal tissue and to predict the efficacy of the treatment based on a single-study patient analysis. Due to the complexity of a binary treatment like BNCT, the role of PET/CT is currently to design new criteria for patient enrolment in treatment protocols: the L-[(18)F]FBPA/PET methodology could be considered as an important tool in newly designed clinical trials to better estimate the concentration ratio of BPA in the tumour as compared to neighbouring normal tissues. Based on these values for individual patients
the decision could be made whether BNCT treatment could be advantageous due to a selective accumulation of BPA in an individual tumour. This approach, applicable in different tumour entities like melanoma, glioblastoma and head and neck malignancies, make this methodology as reliable prognostic and therapeutic indicator for patient undergoing BNCT.


Melanoma of the small intestine.

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Intestinal melanomas can be primary tumours or metastases of cutaneous, ocular, or anal melanomas. Primary intestinal melanoma is extremely rare, whereas metastatic melanoma of the small bowel is common because of the tendency for cutaneous melanoma to metastasise to the gastrointestinal tract. Because distinguishing between primary and metastatic intestinal melanoma can be difficult, the main features of each are discussed, and the diagnostic images used to detect intestinal melanoma are assessed. Routine barium examinations and CT have limited sensitivity, but PET imaging can improve detection of melanoma metastases to the small bowel. Although various treatment strategies have been tried in patients with intestinal melanoma, surgical removal of intestinal metastases is the treatment of choice in patients with resectable tumours. No systemic therapy improves survival in patients with melanoma metastatic to the intestines; thus, the prognosis for these patients is poor. Patients with primary melanoma of the small intestine have a worse prognosis than do patients with metastases of cutaneous melanoma.

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PURPOSE: To prospectively compare contrast material-enhanced harmonic compound ultrasonography (US), computed tomography (CT), and fluorine 18 fluorodeoxyglucose (FDG) positron emission tomography (PET) in detecting nodular infiltration in the spleen of patients with newly diagnosed Hodgkin lymphoma. MATERIALS AND METHODS: After institutional review board approval and informed consent, 100 consecutive patients with Hodgkin lymphoma during pretreatment staging were prospectively investigated for possible spleen involvement by comparing harmonic compound US (integrated with intravenous infusion of microbubbles in 33 patients) with CT and FDG PET. Findings indicative of malignant nodules with the imaging procedures were regarded as lymphoma infiltration; in case of discrepancy, response to treatment was regarded as evidence of lymphoma. RESULTS: Malignant nodules were detected with CT in 13 patients, with FDG PET in 13 patients, and with contrast-enhanced harmonic compound US in 30 patients. Coincidental findings of malignancy with all three imaging techniques occurred in 13 patients; 17 patients had only US-detectable malignant nodules, which showed disappearance or relevant decrease after chemotherapy. Overall, the spleen had nodular infiltration in 30 patients (13 for imaging finding concordance; 17 for typical contrast-enhanced harmonic compound US findings and chemotherapy-related nodule size modifications). Thus, both CT and FDG PET provided false-negative results in 17 of 30 patients compared with contrast-enhanced harmonic compound US, the results of which translated into disease upstaging in 13 patients. CONCLUSION: Harmonic compound US with contrast enhancement for the characterization of possible nodules provides a higher sensitivity than does CT or FDG PET in the detection of splenic involvement by Hodgkin lymphoma.


