Respiratory motion correction for PET oncology applications using affine transformation of list mode data.

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Respiratory motion is a source of artefacts and reduced image quality in PET. Proposed methodology for correction of respiratory effects involves the use of gated frames, which are however of low signal-to-noise ratio. Therefore a method accounting for respiratory motion effects without affecting the statistical quality of the reconstructed images is necessary. We have implemented an affine transformation of list mode data for the correction of respiratory motion over the thorax. The study was performed using datasets of the NCAT phantom at different points throughout the respiratory cycle. List mode data based PET simulated frames were produced by combining the NCAT datasets with a Monte Carlo simulation. Transformation parameters accounting for respiratory motion were estimated according to an affine registration and were subsequently applied on the original list mode data. The corrected and uncorrected list mode datasets were subsequently reconstructed using the one-pass list mode EM (OPL-EM) algorithm. Comparison of corrected and uncorrected respiratory motion average frames suggests that an affine transformation in the list mode data prior to reconstruction can produce significant improvements in accounting for respiratory motion artefacts in the lungs and heart. However, the application of a common set of transformation parameters across the imaging field of view does not significantly correct the respiratory effects on organs such as the stomach, liver or spleen.
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OBJECTIVE: The purpose of this study was to compare the diagnostic performance of manually fused PET images obtained using 18F-FDG and CT images with that of CT alone, PET alone, and conventional side-by-side review of PET images and CT images (hereafter referred to as "PET + CT") in patients with suspected recurrent colorectal cancer. MATERIALS AND METHODS: Ethics committee approval and informed consent were obtained. Sixty-three patients with suspected recurrent colorectal cancer underwent whole-body 18F-FDG PET followed by diagnostic CT. The acquired PET and CT images were merged on a workstation on a pixel-to-pixel basis. CT, PET, PET + CT, and fused images were evaluated separately in terms of the presence or absence of recurrence, new metastases, or both using a 5-point grading scale (0 = definitely negative, 1 = probably negative, 2 = equivocal, 3 = probably positive, and 4 = definitely positive). Lesions determined to be grade 3 or 4 were considered positive, and diagnostic accuracy and certainty were evaluated with statistical analysis using the chi-square test for independence. RESULTS: Of 119 pathologically or clinically confirmed lesions in 36 patients, evaluation of CT, PET, PET + CT, and fused images resulted in the detection of 75 (65%), 84 (71%), 91 (76%), and 111 (93%) lesions, respectively (p < 0.01) with the number of grade 4 lesions detected being 59 (50%), 72 (61%), 84 (71%), and 108 (91%), respectively (p < 0.01). Overall, the diagnostic accuracy of CT, PET, PET + CT, and fused images according to patient were 78%, 79%, 84%, and 92%, respectively (p = 0.13). CONCLUSION: Interpreting fused images provided more accurate diagnoses than interpreting CT, PET, or PET + CT images. This method of manually fusing separately obtained PET and CT images increased the diagnostic certainty for detecting colorectal cancer recurrence and decreased the number of equivocal cases.

**Combined CT colonography and 18F-FDG PET of colon polyps: potential technique for selective detection of cancer and precancerous lesions.**


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OBJECTIVE: The purpose of this study was to determine the feasibility of imaging the colon with fused CT colonography (CTC) and 18F-FDG PET and to correlate the findings with the histologic features of polyps. SUBJECTS AND METHODS: Eighteen patients with suspected colorectal polyps enrolled in this prospective study. Before colonoscopy, 17 of the patients underwent a combination of FDG PET and CTC. CTC consisted of 4-MDCT merged with PET. PET of the abdomen and pelvis was performed after each CTC scan. One radiologist and one nuclear medicine physician in consensus analyzed PET and CTC fusion data. PET standard uptake value was correlated with the findings at histologic examination of polyps. Patient feasibility was defined as the ability to tolerate prolonged scanning with good colonic distention. Technical feasibility was determined by how closely anatomically matched polyps overlapped on fusion images. RESULTS: Seventeen of 18 patients tolerated scanning. Eighty-five percent of colon segments were optimally distended. Twenty-three of 27 FDG-avid polyps measuring 10 mm or more had excellent overlap at fusion imaging. PET depicted 23 of 39 premalignant polyps and even showed increased tracer activity associated with four small tubular adenomas (4-6 mm). Sixteen benign polyps (10-25 mm) were not depicted on PET. All nine cases of cancer (tumors measuring 11-60 mm) were detected with both PET and CTC. The standard uptake value of malignant tumors ranged from 4 to 20 (mean, 9). However, six benign flat polyps did not exhibit FDG avidity. CONCLUSION: The novel combination of CTC and PET was feasible in 17 of 18 patients and allowed excellent image correlation in 23 of 27 proven polyps measuring 10 mm or more on PET-CTC fusion. This technique shows promise in accurate anatomic correlation of both malignant and premalignant lesions evaluated with FDG PET.

**Unsuspected FDG-PET findings in the follow-up of patients with lymphoma.**


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18F-Fluorodeoxyglucose-positron emission tomography (FDG-PET) plays an increasing role in the management of patients with lymphoma, for which it is successfully used for staging and treatment monitoring. We report seven patients with a history of lymphoma who presented a positive FDG-PET suggestive of lymphoma relapse and for which FDG-PET oriented biopsies revealed alternative diagnoses. Early in lymphoma follow-up, persistence of focal increased FDG activity corresponded to inflammatory or infectious lesions in two patients: one aspergillosis and one sarcoidosis. Later in the follow-up, five cases of secondary malignancies were identified (three lung cancers, one epithoid carcinomas, and one villous tumor) in this particularly exposed population. The routine use of FDG PET to evaluate lymphoma significantly increases the probability of detecting unexpected diseases. These cases illustrate the potential pitfalls in PET follow-up. Because FDG is not lymphoma-specific, a relapse suspected only on FDG-PET imaging requires biopsy, as alternative diagnoses-infectious or malignant-are possible. Our data draws clinician's attention to potential false-positive FDG-PET findings, which may lead to therapeutic mistakes. Our data also suggests that FDG-PET might be a new imaging modality for long-term monitoring of late effects, especially second cancer occurrence.

**Positron Emission Tomography (PET) and Mammography (PEM) for Breast Cancer: Importance to Surgeons.**

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PET-Oncology

FDG-PET Detected Thyroid Incidentalomas: Need for Further Investigation?


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BACKGROUND: Incidental thyroid abnormalities are increasingly detected in patients undergoing PET scans. The aim of this study was to review our experience with the management of PET detected thyroid incidentalomas in a large single institution series. METHODS: All PET scans performed from May 2003 to July 2005 were reviewed and patients with incidental thyroid abnormalities were identified. From this group, patients that underwent further investigation were analyzed. Data relating to PET scan findings, FNA diagnoses, operative details, and histopathology was reviewed. RESULTS: In 8,800 patients, 16,300 PET scans were performed of whom 263 patients (2.9% of patients and 1.6% of PET scans) had findings positive for thyroid abnormalities. Thyroid malignancy was noted in 42% (24 patients) of the 57 patients that underwent FNA. In the group of 27 patients that were subjected to operative intervention, 74% (20 patients) were noted to have a malignant diagnosis. The final histopathology revealed primary thyroid carcinoma in all these 20 patients (19 patients with papillary carcinoma and one patient with primary thyroid lymphoma). The factors that correlated with an increased risk of malignancy were the presence of physical finding (p = 0.01) and focal (p < 0.01) or unilateral uptake (p < 0.01) on PET scan. The average SUV was not useful in differentiating benign (9.2) from malignant lesions (8.2, p = 0.7). CONCLUSIONS: PET detected incidental thyroid abnormalities are rare. In patients with positive PET scan findings and suspicious features, the incidence of primary thyroid malignancy is very high. These patients warrant further investigation followed by possible operative intervention.


11C-acetate and 18F-fluorodeoxyglucose positron emission tomography of pulmonary adenocarcinoma.

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Positron emission tomography (PET) with 11C-acetate has been recently reported in detection of slow-growing tumors, such as well-differentiated adenocarcinomas of the lung, which are often negative with 18F-fluorodeoxyglucose (FDG) PET. Here we present findings of acetate-PET and FDG-PET in a case of adenocarcinoma that was comprised of peripheral ground glass opacity and solid central components, and was histologically comprised of both a well-differentiated and a moderately-differentiated adenocarcinoma, respectively. Acetate-PET was positive in both components, whereas FDG-PET was only positive in the solid central component. The present case demonstrates the figurative findings of acetate-PET and FDG-PET in lung adenocarcinoma.


Oligometastatic non-small cell lung cancer: a multidisciplinary approach in the positron emission tomographic scan era.


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BACKGROUND: We have assessed the survival rate of patients with non-small cell lung cancer and synchronous hematogenous solitary metastasis identified with complete staging workup, including total body [18F]fluorodeoxyglucose positron emission tomography scan, and treated with a multidisciplinary approach. METHODS: We examined the database of all patients who underwent surgery for primary non-small cell lung cancer in our institute. The criteria required for inclusion in this analysis were diagnosis of non-small cell lung cancer with synchronous hematogenous solitary metastasis by staging workup with total body computed tomography scan and brain magnetic resonance if indicated, total body positron emission tomography scan, radical surgery for the primary tumors, local treatment of the solitary metastasis, and systemic chemotherapy administration. RESULTS: We analyzed the data from 1,509 patients treated from January 2000 to December 2005: 10 patients (0.7%) satisfied the selection criteria. The median overall survival was 26 months, and the median time to progression was 20 months; 6 patients were alive at the time of analysis, with a median follow-up of 30 months. Four patients were tumor progression-free after 9, 18, 23, and 32 months from the start of their treatment. CONCLUSIONS: The presentation of non-small cell lung cancer with a synchronous hematogenous solitary metastasis identified by [18F]fluorodeoxyglucose positron emission tomography containing complete staging workup is extremely rare. This subset of patients can achieve long-term survival after a multidisciplinary treatment approach.


Detection of interval distant metastases: clinical utility of integrated CT-PET imaging in patients with esophageal carcinoma after neoadjuvant therapy.

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BACKGROUND: The objective of the study was to determine the utility of integrated computed tomography / positron emission tomography (CT-PET) imaging for detecting interval distant metastases and assessing therapeutic response in patients with locally...
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advanced, potentially resectable esophageal carcinoma after neoadjuvant therapy. METHODS.: A retrospective study was performed of 88 patients with potentially resectable esophageal carcinoma who received neoadjuvant therapy before planned surgical resection. CT-PET before and after completion of neoadjuvant was used for evaluating therapeutic response; response criteria were based on qualitative and semiquantitative analyses. RESULTS.: Neoadjuvant therapy comprised chemoradiotherapy in 85 patients, with prior induction chemotherapy in 39 patients. Fifty-five patients proceeded to esophagectomy. Repeat CT-PET was performed after induction chemotherapy (n = 23) and after completing chemoradiotherapy (n = 85). CT-PET identified the interval appearance of metastatic disease in 7 (8%) patients. For assessment of locoregional therapeutic response, CT-PET was unable to predict pathological response to neoadjuvant therapy in the primary tumor or locoregional lymph nodes. CT-PET had sensitivity, specificity, and positive and negative predictive values of 57%, 46%, 39%, and 64%, respectively, for detection of residual macroscopic malignancy within the primary tumor; and sensitivity, specificity, and positive and negative predictive values of 0%, 90%, 0%, and 69% for detection of residual malignancy within resected lymph nodes. CONCLUSIONS.: CT-PET performed after neoadjuvant therapy in patients with potentially resectable esophageal carcinoma is important for detecting interval metastases that preclude surgical resection, but is of limited utility for assessing locoregional therapeutic response. Cancer 2007. (c) 2006 American Cancer Society.

How do oncologists deal with incidental abnormalities on whole-body fluorine-18 fluorodeoxyglucose PET/CT?

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BACKGROUND.: Combined positron emission tomography (PET)/computed tomography (CT) using fluorine-18 fluorodeoxyglucose (FDG) is an exciting technique for cancer evaluation, but false-positive results are a recognized limitation. The aim of the study was to evaluate how oncologists deal with focal extrathyroidal FDG abnormalities considered by imaging specialists to be unrelated to the referral indication. METHODS.: PET scan reports from a 12-month period from August 2002 to July 2003 in 1727 consecutive patients (mean age, 63 years) were reviewed. Incidental, nonphysiologic FDG abnormalities were classified based on the report conclusion. The frequency with which such abnormalities were investigated by oncologists and the final diagnosis were compared with the imaging diagnosis with a minimum potential follow-up of 2 years (mean, 27.5 months). RESULTS.: Incidental FDG abnormalities were reported in 199 (12%) of 1727 patients, including 181 with adequate follow-up. Of 59 cases with a suspected second malignancy, 34 (58%) were actively investigated, with 14 confirmed, 7 unexpected metastatic sites, and 10 other active pathologies. Only 1 further cancer was subsequently detected in the 25 (42%) patients not actively investigated. Conversely, of 122 sites presumed to be benign, only 10 (8%) were actively investigated. Only 2 were proven to relate to malignancy. CONCLUSIONS.: Although incidental abnormalities were common, most were benign and appropriately categorized by experienced readers. For actively investigated extrathyroidal abnormalities, a neoplastic basis was confirmed in over 60% of cases. Conversely, for cases deemed most likely benign by the PET/CT report or after review of readily available clinical information by the referring oncologist, the rate of malignancy was less than 2%. Cancer 2007. (c) 2006 American Cancer Society.

Incidental PET/CT Detection of Thyroid and Breast Cancer During Recurrence of Colorectal Carcinoma.

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F-18 FDG PET/CT provides an accurate staging and posttherapeutic surveillance of cancer. In the process of detecting high metabolic malignancy, this combined functional and anatomic imaging modality may demonstrate unexpected remote metastases or incidental additional primary cancers. The author presents a rare instance of concomitant thyroid papillary cancer and breast ductal carcinoma diagnosed during PET/CT evaluation of colorectal carcinoma recurrence.

Adenocarcinoma in an Indiana Pouch on PET-CT.

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We report the PET-CT appearance of adenocarcinoma in an Indiana pouch in a patient with a history of squamous cell carcinoma of the cervix diagnosed 17 years ago. As a part of her treatment regimen, an Indiana pouch was constructed. The patient was recently found to have a mass in the diversion pouch after presenting with hematuria, and subsequent biopsy confirmed moderately differentiated adenocarcinoma.

Round Pneumonia Mimicking Pulmonary Malignancy on F-18 FDG PET/CT.

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Round pneumonia is well known in the pediatric population; however, it is relatively uncommon in adults. The appearance of round pneumonia may be difficult to distinguish from lung carcinoma on anatomic images. This case illustrates a round pneumonia mimicking a pulmonary malignancy on PET/CT. In patients found to have rapid development of a round pulmonary lesion and clinical manifestations of pneumonia, it may be prudent to treat with empiric antibiotics before invasive diagnostic procedures for malignancy.


F-18 FDG PET/CT Demonstration of an Adrenal Metastasis in a Patient With Anaplastic Thyroid Cancer.

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An adrenal metastasis was identified on an F-18 FDG PET/CT scan in a patient with anaplastic thyroid cancer. There are very few reports of thyroid cancer, even anaplastic thyroid cancer, metastasizing to the adrenal.


Mismatch of F-18 Fluorodeoxyglucose (FDG) Positron Emission Tomography (PET) and Tc-99m Pertechnetate Single Photon Emission Computed Tomography (SPECT) in a Euthyroid Multinodular Goiter.

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Imaging results of F-18 fluorodeoxyglucose (FDG) PET/CT scanning and Tc-99m pertechnetate scintigraphy of the thyroid gland are described and compared with pathology in a patient who was followed after left nephrectomy for renal cell carcinoma diagnosed 10 years earlier. On F-18 FDG PET/CT scanning, a multinodular struma with increased localized F-18 FDG uptake in 4 nodules was seen. Two nodules with increased glucose metabolism appeared normal on Tc-99m pertechnetate scintigraphy. Pathology indicated hyperplastic nodules. High focal F-18 FDG uptake was also seen in a lesion that corresponded with a "cold" nodule on Tc-99m pertechnetate scintigraphy, suggesting malignant disease. However, pathology revealed hyperplastic nodules with a background of aspecific lymphocytic thyroiditis. A fourth nodule with increased F-18 FDG uptake appeared mixed ("cold"/"hot") on Tc-99m pertechnetate scintigraphy. On pathology, a well-differentiated follicular carcinoma was found. These findings, in a single patient, illustrate the wide spectrum of matched and mismatched F-18 FDG and Tc-99m pertechnetate thyroid uptake along with their variable pathologic correlates.


Integrated CT-PET Imaging of Esophageal Cancer: Unexpected and Unusual Distribution of Distant Organ Metastases.

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CT-PET imaging is being increasingly used for the initial staging, assessment of treatment response, and follow-up of patients with esophageal carcinoma, primarily because of its superior detection of distant metastases compared to conventional methods. Our recent experience has shown that metastases from esophageal cancer can occur in unusual locations and have an unexpected presentation. Recognition of the distribution and appearance of esophageal metastases is important for optimal image interpretation in order to avoid confusion with more benign disease. This article reviews the location and appearance of metastases detected by CT-PET imaging in patients with esophageal cancer either at presentation or after preoperative or definitive chemoradiation therapy.