[Evaluation of PET-CT : product safety, clinical usefulness, reimbursement in Germany and the USA]

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Since 1994, PET - and later PET-CT - have gained significant clinical importance. Since 2002, PET-CT systems (PET + multislice CT) are available. The combination of high sensitivity PET images fused with high resolution CT images has gained widespread clinical acceptance for diagnosis, staging and re-staging as well as prediction of response to chemotherapy in oncology. Besides oncology, there are clear indications in diseases of the heart and the brain. The development of new systems in mainly based on multislice CT (64 slice). Radiopharmacology is advancing quickly, especially in the fields of oncology and neurological disorders. However, the limited reimbursement in Germany hampers this development.
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**Case study of anti-1-amino-3-F-18 fluorocyclobutane-1-carboxylic acid (anti-[F-18] FACBC) to guide prostate cancer radiotherapy target design.**

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PURPOSE OF THE REPORT: Anti-1-amino-3-F-18 fluorocyclobutane-1-carboxylic acid (FACBC) is a novel radiotracer, which has shown some promise for use with positron emission tomography (PET)/computed tomography (CT) for visualizing prostate cancer. Here we describe a case of a prostate cancer patient who underwent radiation treatment and had an FACBC scan obtained as part of a pilot study. METHODS: We explored the potential impact of FACBC on treatment planning. We registered the FACBC acquisition with the PET/CT, which required a simple translation. Then, we did a deformable image registration of the PET/CT with the planning CT-this process allowed the FACBC-defined gross tumor volume (GTVFACBC) to be projected into the planning CT. An intensity-modulated radiotherapy (IMRT) plan (plan A) not including GTVFACBC (with final dose to 81.0 Gy) was generated, as was an IMRT plan including the GTVFACBC to a final dose of 86.4 Gy (plan B). Target coverage and normal tissue dose volume histogram (DVH) endpoints were tabulated. RESULTS: In this particular patient, bladder constraints could not be met on any plan due to anatomic limitations. However, the impact on the rectal DVH could be assessed, and inclusion of the GTVFACBC did permit rectal DVH constraints to be met in plan B while maintaining target coverage and inhomogeneity constraints. CONCLUSION: In our test case, it was feasible to use FACBC to guide IMRT, and highlights the role of deformable image registration of the PET/CT with the planning CT. These findings can guide future studies incorporating FACBC into treatment planning.


**Detection of solitary humeral metastasis from pancreatic adenocarcinoma with F-18 FDG PET/CT.**

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**F-18 FDG PET/CT of polymyalgia rheumatica.**


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**The role of 18F-FDG PET in assessing therapy response in cancer of the cervix and ovaries.**

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For locally advanced cervical cancer, the current literature supports the use of (18)F-FDG PET for assessing treatment response 3 mo after the completion of concurrent chemoradiation. (18)F-FDG PET can provide reliable long-term prognostic information for these patients and, in the future, may be used to guide additional therapy. Investigational areas include the use of (18)F-FDG PET for monitoring response during radiotherapy and chemotherapy in the metastatic and neoadjuvant settings. For ovarian masses, the performance of (18)F-FDG PET in the detection of borderline tumors is limited, and the presence of physiologic (18)F-FDG uptake in normal ovaries of premenopausal women poses another limitation. Preliminary data suggest that the performance of (18)F-FDG PET and (18)F-FDG PET/CT is superior to that of CT alone in initial staging, but the sensitivity of both in the detection of carcinomatosis is limited. Preliminary data also suggest that (18)F-FDG PET may be promising for early prediction of response to chemotherapy and for prediction of response after the completion of chemotherapy. (18)F-FDG PET and (18)F-FDG PET/CT are most helpful in the evaluation of patients with suspected recurrent ovarian carcinoma, especially when CA-125 levels are rising and CT findings are normal or equivocal. PET and CT are complementary, and PET/CT should be used when available. Preliminary data suggest that the addition of (18)F-FDG PET/CT to the evaluation of these patients changes management in approximately a third and reduces overall treatment costs by accurately identifying patients who will or will not benefit from surgery.
PET/CT for therapy response assessment in lymphoma.

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PET with (18)F-FDG is a standard staging procedure for most lymphoma subtypes. Performed during and after therapy for Hodgkin lymphoma (HL) and aggressive non-Hodgkin lymphoma (NHL), (18)F-FDG PET results have a high prognostic value and correlate with survival. (18)F-FDG PET has been incorporated into revised response criteria for aggressive lymphomas, and several ongoing trials are under way to investigate the value of treatment adaptation based on early (18)F-FDG PET results for HL and aggressive NHL. There is little evidence to support the use of (18)F-FDG PET for monitoring of the treatment of indolent lymphomas and for routine use in the surveillance setting. So that trial results can be compared and translated easily into clinical practice, uniform and evidence-based guidelines for the interpretation and reporting of response monitoring scans are warranted. Because it is still not proven that the use of interim (18)F-FDG PET can improve patient outcomes, we recommend examination of the use of (18)F-FDG PET for response monitoring in appropriately designed clinical trials.

Standards for PET image acquisition and quantitative data analysis.

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Quantitative (18)F-FDG PET is increasingly being recognized as an important tool for diagnosis, determination of prognosis, and response monitoring in oncology. However, PET quantification with, for example, standardized uptake values (SUVs) is affected by many technical and physiologic factors. As a result, some of the variations in the literature on SUV-based patient outcomes are explained by differences in (18)F-FDG PET study methods. Various technical and clinical studies have been performed to understand the factors affecting PET quantification. On the basis of the results of those studies, several recommendations and guidelines have been proposed with the aims of improving the image quality and the quantitative accuracy of (18)F-FDG PET studies. In this contribution, an overview of recommendations and guidelines for quantitative (18)F-FDG PET studies in oncology is provided. Special attention is given to the rationale underlying certain recommendations and to some of the differences in various guidelines.

Phase 1 trial of high-dose exogenous testosterone in patients with castration-resistant metastatic prostate cancer.


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BACKGROUND: Growth of selected castration-resistant prostate cancer (CRPC) cell lines and animal models can be repressed by reexposure to androgens. Low doses of androgens, however, can stimulate tumor growth. OBJECTIVE: We performed a phase 1 clinical trial to determine the safety of high-dose exogenous testosterone in patients with castration-resistant metastatic prostate cancer (CRMPC). DESIGN, SETTING, AND PARTICIPANTS: Patients with progressive CRMPC who had been castrate for at least 1 yr received three times the standard replacement dose of transdermal testosterone. INTERVENTION: Cohorts of 3-6 patients received testosterone for 1 wk, 1 mo, or until disease progression. MEASUREMENTS: Toxicities, androgen levels, prostate-specific antigen (PSA) assays, computed tomography (CT) scans, bone scintigraphy, positron emission tomography (PET) scans, and metastatic tumor biopsy androgen receptor levels were assessed. RESULTS AND LIMITATIONS: Twelve patients were treated-three in cohorts 1 and 2 and six in cohort 3. No pain flares were noted. One patient came off study because of epidural disease, which was treated with radiation. Average testosterone levels were within normal limits, although dihydrotestosterone (DHT) levels on average were supraphysiologic in cohort 3. One patient achieved a PSA decline of >50% from baseline. No objective responses were seen. For cohort 3, median time on treatment was 84 d (range: 23-247 d). CONCLUSIONS: We have demonstrated that patients with CRMPC can be safely treated in clinical trials using high-dose exogenous testosterone. Patients did not, on average, achieve sustained supraphysiologic serum testosterone levels. Future studies should employ strategies to maximize testosterone serum levels, use contemporary methods of identifying patients with androgen receptor overexpression, and utilize PSA Working Group II Consensus Criteria clinical trial end points.
Conclusion: The RC derived from volumetric analysis of daily MVCT is prognostic and predictive for local response in patients who will eventually achieve an MCR. The total cumulative percentage of esophageal grade 3 or more toxicity was 46.7%. A proposed cut-off value for the RC of 0.0380% of the non-responders will be detected correctly while misclassifying 16.4% of evaluation was done with positron emission tomography using the radio-labeled glucose analogue F18 fluorodeoxyglucose (FDG-PET). RESULTS: The mean volume decrease (+/-standard deviation) was 73% (+/-18%). With a mean treatment time of 42 days this treatment schedule resulted in a mean decrease of 1.74%/day. Of the 13 evaluable patients seven developed a metabolic complete remission (MCR). The mean RC of the patients with MCR is 0.050 versus a mean RC of 0.023 in non-responders (p = 0.0074). Using PET/CT in defining splenic lesions in the pediatric population remains to be defined.  