The role of PET scanning in determining pharmacoselective doses in oncology drug development.

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Molecular imaging is the most sensitive and specific method for measuring in vivo molecular pathways in man. Its use in oncology has developed significantly over the last 5-10 years. Molecules can be labelled with positron emitting isotopes and the emitted radiation is detected using sensitive positron emission tomography (PET) cameras. It is now possible to measure in vivo and normal tissue pharmacokinetics of anti-cancer drugs and investigate their mechanism of action. Radiolabelling of tracers can be used to measure specific pharmacodynamic endpoints and target identification. Increasing evidence shows how these technologies, when added to early drug development, can rapidly reduce the time for entry into man and early identification of mechanisms of action. With the move towards more segmented markets and identification of specific subgroups, PET's use for noninvasive biomarkers will become increasingly important. However, much international effort between academia and industry is required with prioritisation of development of this technology.
Bone involvement in patients with lymphoma: the role of FDG-PET/CT.

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PURPOSE: To evaluate the diagnostic impact and clinical significance of FDG-avid bone lesions detected by FDG-PET/CT in patients with lymphoma. METHODS: The study population comprised 50 consecutive patients (mean age 41.7±15.5 years; 27 female, 23 male; 41 staging, 9 restaging) with Hodgkin's disease (n=22) or aggressive non-Hodgkin's lymphoma (n=28) in whom FDG-avid bone lesions were detected by FDG-PET/CT. All patients had either direct biopsy of the FDG-avid bone lesion (n=18), standard bone marrow biopsy at the iliac crest (BMB; n=43) or both procedures (n=11). In 15 patients, additional MRI of the bone lesions was performed. All patients underwent FDG-PET/CT after the end of treatment. All CT images of FDG-PET/CT scans were analysed independently regarding morphological osseous changes and compared with FDG-PET results. RESULTS: In the 50 patients, 193 FDG-avid lesions were found by PET/CT. The mean standardised uptake value was 6.26 (+/-3.22). All direct bone biopsies (n=18) of the FDG-avid lesions proved the presence of lymphomatous infiltration. BMB (n=43) was positive in 12 patients (27.9%). In CT, 32 of 193 (16.6%) lesions were detected without the PET information. No additional morphological bone infiltration was detected on CT compared with FDG-PET. All morphological bone alterations on CT scans persisted after the end of therapy. Additional PET/CT information regarding uni- or multifocal bone involvement resulted in lymphoma upstaging in 21 (42%) patients compared with the combined information provided by CT and BMB. CONCLUSION: In patients with FDG-avid bone lesions, FDG-PET is superior to CT alone or in combination with unilateral BMB in detecting bone marrow involvement, leading to upstaging in a relevant proportion of patients.

Value of (11)C-choline PET and PET/CT in patients with suspected prostate cancer.

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PURPOSE: The value and limitations of (11)C-choline PET and PET/CT for the detection of prostate cancer remain controversial. The aim of this study was to investigate the diagnostic efficacy of (11)C-choline PET and PET/CT in a large group of patients with suspected prostate cancer. METHODS: Fifty-eight patients with clinical suspicion of prostate cancer underwent (11)C-choline PET (25/58, Siemens ECAT Exact HR+) or PET/CT (33/58, Philips Gemini) scanning. On average, 500 MBq of (11)C-choline was administered intravenously. Studies were interpreted by raters blinded to clinical information and other diagnostic procedures. Qualitative image analysis as well as semiquantitative SUV measurement was carried out. The reference standard was histopathological examination of resection specimens or biopsy. RESULTS: Prevalence of prostate cancer in this selected patient population was 63.8% (37/58). (11)C-choline PET and PET/CT showed a sensitivity of 86.5% (32/37) and a specificity of 61.9% (13/21) in the detection of the primary resection specimens or biopsy. Results: Prevalence of prostate cancer in this selected patient population was 63.8% (37/58). (11)C-choline PET and PET/CT showed a sensitivity of 86.5% (32/37) and a specificity of 61.9% (13/21) in the detection of the primary malignancy. With regard to metastatic spread, PET showed a per-patient sensitivity of 81.8% (9/11) and produced no false positive findings. CONCLUSION: Based on our findings, differentiation between benign prostatic changes, such as benign prostatic hyperplasia or prostatitis, and prostate cancer is feasible in the majority of cases when image interpretation is primarily based on qualitative characteristics. SUV(max) may serve as guidance. False positive findings may occur due to an overlap of (11)C-choline uptake between benign and malignant processes. By providing functional information regarding both the primary malignancy and its metastases, (11)C-choline PET may prove to be a useful method for staging prostate cancer.

Diagnostic value of kinetic analysis using dynamic FDG PET in immunocompetent patients with primary CNS lymphoma.

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PURPOSE: The purpose of this study was to investigate the accumulation of FDG in immunocompetent patients with primary central nervous system (CNS) lymphoma using qualitative and quantitative PET images and to compare baseline with follow-up PET after therapy. METHODS: Twelve immunocompetent patients with CNS lymphoma were examined. Dynamic emission data were acquired for 60 min immediately following injection of FDG. In seven patients, repeated PET studies were performed after treatment. Applying a three-compartment five-parameter model, K (1), k (2), k (3), k (4), vascular fraction (V (B)) and cerebral metabolic rate of glucose (CMR(Glc)) were obtained. We evaluated the FDG uptake visually using qualitative and parametric images and quantitatively using parametric images. RESULTS: A total of 12 lesions were identified in ten patients with newly diagnosed CNS lymphoma. On visual analysis, ten lesions showed an increase on qualitative images, eight showed an increase on K (1) images, 12 showed an increase on k (3) images and ten showed an increase on CMR(Glc) images. On quantitative analysis, k (2), k (3) and CMR(Glc) values of the lesion were significantly different from those of the normal grey matter (p<0.02-0.0005). A total of three lesions were identified in two patients with recurrent tumour. All three lesions showed an increase on qualitative, k (3) and CMR(Glc) images. The K (1), k (2), k (3) and CMR(Glc) values after treatment were significantly different from those obtained before treatment (p<0.04-0.008). CONCLUSION: Kinetic analysis, especially with respect to k (3), using dynamic FDG PET might be helpful for diagnosis of CNS lymphoma and for monitoring therapeutic assessment.
Uptake of 4-borono-2-[(18)F]fluoro-L-phenylalanine in sporadic and neurofibromatosis 2-related schwannoma and meningioma studied with PET.


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PURPOSE: Meningiomas and schwannomas associated with neurofibromatosis 2 (NF2) are difficult to control by microsurgery and stereotactic radiotherapy alone. Boron neutron capture therapy (BNCT) is a chemically targeted form of radiotherapy requiring increased concentration of boron-10 in tumour tissue. PET with the boron carrier 4-borono-2-[(18)F]fluoro-L-phenylalanine ([(18)F]FBPA) allows investigation of whether 4-borono-L-phenylalanine (BPA) concentrates in NF2 tumours, which would make BNCT feasible.

METHODS: We studied dynamic uptake of [(18)F]FBPA in intracranial meningiomas (n=4) and schwannomas (n=6) of five sporadic and five NF2 patients. Tracer input function and cerebral blood volume were measured. [(18)F]FBPA uptake in tumour and brain was assessed with a three-compartmental model and graphical analysis. These, together with standardised uptake values (SUVs), were used to define tumour-to-brain [(18)F]FBPA tissue activity gradients.

RESULTS: Model fits with three parameters (K (1) (transport), k (2) (reverse transport) and k (3) (intracellular metabolism)) were found to best illustrate [(18)F]FBPA uptake kinetics. Maximum SUV was two- to fourfold higher in tumour as compared with normal brain and independent of NF2 status. The increased uptake was due to higher transport of [(18)F]FBPA in tumour. In multiple-time graphical analysis (MTGA, Gjedde-Patlak plot) the tumour-to-brain [(18)F]FBPA influx constant (K (i) -MTGA) ratios varied between 1.8 and 5.4 in NF2-associated tumours while in sporadic tumours the ratio was 1-1.4.

CONCLUSION: [(18)F]FBPA PET offers a viable means to evaluate BPA uptake in meningiomas and schwannomas in NF2. Based on our results on tumour uptake of [(18)F]FBPA, some of these benign neoplasms may be amenable to BNCT.

Low dose non-enhanced CT versus standard dose contrast-enhanced CT in combined PET/CT protocols for staging and therapy planning in non-small cell lung cancer.


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PURPOSE: To evaluate low dose non-enhanced CT and standard dose contrast-enhanced CT in combined PET/CT protocols for staging and therapy planning of non-small cell lung cancer (NSCLC). METHODS: Retrospective analysis was performed of 50 consecutive patients with proven NSCLC who had been referred for primary staging (n=41) or restaging (n=9). All patients underwent a multi-phase PET/CT consisting of a low dose non-enhanced attenuation scan and an arterial and portal-venous contrast-enhanced CT scan followed by whole-body PET. Fused datasets of non-enhanced and contrast-enhanced PET/CT were compared per patient by using the TNM staging system, and per lesion regarding localisation, characterisation and delineation of tumour lesions. The staging results were validated either by histopathology or by clinical-radiological follow-up for >6 months. RESULTS: In 47/50 patients, the results of T staging did not differ between the two PET/CT protocols. Three patients could only be correctly classified as having T4 tumours after contrast application. Regarding N staging, both protocols yielded the same results. In M staging, there was only one patient with an improvement of the results of M staging as a result of a contrast application. The lesion-based analysis of 92 sites showed no difference in the accuracy of lesion localisation and only one revision of lesion characterisation by contrast-enhanced PET/CT. The assessment of tumour delineation was altered by contrast application in 58/92 sites (p<0.0001). In 10/50 patients, contrast-enhanced PET/CT detected additional clinically important findings. CONCLUSION: In patients with advanced NSCLC, contrast-enhanced CT as part of the PET/CT protocol more accurately assessed the TNM stage in 8% of patients compared with non-contrast PET/CT. However, for planning of 3D conformal radiotherapy and non-conventional surgery, contrast-enhanced PET/CT protocols are indispensable owing to their superiority in precisely defining the tumour extent.

Impact of staging with (18)F-FDG-PET on outcome of patients with stage III non-small cell lung cancer: PET identifies potential survivors.


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PURPOSE: The aim of this study was to analyse the impact of FDG-PET staging on treatment results of neo-adjuvant radiochemotherapy in patients with advanced non-small cell lung cancer (NSCLC). We compared prospectively the outcome of two patient groups with stage III NSCLC undergoing the same neo-adjuvant radio-chemotherapy (NARCT). In one group, FDG-PET was part of the pretherapeutic staging, whereas in the other group, no PET scans were performed. METHODS: One hundred and eighty-eight patients with advanced stage III NSCLC were selected for a phase II trial of NARCT. The first 115 patients underwent conventional workup (CWU) and FDG-PET before inclusion (group I); the remaining 73 patients underwent CWU only (group II). All patients were followed up according to a standardised protocol for at least 11 months (up to 64 months). Overall survival and disease-free survival were used as parameters of therapeutic success and analysed statistically. RESULTS: After staging, 157/188 patients were included in the clinical trial. Thirty-one were excluded owing to the results of FDG-PET, in most cases because of the detection of previously unknown distant metastases. Overall survival and metastasis-free survival were significantly longer in patients of group I stratified by FDG-PET than in group II (p=0.006 and 0.02 respectively). Another significant factor for survival was complete tumour resection (p=0.02). Gender, histological tumour type, tumour grade and UICC stage had no significant influence. CONCLUSION: Pretherapeutic
staging by FDG-PET significantly influences the results of NARCT and subsequent surgery by identifying patients not eligible for curative treatment.

**Impact of hybrid fluorodeoxyglucose positron-emission tomography/computed tomography on radiotherapy planning in esophageal and non-small-cell lung cancer.**


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Purpose: The aim of this study was to investigate the impact of a hybrid fluorodeoxyglucose positron-emission tomography/computed tomography (FDG-PET/CT) scanner in radiotherapy planning for esophageal and non-small-cell lung cancer (NSCLC). Methods and Materials: A total of 30 patients (16 with esophageal cancer, 14 with NSCLC) underwent an FDG-PET/CT for radiotherapy planning purposes. Noncontrast total-body spiral CT scans were obtained first, followed immediately by FDG-PET imaging which was automatically co-registered to the CT scan. A physician not involved in the patients' original treatment planning designed a gross tumor volume (GTV) based first on the CT dataset alone, while blinded to the FDG-PET dataset. Afterward, the physician designed a GTV based on the fused PET/CT dataset. To standardize PET GTV margin definition, background liver PET activity was standardized in all images. The CT-based and PET/CT-based GTVs were then quantitatively compared by way of an index of conformality, which is the ratio of the intersection of the two GTVs to their union. Results: The mean index of conformality was 0.44 (range, 0.00-0.70) for patients with NSCLC and 0.46 (range, 0.13-0.80) for patients with esophageal cancer. In 10 of the 16 (62.5%) esophageal cancer patients, and in 12 of the 14 (85.7%) NSCLC patients, the addition of the FDG-PET data led to the definition of a smaller GTV. Conclusion: The incorporation of a hybrid FDG-PET/CT scanner had an impact on the radiotherapy planning of esophageal cancer and NSCLC. In future studies, we recommend adoption of a conformality index for a more comprehensive comparison of newer treatment planning imaging modalities to conventional options.

**Adaptive brachytherapy treatment planning for cervical cancer using FDG-PET.**


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Purpose: A dosimetric study was conducted to compare intracavitary brachytherapy using both a conventional and a custom loading intended to cover a positron emission tomography (PET)-defined tumor volume in patients with cervix cancer. Methods and Materials: Eleven patients who underwent an [(18)F]-fluoro-deoxy-D-glucose (FDG)-PET in conjunction with their first, middle, or last brachytherapy treatment were included in this prospective study. A standard plan that delivers 6.5 Gy to point A under ideal conditions was compared with an optimized plan designed to conform the 6.5-Gy isodose surface to the PET-defined volume. Results: A total of 31 intracavitary brachytherapy treatments in conjunction with an FDG-PET were performed. The percent coverage of the target isodose surface for the first implant with and without optimization was 73% and 68% (p = 0.21). The percent coverage of the target isodose surface for the mid/final implant was 83% and 70% (p = 0.02), respectively. The dose to point A was higher with the optimized plans for the first implant (p = 0.02) and the mid/last implants (p = 0.008). The dose to 2 cm(3) and 5 cm(3) of both the bladder and rectum were not significantly different. Conclusions: FDG-PET based treatment planning allowed for improved dose coverage of the tumor without significantly increasing the dose to the bladder and rectum.

**Oncogenic osteomalacia: exact tumor localization by co-registration of positron emission and computed tomography.**

Hesse E, Moessinger E, Rosenthal H, Laenger F, Brabant G, Petrich T, Gratz KF, Bastian L.

In oncogenic osteomalacia, the causative tumor is almost always difficult to find. A novel diagnostic approach is presented that facilitates a precise and rapid localization of the associated lesion by PET-CT co-registration using the radiotracer (68)Ga-DOTANOC. Introduction: Oncogenic osteomalacia (OOM) is an uncommon disorder characterized by hyperphosphaturia, hypophosphatemia, decreased vitamin D(3) serum levels, and osteomalacia. The paraneoplastic syndrome is exclusively driven by a small somatostatin receptor (sst)-positive tumor that produces phosphatonin proteins that cause renal phosphate loss. OOM can be cured completely on decreased vitamin D(3) serum levels, and osteomalacia. The paraneoplastic syndrome is exclusively driven by a small somatostatin receptor (sst)-positive tumor that produces phosphatonin proteins that cause renal phosphate loss. OOM was suspected, and a meticulous search for the tumor was initiated by conventional imaging techniques, sst-mediated imaging using (111)In-octreotide scintigraphy, and (68)Ga-DOTANOC-based positron emission tomography (PET)-CT co-registration. (68)Ga-DOTANOC is a novel radiopharmaceutical compound in which the somatostatin analog octreotide is modified at position 3, chelated with DOTA, and complexed with (68)Gallium. (68)Ga-DOTANOC has an improved affinity to sst2 and sst5 relative to other radiodeptides. Results: Whereas common imaging techniques such as CT failed to localize the tumor, (111)In-octreotide scintigraphy was able to detect the tumor, but only PET-CT using (68)Ga-DOTANOC revealed the exact tumor localization in the right femoral head. On tumor resection, the well being of the patient improved significantly, and biochemical parameters returned to normal. Conclusions: (68)Ga-DOTANOC-based PET-CT is a novel and powerful approach to detect sst-positive tumors in a timely manner and to provide highly resolved images facilitating the development of a therapeutic strategy.
T cell homing to tumors detected by 3D-coordinated positron emission tomography and magnetic resonance imaging.