Volumetric response analysis during chemoradiation as predictive tool for optimizing treatment strategy in locally advanced unresectable NSCLC.


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Purpose: To study the feasibility of measuring volumetric changes in the primary tumor on megavoltage-computed tomography (MVCT) during chemoradiation and to examine the correlation with local response. Patients and Methods: Fifteen consecutive patients with stage III, inoperable, locally advanced non-small cell lung cancer (NSCLC) were treated in a prospective dose escalation study protocol of concurrent chemoradiation. They were monitored for acute toxicity and evaluated with daily MVCT imaging. The volumetric changes were fitted to a negative exponential resulting in a regression coefficient (RC). Local response evaluation was done with positron emission tomography using the radio-labeled glucose analogue F18 fluorodeoxyglucose (FDG-PET). RESULTS: The mean volume decrease (+/-standard deviation) was 73% (+/-18%). With a mean treatment time of 42 days this treatment schedule resulted in a mean decrease of 1.74%/day. Of the 13 evaluable patients seven developed a metabolic complete remission (MCR). The mean RC of the patients with MCR is 0.050 versus a mean RC of 0.023 in non-responders (p = 0.0074). Using a proposed cut-off value for the RC of 0.0380% of the non-responders will be detected correctly while misclassifying 16.4% of patients who will eventually achieve an MCR. The total cumulative percentage of esophageal grade 3 or more toxicity was 46.7%. Conclusion: The RC derived from volumetric analysis of daily MVCT is prognostic and predictive for local response in patients treated with chemoradiation for a locally advanced NSCLC. Because this treatment schedule is toxic in nearly half of the patient population, MVCT is a tool in the implementation of patient-individualized treatment strategies.


Predictive value of early 18F-fluorodeoxyglucose positron emission tomography (FDG-PET) during salvage chemotherapy in relapsing/refractory Hodgkin lymphoma (HL) treated with high-dose ch


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This retrospective study evaluated whether early 2-[fluorine-18]fluoro-2-deoxy-D-glucose positron emission tomography (FDG-PET) after two cycles of salvage chemotherapy (PET2) could predict survival after high-dose chemotherapy (HDC). Twenty-four Hodgkin lymphoma (HL) patients were included. PET2 was negative in 58% and positive in 42% of patients. Ninety per cent of patients (9/10) with positive PET2 relapsed after HDC while all but one patient with negative PET2 maintained a complete remission. The 2-year progression-free survival was 93% vs. 10% for patients with negative and positive PET2, respectively (P < 0.001). This study shows that interim PET can predict the outcome after high-dose chemotherapy in HL patients.


Splenic hamartoma in a child in the era of PET-CT.

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We present a case of a healthy 7-year-old female with an incidental finding of a growing splenic lesion, diagnosed as a splenic hamartoma after splenectomy. This case highlights the diagnostic challenge of splenic lesions and that the role of positron emission tomography/computed tomography (PET/CT) in defining splenic lesions in the pediatric population remains to be defined.


The impact of hybrid PET-CT scan on overall oncologic management, with a focus on radiotherapy planning: a prospective, blinded study.