A general hindrance to progress in adoptive cellular therapy is the lack of detailed knowledge of the fate of transferred cells in the body of the recipient. In this study, we present a novel technique for tracking of 124I-labeled cells in situ, which combines the high spatial resolution of magnetic resonance imaging with the high sensitivity and spatial accuracy of positron emission tomography. We have used this technique, together with determination of tissue radioactivity, flow cytometry, and microscopy, to characterize and quantitate the specific accumulation of transferred CD8+ T cells in tumor tissue in a mouse model. Transgenic CD8+ T cells, specific for the ovalbumin peptide SIINFEKL, were adaptively transferred to recipients carrying a subcutaneous tumor of the ovalbumin-expressing malignant melanoma cell line B16-OVA. The number of SIINFEKL-specific CD8+ cells in the tumor tissue was determined by flow cytometry each day for 8 consecutive days after adoptive transfer. From low levels 1 day after injection, their number gradually increased until day 5 when an average of 3.3x10^6 SIINFEKL-specific cells per gram tumor tissue was found. By applying the combined positron emission tomography/magnetic resonance imaging technique we were able to determine the position of the transferred, 124I-labeled SIINFEKL-specific T cells in 3 dimensions in recipient mice, and could demonstrate a highly significant accumulation of the 124I label in and around the subcutaneous B16-OVA tumors compared with normal tissue. Accumulation of 124I was significantly higher in B16-OVA than in B16 tumors not expressing the OVA antigen.
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Clinical Role of 18F-FDG PET/CT in the Management of Squamous Cell Carcinoma of the Head and Neck and Thyroid Carcinoma.

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(18)F-FDG PET/CT has rapidly become a widely used imaging modality for evaluating a variety of malignancies, including squamous cell carcinoma of the head and neck and thyroid cancer. Using both published data and the multidisciplinary experience at our institution, we provide a practical set of guidelines and algorithms for the use of (18)F-FDG PET/CT in the evaluation and management of head and neck cancer and thyroid cancer.

Can PET/CT Replace Separate Diagnostic CT for Cancer Imaging? Optimizing CT Protocols for Imaging Cancers of the Chest and Abdomen.


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Stage-adapted treatment in oncology relies on correct tumor staging for patients with malignant diseases. To ensure accurate assessment of the tumor stage in thoracic and abdominal diseases by PET/CT, both CT and PET need to be optimized. In this setting, different malignant diseases require customized imaging protocols. Although in the clinical setting of therapy assessment, PET/CT with integration of low-dose, nonenhanced CT may be sufficient, tumor staging may require a more sophisticated CT protocol. This review focuses on potential CT protocols for imaging cancers of the chest and abdomen. Examples of CT protocols are presented and discussed for non-small cell lung cancer, breast cancer, colorectal cancer, gastrointestinal stromal tumors, and interventional liver therapy.

Monitoring Cancer Treatment with PET/CT: Does It Make a Difference?

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PET with the glucose analog (18)F-FDG is increasingly being used to monitor the effectiveness of therapy in patients with malignant lymphomas and a variety of solid tumors. The use of integrated PET/CT instead of stand-alone PET for treatment monitoring poses some methodologic challenges for the quantitative analysis of PET scans but also provides the opportunity to integrate morphologic information and functional information. This integration may allow the definition of new parameters for assessment of the tumor response and will also facilitate the use of PET in research studies as well as in clinical practice. This review addresses how CT-based attenuation correction may affect the quantitative analysis of (18)F-FDG PET scans and summarizes the results of recent studies with PET/CT for treatment monitoring for lung cancer and gastrointestinal stromal tumors. The review concludes with an outlook on how PET/CT could make a difference in drug development and clinical management for patients.

Early Detection of Cancer Recurrence: 18F-FDG PET/CT Can Make a Difference in Diagnosis and Patient Care.

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Early detection of recurrence is clinically important and can improve the prognosis and survival of patients with cancer. CT, considered the primary method of investigation because of its low cost and widespread availability, provides high-resolution anatomic details but may underestimate the actual tumor burden by overlooking small tumor clusters in areas of distorted anatomy after treatment. (18)F-FDG PET is an effective whole-body imaging technique that detects metabolic changes preceding structural findings. However, the specificity of PET is impaired by false-positive or equivocal results attributable to the lack of precise anatomic landmarks and to sites of increased (18)F-FDG uptake of nonmalignant etiology. PET/CT provides fused images that demonstrate the complementary roles of functional and anatomic assessments in the diagnosis of cancer recurrence through the precise localization of suspected (18)F-FDG foci and their characterization as malignant or benign. In addition to the accurate diagnosis and definition of the whole extent of recurrent cancer, PET/CT has an impact on patient management because it can assist in defining potential candidates for surgery for cure, planning the appropriate surgical or radiotherapy approach, and referring patients with unresectable disease to other therapeutic options.
**Screening for Cancer with PET and PET/CT: Potential and Limitations.**

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Screening for cancer remains a very emotional and hotly debated issue in contemporary medical practice. An analysis of published data reveals a multitude of opinions based on a limited amount of reliable data. Even for breast cancer screening, which is now widely practiced in the United States and many European countries, there is continuing controversy regarding the appropriate age limits for screening mammography and, in fact, concerning the value of mammography itself. Similarly, there is no agreement as to whether screening for lung or prostate cancer is meaningful as currently practiced. Recommendations and decisions regarding cancer screening should be based on reliable data, not good intention, assumptions, or speculation. Therefore, we first explain the underlying principles and premises of screening and then briefly discuss current controversies regarding screening for breast, prostate, and lung cancers. Recently, some authors advocated CT, PET, or PET/CT for whole-body screening without support from reliable data. We discuss the potential financial, legal, and radiation safety implications associated with whole-body CT or PET cancer screening. We conclude from the available data that neither CT nor PET/CT cancer screening is currently warranted. Far from providing a desirable binary answer (presence of absence of cancer), in nonselected populations the procedures frequently yield equivocal or indeterminate findings that require further evaluation, with associated costs and potential complications. The clinical and statistical relevance of occasionally detected cancers is likely too low to justify population-wide screening efforts with these 2 imaging modalities. Ultimately, the true utility, or lack thereof, of PET and PET/CT for cancer screening can be assessed only in a prospective randomized trial. Because of prohibitive costs and the required length of follow-up, it is unlikely that such a trial will ever be conducted. Rather than spending time and resources on screening studies, medical practitioners should continue using whole-body PET/CT for diagnosing, staging, and restaging cancer and for monitoring treatment effects. Researchers should also investigate the utility of whole-body PET/CT for the surveillance of selected groups of patients who have cancer, who have completed curative treatment, but who remain at high risk for recurrent disease.

**Prediction of Absorbed Dose to Normal Organs in Thyroid Cancer Patients Treated with 131I by Use of 124I PET and 3-Dimensional Internal Dosimetry Software.**


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The objective of this work was to determine normal organ (131)I dosimetry in patients undergoing radiodine therapy for thyroid cancer by use of serial scanning with (124)I PET. METHODS: A total of 26 patients who had papillary and follicular metastatic thyroid cancer and who were already enrolled in a Memorial Sloan-Kettering Cancer Center (131)I thyroid cancer protocol were selected for this study. Imaging before (131)I therapy consisted of multiple, whole-body (124)I PET studies over a period of 2-8 d, an (18)F-FDG PET scan and, for some, a diagnostic CT scan. With a set of in-house-developed software tools (3-dimensional internal dosimetry [3D-ID] and Multiple Image Analysis Utility [MIAU]), the following procedures were performed: all PET emission and transmission and CT image sets were investigated. Imaging before (131)I therapy consists of multiple, whole-body (124)I PET studies over a period of 2-8 d, an (18)F-FDG PET scan and, for some, a diagnostic CT scan. With a set of in-house-developed software tools (3-dimensional internal dosimetry [3D-ID] and Multiple Image Analysis Utility [MIAU]), the following procedures were performed: all PET emission and transmission and CT image sets were investigated; half-life-corrected tomographic images of (131)I activity were integrated voxel by voxel to produce cumulated (131)I activity images; and the latter images were, in turn, convolved with a (131)I electron-photon point kernel to produce images of (131)I dose distribution. Cumulated activity values and calculated residence times obtained from our patient-specific dosimetry software (3D-ID)
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were used as inputs to OLINDA, and volume difference-adjusted comparisons were made between the mean dose estimates. RESULTS: With 3D-ID, dose volume histograms and mean doses were calculated for 14 organs, and results were expressed in Gy/GBq. The highest mean dose, 0.26 Gy/GBq, was seen in the right submandibular gland, whereas the lowest mean dose, 0.029 Gy/GBq, was seen in the brain. CONCLUSION: This is the first comprehensive study of normal organ dosimetry in patients by use of a quantitative tomographic imaging modality.


Segmentation of PET Volumes by Iterative Image Thresholding.

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The segmentation of metastatic volumes in PET is usually performed by thresholding methods. In a clinical application, the optimum threshold obtained from the adaptive thresholding method requires a priori estimation of the lesion volume from anatomic images such as CT. We describe an iterative thresholding method (ITM) used to estimate the PET volumes without anatomic a priori knowledge and its application to clinical images. METHODS: The ITM is based on threshold-volume curves at varying source-to-background (S/B) ratio acquired from a body phantom. The spheres and background were filled either with (18)F-FDG or Na[124]I ([124]I). These calibrated S/B-threshold-volume curves were used in estimating the volume by applying an iterative procedure. The ITM was validated with a PET phantom containing spheres and with 39 PET tumors that were discernable on CT by using whole-body (18)F-FDG (15 patients) and (124)I PET/CT (9 patients): The measured S/B ratios of the lesions were estimated from PET images, and their volumes were iteratively calculated using the calibrated S/B-threshold-volume curves. The resulting PET volumes were then compared with the known inner volume and CT volumes of tumors that served as gold standards. RESULTS: Phantom data analysis showed that the S/B-threshold-volume curves of (18)F-FDG and (124)I were similar. The average absolute deviation (expressed as a percentage of the expected volume) obtained in the PET validation phantom was 10% for volumes larger than 1.0 mL; sphere volumes of 0.5 mL showed a significantly larger deviation. For patients, the average absolute deviation for volumes between 0.8 and 7.5 mL was about 9% (31 lesions), whereas volumes larger than 7.5 mL showed an average volume mismatch of 15% (8 lesions). CONCLUSION: The ITM sufficiently estimated the clinical volumes in the range of 0.8-7.5 mL; volumes larger than 7.5 mL showed greater deviations that were still acceptable. These findings are associated with the limitation of the ITM. The ITM is especially useful for lesions that are only visible on PET. As a consequence, the lesion dosimetry is feasible with sufficient accuracy using PET images only.


Initial Experience with the Radiotracer Anti-1-Amino-3-18F-Fluorocyclobutyl-1-Carboxylic Acid with PET/CT in Prostate Carcinoma.


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Conventional imaging techniques have serious limitations in the detection, staging, and restaging of prostate carcinoma. Anti-1-amino-3-(18)F-fluorocyclobutane-1-carboxylic acid (anti-(18)F-FACBC) is a synthetic l-leucine analog that has excellent in vitro uptake within the DU-145 prostate carcinoma cell line and orthotopically implanted prostate tumor in nude rats. There is little renal excretion compared with (18)F-FDG. The present study examines anti-(18)F-FACBC uptake in patients with newly diagnosed and recurrent prostate carcinoma. METHODS: Fifteen patients with a recent diagnosis of prostate carcinoma (n = 9) or suspected recurrence (n = 6) underwent 65-min dynamic PET/CT of the pelvis after intravenous injection of 300-410 MBq anti-(18)F-FACBC followed by static body images. Each study was evaluated qualitatively and quantitatively. Maximum standardized uptake values were recorded in the prostate or prostate bed, and within lymph nodes at 4.5 min (early) and 20 min (delayed), and correlated with clinical, imaging and pathologic follow-up. Time-activity curves were also generated for benign and malignant tissue. RESULTS: In the 6 patients with newly diagnosed prostate carcinoma who underwent dynamic scanning, visual analysis correctly identified the presence or absence of focal neoplastic involvement in 40 of 48 prostate sextants. Pelvic nodal status correlated with anti-(18)F-FACBC findings in 7 of 9 patients and was indeterminate in 2 of 9. In all 4 patients in whom there was proven recurrence, visual analysis was successful in identifying disease (1 prostate bed, 3 extraprostatic). In 3 of these patients, (111)In-capromab-pendetide had no significant uptake at nodal and skeletal foci. Malignant lymph node uptake was seen in both the staging and restaging patients was significantly higher than benign nodal uptake. Though uptake faded with time, in all 6 patients with either lymph node metastases or recurrent prostate bed carcinoma, there was intense persistent uptake at 65 min. CONCLUSION: Anti-(18)F-FACBC is a promising radiotracer for imaging prostate carcinoma. Radiotracer uptake was demonstrated in primary and metastatic disease. Future research should investigate the mechanism of radiotracer uptake in normal and pathologic tissue and develop a clinical imaging strategy for initial staging and restaging.


A Preliminary Study of Anti-1-Amino-3-18F-Fluorocyclobutyl-1-Carboxylic Acid for the Detection of Prostate Cancer.


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We evaluated the feasibility of anti-1-amino-3-(18)F-fluorocyclobutyl-1-carboxylic acid (anti-(18)F-FACBC) in diagnosing prostate cancer (PCa), using a rat orthotopic prostate cancer transplantation (OPCT) model. Furthermore, using in vivo experiments, we examined the potential of anti-(18)F-FACBC for differentiating between PCa and inflammation and between PCa and benign prostatic hyperplasia.
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(BPH). METHODS: The OPCT model was developed by transplanting DU145, a human PCA cell line, into the ventral prostate of athymic F344 rats. To develop a dual PCA and inflammation (DPCI) model, MAT-Ly-Lu-B2-a rat PCA cell line was transplanted subcutaneously into male Copenhagen rats. Streptozotocin was injected into the hind footpad of these rats for inducing papillotal lymphadenitis. For inducing the BPH, normal F344 rats were castrated and injected subcutaneously with testosterone propionate. In biodistribution studies, the rats were injected with anti-(18)F-FACBC or (18)F-FDG and sacrificed at 15 or 60 min after injection. We performed dynamic small-animal PET of the abdominal portion of the OPCT rats for 60 min after the injection of anti-(18)F-FACBC or (18)F-FDG. RESULTS: The biodistribution in the OPCT rats at 60 min after injection showed that the uptake of anti-(18)F-FACBC and (18)F-FDG into the PCA tissue was 1.58 +/- 0.40 %ID/cm(3) (percentage injected dose per cm(3)) and 1.48 +/- 0.90 %ID/cm(3), respectively (P > 0.05). The accumulation of anti-(18)F-FACBC in the urinary bladder at 60 min after injection was 3.09 +/- 1.43 %ID/cm(3), whereas that of (18)F-FDG was 69.31 +/- 16.55 %ID/cm(3) (P < 0.05). Consequently, small-animal imaging with anti-(18)F-FACBC facilitated the visualization of the PCA tissue of the OPCT rats with higher contrast than (18)F-FDG. Furthermore, in comparison with (18)F-FDG, apparently higher ratios of PCA to inflammation and PCA to BPH accumulation of anti-(18)F-FACBC were demonstrated in the animal models. CONCLUSION: FACBC PET is believed to be useful not only for the visualization of human PCA but also for differentiating between PCA and inflammation and between PCAs and BHP.

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Small pulmonary nodules with little or no perceptible (18)F-FDG uptake are relatively common findings on combined PET/CT images of patients with nonthoracic malignancies. Interpreting such nodules is often a diagnostic challenge, and this study aimed to evaluate the clinical significance of the nodules. METHODS: Patients with pulmonary nodules </=1 cm in diameter showing no (18)F-FDG uptake or uptake less than the mediastinal background were included. Nodules with clearly benign or metastatic findings on CT were excluded. One hundred twenty-one patients had either tissue confirmation or clinical follow-up with additional chest images. The subjects were studied by 3 variables: (i) solitary versus multiple nodules, (ii) presence of accompanying benign lung lesion versus absence, and (iii) imperceptible (18)F-FDG uptake versus faint (18)F-FDG uptake. The malignancy rates were calculated for each variable. RESULTS: Of the 121 patients, 24 had malignancy, with a strong possibility of pulmonary metastasis (19.8%). Six of the 44 patients with solitary nodules (13.6%) and 18 of the 77 patients with multiple nodules (23.4%) had malignancies, though there was no statistically significant difference in the incidences of malignancy between the solitary and multiple groups. On the other hand, there was a statistically significant difference (P = 0.040) between the accompanying lung lesion present (8.3%) and absent (24.7%) groups. No statistically significant difference was noted between the (18)F-FDG uptake imperceptible group and faint (18)F-FDG uptake group (20.7% vs. 17.2%). CONCLUSION: For patients with incidental lung nodules of indeterminate nature with no (18)F-FDG uptake or uptake less than that of the mediastinum on PET/CT images, >19% of the cases turned out to be malignant. The nodule was more likely to be malignant when no other benign pulmonary lesions could be identified elsewhere in the lung field. Thus, regardless of the number of nodules and (18)F-FDG uptake, tissue confirmation or close imaging follow-up is necessary when small nodules with imperceptible or faint (18)F-FDG activity are present on the PET/CT images, especially in the absence of accompanying benign lung lesions.

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Utility of 18F-FDG PET/CT Uptake Patterns in Waldeyer's Ring for Differentiating Benign from Malignant Lesions in Lateral Pharyngeal Recess of Nasopharynx.