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Functional imaging using fluorodeoxyglucose positron-emission tomography (FDG-PET) has been increasing incorporated into radiotherapy planning in conjunction with computed tomography (CT). Hybrid FDG-PET/CT scanners allow these images to be obtained in very close temporal proximity without the need for repositioning patients, thereby minimizing imprecision when overlaying these images. To prospectively examine the impact of hybrid PET/CT imaging on overall oncologic impact, with a focus
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on radiotherapy planning, we performed a prospective, blinded trial in 111 patients. Patients with lung cancer (n=38), head-and-neck squamous cell carcinoma (n=23), breast (n=8), cervix (n=15), esophageal (n=9), and lymphoma (n=18) underwent hybrid PET/CT imaging at the time of radiation therapy planning. A physician blinded to the PET dataset designed a treatment plan using all clinical information and the CT dataset. The treating physician subsequently designed a second treatment plan using the hybrid PET/CT dataset. The two treatment plans were compared to determine if a major alteration in overall oncologic management occurred. In patients receiving potentially curative radiotherapy the concordance between CT-based and PET/CT-based GTVs was quantified using an index of conformality (CI). In 76/111 (68%) of patients, the PET/CT data resulted in a change in one or more of the following: GTV volume, regional/local extension, prescribed dose, or treatment modality selection. In 35 of these 76 cases (46%; 31.5% of the entire cohort) the change resulted in a major alteration in the oncologic management (dose, field design, or modality change). Thus, nearly a third of all cases had a major alteration in oncologic management as a result of the PET/CT data, and 29 of 105 patients (27.6%) who underwent potentially curative radiotherapy had major alterations in either dose or field design. Hybrid PET/CT imaging at the time of treatment planning may be highly informative and an economical manner in which to obtain PET imaging, with the dual goals of staging and treatment planning.


Early 2'-deoxy-2'-(18F)fluoro-D-glucose PET metabolic response after corticosteroid therapy to differentiate cancer from sarcoidosis and sarcoid-like lesions.

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PURPOSE: We aimed at investigating whether early metabolic response to corticosteroid therapy may be used as a diagnostic tool to discriminate between cancer and sarcoidosis, a well-known cause of false-positive 2-deoxy-2-[F-18]fluoro-D-glucose-positron emission tomography (FDG-PET) findings in oncology. PROCEDURE: Two cancer patients with biopsy-proven sarcoidosis or sarcoid-like reaction had multiple thoracic FDG foci. After infectious disease had been excluded, patients received oral corticosteroids for 16 and 14 days, respectively, and underwent posttherapeutic FDG-PET examination. RESULTS: Posttreatment PET revealed a complete metabolic response in both patients, and clinical and imaging follow-up showed no sign of cancer progression. CONCLUSION: Early metabolic response to systemic corticosteroid treatment may be used as a tool in the establishment of final diagnosis when sarcoidosis is suspected in a cancer patient and could be capable of differentiating cancer from sarcoidosis in the case of coexisting diseases.


Identification of residual metabolic-active areas within individual NSCLC tumours using a pre-radiotherapy (18)F-fluorodeoxyglucose-PET-CT scan.


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BACKGROUND AND PURPOSE: Non-small cell lung cancer (NSCLC) tumours are mostly heterogeneous. We hypothesized that areas within the tumour with a high pre-radiotherapy (18)F-deoxyglucose (FDG) uptake, could identify residual metabolic-active areas, ultimately enabling selective-boosting of tumour sub-volumes. MATERIAL AND METHODS: Fifty-five patients with inoperable stage I-III NSCLC treated with chemo-radiotherapy or with radiotherapy alone were included. For each patient one pre-radiotherapy and one post-radiotherapy FDG-PET-CT scans were available. Twenty-two patients showing persistent FDG uptake in the primary tumour after radiotherapy were analyzed. Overlap fractions (OFs) were calculated between standardized uptake value (SUV) threshold-based auto-delineations on the pre- and post-radiotherapy scan. RESULTS: Patients with residual metabolic-active areas within the tumour had a significantly worse survival compared to individuals with a complete metabolic response (p=0.002). The residual metabolic-active areas within the tumour largely corresponded (OF>70%) with the 50%SUV high FDG uptake area of the pre-radiotherapy scan. The hotspot within the residual area (90%SUV) was completely within the GTV (OF=100%), and had a high overlap with the pre-radiotherapy 50%SUV threshold (OF>84%). CONCLUSIONS: The location of residual metabolic-active areas within the primary tumour after therapy corresponded with the original high FDG uptake areas pre-radiotherapy. Therefore, a single pre-treatment FDG-PET-CT scan allows for the identification of residual metabolic-active areas.