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Focally increased (18)F-FDG uptake in the lateral pharyngeal recess (LPR) of the nasopharynx due to a benign or malignant lesion is not an uncommon finding on PET images. The aim of this study was to evaluate whether, on PET/CT images, (18)F-FDG uptake occurs with characteristic patterns and intensities in various regions of Waldeyer's ring that can improve our ability to differentiate benign from malignant lesions. METHODS: Data generated from the (18)F-FDG PET/CT images of 1,628 subjects in our cancer-screening program were analyzed. Increased uptake in the LPR was observed in 80 subjects (4.9%) presenting with benign lesions, including 27 subjects without and 27 subjects with symptoms of upper airway discomfort. In addition, 30 healthy controls and 21 patients with newly diagnosed nasopharyngeal carcinoma were recruited for this study. Visual uptake, measurements of the lesions' standardized uptake value (SUV), and any abnormalities on PET/CT were evaluated. The receiver-operating-characteristic curve and area under the curve were applied to evaluate the discriminating power. RESULTS: Increased (18)F-FDG uptake (SUV, mean +/- SD) was found in the LPR, with a statistically significant (P < 0.001) difference between benign lesions (3.0 +/- 1.16) and malignant lesions (7.03 +/- 3.83). However, associated increased uptake exclusively in the palatine tonsil, lingual tonsil, and submandibular gland was found in both asymptomatic and symptomatic subjects. The ratio of LPR uptake to palatine tonsil uptake (N/P ratio) in benign lesions (0.81 +/- 0.37) was significantly (P < 0.001) lower than that in malignant lesions (2.30 +/- 1.62). Higher incidences of asymmetric (18)F-FDG LPR uptake, cervical lymph node uptake, and asymmetric wall thickening of the LPR on CT were observed in patients with nasopharyngeal carcinoma. When an SUV of less than 3.9 and an N/P ratio of less than 1.5 were used as cutoff points in subjects showing the combination of symmetric uptake in the LPR and normal or symmetric wall thickening, and detectable lymph node uptake, the area under the curve for benign lesions on PET/CT was 0.932 +/- 0.042 (95% confidence interval, 0.86-0.98), with a sensitivity of 90.4% and
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a specificity of 93.8%. CONCLUSION: The intensity and patterns of (18)F-FDG uptake in various regions of Waldeyer's ring along with CT scan findings provide a feasible modality to differentiate benign from malignant nasopharyngeal lesions.


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OBJECTIVES: 2-Deoxy-2-[F-18]fluoro-D-glucose (FDG)-positron emission tomography (PET/computed tomography (CT) is widely available as a powerful imaging modality, combining the ability to detect active metabolic processes and their morphologic features in a single exam. The role of FDG-PET is proven in a variety of cancers, including melanoma, but the estimates of sensitivity and specificity are based in the majority of the published studies on dedicated PET, not PET/CT. Therefore, we were prompted to review our experience with FDG-PET/CT in the management of melanoma. METHODS: This is a retrospective study on 106 patients with melanoma (20-87 years old; average: 56.8 +/- 15.9), who had whole-body FDG-PET/CT at our institution from January 2003 to June 2005. Thirty-eight patients (35.9%) were women and 68 patients (64.1%) were men. Reinterpretation of the imaging studies for accuracy and data analysis from medical records were performed. RESULTS: All patients had the study for disease restaging. The primary tumor depth (Breslow's thickness) at initial diagnosis was available for 76 patients (71.7%) and ranged from 0.4 to 25 mm (average: 3.56 mm). The anatomic level of invasion in the skin (Clark's level) was determined for 70 patients (66%): 3, level II; 13, level III; 43, level IV; 11, level V. The administered dose of (18)F FDG ranged from 9.8 to 21.6 mCi (average: 15.4 +/- 1.8 mCi). FDG-PET/CT had a sensitivity of 89.3% [95% confidence interval (CI): 78.5-95] and a specificity of 88% (95% CI: 76.2-94.4) for melanoma detection. CONCLUSION: This study confirms the good results of FDG-PET/CT for residual/recurrent melanoma detection, as well as for distant metastases localization. PET/CT should be an integral part in evaluation of patients with high-risk melanoma, prior to selection of the most appropriate therapy.


Assessment of response to treatment of unresectable liver tumours with 90Y microspheres: Value of FDG PET versus computed tomography.


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INTRODUCTION: Selective internal radiation therapy (SIRT) with SIR spheres (Y microspheres) is a treatment option for liver tumours in patients in whom other therapies are inappropriate or have failed. This study aims to assess the value of FDG PET in assessing the response to SIRT as compared to computed tomography (CT). MATERIAL AND METHODS: Twenty-one patients (11 F, 10 M; age range 40-75 years, mean, 58 years) received SIR spheres at the Hammersmith Hospital. One patient received two treatments. Most response to SIRT as compared to computed tomography (CT).

MATERIAL AND METHODS: Twenty-one patients (11 F, 10 M; age range 40-75 years, mean, 58 years) received SIR spheres at the Hammersmith Hospital. One patient received two treatments. Most response to SIRT as compared to computed tomography (CT).

RESULTS: Surgical pathology and follow-up with serial computed tomography scans for at least 24 months revealed 18 malignant lung lesions and 24 benign lesions less than 3.0 cm in size. The mean dose was 1.9 GBq (range, 1.2-2.5 GBq). Follow-up was done with FDG PET and CT at 6 weeks, and 6-monthly thereafter. Pre-therapy and post-therapy CT and PET scans were assessed visually (RECISt criteria for CT) and semi-quantitative for PET using the standardized uptake value (SUV). RESULT: Eighty-six percent of patients showed decreased PET activity at 6 weeks while only 13% showed a partial response in the size of tumour on CT scan. The mean pre-treatment SUV was 12.2 +/- 3.7 and the mean post-treatment SUV was 9.3 +/- 3.7 (P=0.01). CT imaging showed progressive disease in 27% patients and stable liver disease in 60% patients. Based on FDG PET results one patient had surgery for down-staged tumour. CONCLUSION: FDG PET imaging is more sensitive than CT in the assessment of early response to SIR spheres, allowing clinicians to proceed with further therapeutic options.


Comparison of lesion-to-cerebellum uptake ratios and standardized uptake values in the evaluation of lung nodules with 18F-FDG PET.

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OBJECTIVE: To evaluate the clinical performance of the lesion-to-cerebellum uptake ratio (LCR), a semiquantitative index for differentiating malignant from benign lung nodules with [18]fluorodeoxyglucose positron emission tomography (F-FDG PET). METHODS: Thirty-six patients (16 females, 20 males; median age, 73 years; range, 41-87 years) with 42 known or suspected malignant lung nodules underwent whole-body PET imaging after an intravenous injection of a mean dose of 543 +/- 69 MBq (14.7 +/- 1.9 mCi) of F-FDG. The standardized uptake value (SUV) and the LCR were calculated for each nodule and receiver operating characteristic (ROC) curves were analyzed using the ROCKIT 0.9B software package. RESULTS: Surgical pathology and follow-up with serial computed tomography scans for at least 24 months revealed 18 malignant lung lesions and 24 benign lesions less than 3.0 cm in size. The mean LCR was 0.70 +/- 0.40 for malignant nodules and 0.23 +/- 0.12 for benign nodules (P<0.001, two-tailed test). The area under the estimated ROC curve was 0.8660 for SUV data and 0.9197 for LCR data (P=0.2408, two-tailed test). CONCLUSIONS: The LCR method appears to be a valuable semiquantitative index for the evaluation of malignancy in pulmonary nodules with F-FDG PET, which is simple to perform clinically and does not require accurate measurements of body weight or the residual activity in the syringe utilized for F-FDG injection.
The role of integrated computed tomography positron-emission tomography in esophageal cancer: staging and assessment of therapeutic response.

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Computed tomography (CT) and endoscopy/endoscopic ultrasonography are usually performed to initially stage patients with esophageal cancer, to determine primary tumor response, and to detect nodal and distant metastases after preoperative therapy. Positron-emission tomography (PET) with [18F]-fluoro-2-deoxy-D-glucose and integrated CT-PET are useful in the initial staging of patients with esophageal cancer as well as in the prediction of pathologic response, disease-free interval, and overall survival after preoperative therapy. Importantly, integrated CT-PET imaging decreases the number of futile attempts at surgical resection, mainly because of the detection of occult distant metastases. The following sections review the use of integrated CT-PET imaging in determining the T, N, and M descriptors of the American Joint Commission on Cancer’s 2002 guidelines for pathologic and clinical staging at initial diagnosis and after chemoradiation therapy in those patients being considered for surgical resection.

PET/CT and MR imaging in myeloma.