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Metabolic control probability in tumour subvolumes or how to guide tumour dose redistribution in non-small cell lung cancer (NSCLC): an exploratory clinical study.


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PURPOSE: To characterize the relationship between pre-radiotherapy (18)Fluorodeoxyglucose (FDG) uptake in a tumour voxel, radiation dose and the probability to achieve metabolic control in the tumour voxel after radiotherapy. MATERIALS AND METHODS: Thirty-nine patients with inoperable stage I-II non-small cell lung cancer, treated with radiotherapy (RT) alone or sequential chemo radiation were analysed retrospectively. Twenty-two showed metabolic active areas in the tumour 3 months post-radiotherapy, which is known to be a surrogate for persistent local tumour failure and worse survival. Pre- and post-RT FDG-PET-CT scans were registered and the metabolic active zones within the tumour after RT were projected on the pre-RT scan. Multi-level logistic regression was performed to determine the relation between the FDG uptake if a voxel pre-RT and its metabolic state after RT. RESULTS: The probability that a voxel is metabolically controlled (mVCP), decreased significantly with increasing FDG uptake in a voxel (SUV) (OR=0.72), increasing tumour volume (20 cm(3)) (OR=0.89) and increasing dose (Gy) (OR=0.99). Inter-patient differences in mVCP were substantial. CONCLUSION: A methodology was presented to derive relationships between FDG uptake, dose and metabolic control. Although no strong dose effect relation was demonstrated, mVCP decreased with increasing FDG uptake and tumour volume.


Splenic metastasis from endometrial carcinoma: report of a case and review of literature.

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INTRODUCTION: Splenic metastasis from endometrial carcinoma is a rare clinical event, with only 11 cases documented previously in the literature. CASE REPORT: A 58-year-old woman had surgery and radiotherapy for stage IIB endometrial carcinoma. Eighteen months later, PET scan discovered a hypermetabolic splenic mass and two hypermetabolic lung nodules. Spleen biopsy showed metastasis from endometrial carcinoma. Chemotherapy with six cycles of cyclophosphamide, adriamycin and cisplatin effected a partial response of the splenic and lung metastasis. After few months, however, splenectomy was performed because of substantial growth of the splenic metastasis and it confirmed that the splenic metastasis was of endometrial origin and solitary in the peritoneal cavity. After splenectomy, the patient received chemotherapy with six cycles of paclitaxel. To date, 6 months after splenectomy, she is alive with no intraperitoneal disease and with few stable lung metastases. CONCLUSION: This is the 12th reported case of splenic metastasis from endometrial carcinoma. Splenic metastasis from endometrial carcinoma is usually solitary splenic metastasis limited to the splenic parenchyma. Spleenectomy is an appropriate treatment to avoid splenic rupture, splenic vein thrombosis and painful splenomegaly, to circumvent the splenic metastasis being a source of secondary metastatic disease, and to provide the potential for cure or extended survival. Since patients with splenic metastasis may be asymptomatic and the interval between the diagnoses of endometrial carcinoma and splenic metastasis may be prolonged, careful and extended follow-up after primary treatment of endometrial carcinoma is warranted.


Spectrum of focal benign musculoskeletal 18F-FDG uptake at PET/CT of the shoulder and pelvis.

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OBJECTIVE: The purpose of this article is to illustrate the spectrum of common benign intraarticular and extraarticular disorders associated with focal (18)F-FDG uptake in the shoulder and pelvic areas in oncology patients referred for PET/CT. CONCLUSION: A wide spectrum of benign musculoskeletal disorders associated with focal FDG uptake may be detected in cancer patients. This incidental uptake usually does not seem to be a clinically significant finding, but it can affect quality of life.