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Myeloma is the most common primary bone malignancy. It accounts for 10% of all hematological malignancies and 1% of all cancers. In the United States, there are an estimated 16,000 new cases and over 11,000 deaths yearly due to myeloma. Plasma cell dyscrasias manifest themselves in a variety of forms that range from MGUS (monoclonal gammopathy of undetermined significance) and smoldering myeloma that require no therapy, to the "malignant" form of multiple myeloma. The role of imaging in the management of myeloma includes: an assessment of the extent of intramedullary bone disease, detection of any extramedullary foci, and severity of the disease at presentation; the identification and characterization of complications; subsequent assessment of disease status. This review will focus on the use of PET/CT and MR imaging for myeloma patients at the time of initial diagnosis and for follow-up management, based on current reports in the literature and our practice at the Marlene and Stewart Greenebaum Cancer Center, University of Maryland Medical Center in Baltimore, USA.

Preoperative evaluation of thyroid nodules with 18FDG-PET/CT or MIBI scan?

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Fluorine-18 fluorodeoxyglucose PET in the preoperative staging of colorectal cancer.


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INTRODUCTION: In patients with colorectal cancer (CC), preoperative evaluation and staging should focus on techniques that might alter the preoperative or intraoperative surgical plan. Conventional imaging methods (CT, MRI) have low accuracy for identifying the depth of tumour infiltration and have limited ability to detect regional lymph node involvement. The aim of this study was to evaluate the utility of FDG-PET in the initial staging of patients with CC in comparison with conventional staging methods and to determine its impact on therapeutic management. METHODS: One hundred and four patients with a diagnosis of CC (53 males and 51 females; mean age 66.76 +/- 12.36 years), selected prospectively, were studied for staging using a standard procedure (CT) and FDG-PET. When possible, the reference method was histology. RESULTS: In 14 patients, surgery was contraindicated by FDG-PET owing to the extent of disease (only 6/14 suspected by CT). FDG-PET revealed four synchronous tumours. For N staging, both procedures showed a relatively high specificity but a low diagnostic accuracy (PET 56%, CT 60%) and sensitivity (PET 21%, CT 25%). For M assessment, diagnostic accuracy was 92% for FDG-PET and 87% for CT. FDG-PET results led to modification of the therapy approach in 50% of patients with unresectable disease. FDG-PET findings were important, revealing unknown disease in 19.2%, changing the staging in 13.46% and modifying the scope of surgery in 11.54% (with a change in the therapeutic approach in 17.85% of those patients with rectal cancer). CONCLUSION: Compared with conventional techniques, FDG-PET appears to be useful in pre-surgical staging of CC, revealing unsuspected disease and impacting on the treatment approach.
PET imaging with [(18)F]3'-deoxy-3'-fluorothymidine for prediction of response to neoadjuvant treatment in patients with rectal cancer.


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PURPOSE: Positron emission tomography (PET) using [(18)F]-labelled 3-deoxy-3'-fluorothymidine (FLT) was assessed for therapy monitoring in patients with rectal cancer undergoing neoadjuvant chemoradiotherapy. METHODS: Ten patients with locally advanced rectal cancer were included and underwent long-course preoperative chemoradiotherapy (total dose 45 Gy, 1.8 Gy/day, concomitant 250 mg/m(2) 5-fluorouracil) followed by surgery. FLT-PET was performed prior to chemoradiotherapy, 2 weeks after initiation of chemoradiotherapy and preoperatively (3-4 weeks post chemoradiotherapy). FLT uptake was correlated with histopathological tumour regression and changes in T stage. RESULTS: Mean tumour FLT uptake was 4.2±1.0 SUV before therapy and decreased significantly to 2.9±0.6 SUV 14 days after initiation of chemoradiotherapy (-28.6%±10.7%, p = 0.005). The preoperative scan showed a further decrease to 1.9±0.4 SUV (-54.7%±7.6%, p = 0.005). However, the degree of change in FLT uptake 2 weeks after initiation and after completion of neoadjuvant therapy did not correlate with histopathological tumour regression. CONCLUSION: FLT-PET did not seem to be a promising method for assessment of tumour response in the studied chemoradiotherapy regimen in patients with rectal cancer.
**PET-Oncology**

define the GTV for NSCLC. Although the quantitative absolute target volume is sometimes similar, the qualitative target locations can be substantially different, leading to underdosage of the target when planning is done using CT alone without PET fusion.

Mol Imaging Biol. 2006 Dec 21

**Detection of Occult Medullary Thyroid Cancer Recurrence with 2-Deoxy-2-[F-18]fluoro-D-glucose-PET and PET/CT.**

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PURPOSE: 2-Deoxy-2-[F-18]fluoro-D-glucose (FDG)-positron emission tomography (PET) has an established role in restaging of various cancers, including papillary and undifferentiated thyroid carcinoma. However, controversies exist regarding its ability to reliably assess recurrent medullary thyroid cancer (MTC). We were therefore prompted to review our experience with FDG-PET for detection of occult MTC. METHODS: This is a retrospective study (Apr 1, 1997-Mar 31, 2004) of 13 patients with histologic diagnosis of MTC, who had PET examinations. The group included six men and seven women, 15-62 years old (average: 48 +/- 13). The PET scan request was triggered by rising levels of calcitonin and negative anatomical imaging studies. RESULTS: Recurrent/metastatic disease was identified by PET in seven (54%) of the 13 patients. The lesions were located in superior mediastinum (4), cervical lymph nodes (3), thyroid bed (2), lung (1) and liver (1). The calcitonin levels ranged from 52 to 5,090 pg/ml (average: 1,996 pg/ml) in patients with negative PET scans and from 132 to 9,500 pg/ml (average: 3,757 pg/ml) in patients with positive studies. The sensitivity and specificity of FDG-PET for disease detection in this cohort were 85.7% (95% CI: 48.7-97.4) and 83.3% (95% CI: 43.6-96.9), respectively. CONCLUSION: Our findings suggest a significant role for FDG-PET in patients with suspected MTC recurrence, with sensitivity of 85.7% and specificity of 83.3% for disease detection. FDG-PET provides additional information in a significant fraction of cases (54%) and could be used for restaging of patients with MTC and elevated levels of biomarkers (calcitonin). Additional studies are necessary to further evaluate the role of FDG-PET in MTC.


**Integrated PET/CT as a first-line re-staging modality in patients with suspected recurrence of ovarian cancer.**


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PURPOSE: The aims of this study were to compare CT with PET/CT results in patients with suspected ovarian cancer recurrence and to assess the impact of the PET/CT findings on their clinical management. METHODS: Thirty-two consecutive patients with suspected ovarian cancer recurrence were retrospectively included in the study. Abdominal contrast-enhanced CT and PET/CT with [(18)F]FDG, in addition to conventional follow-up, were performed in all 32 patients. After the comparison between CT and PET/CT results, based on clinical reports, changes in the clinical management of patients (intermodality changes) due to PET/CT information were analysed. RESULTS: Twenty of the 32 patients were positive at CT (62.5%) versus 29 (90.6%) at PET/CT. Intermodality changes in management, i.e. use of a different treatment modality, after PET/CT examination were indicated in 14/32 (44%) patients. In particular, before PET/CT study, the planned management was as follows: wait-and-see in 7/32 (22%), further instrumental examinations in 4/32 (12%), chemotherapy in 10/32 (31%), diagnostic surgical treatment in 6/32 (19%) and surgical treatment in the remaining 5/32 (16%). After PET/CT study, wait-and-see was indicated in 1/32 (3%), further instrumental examinations in 7/32 (22%), chemotherapy in 16/32 (50%), diagnostic surgical treatment in 2/32 (6%) and surgical treatment in the remaining 6/32 (19%). CONCLUSION: Integrated PET/CT could detect tumour relapse in a higher percentage of patients than could CT. A change in the clinical management was observed in 44% of cases when PET/CT information was added to conventional follow-up findings.

Radiol Med (Torino). 2006 Dec 20

**(18)F-FDG PET/CT in the assessment of carcinoma of unknown primary origin.**


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PURPOSE: Metastatic cancers of unknown primary origin are characterised by a poor prognosis, with a survival rate from diagnosis of approximately 12 months. Conventional radiological imaging allows detection of 20%-40% of primary cancers, whereas the detection rate with positron emission tomography (PET) is 24%-40%. The aim of this study was to assess the role of (18)F-fluorodeoxyglucose (FDG) PET/computed tomography (CT) in the identification of occult primary cancers. MATERIALS AND METHODS.: The study population consisted of 38 consecutive patients with histologically proven metastatic disease and negative or nonconclusive conventional diagnostic procedures. All patients were studied by (18)F-FDG PET performed according to the standard procedure (6 h of fasting, intravenous injection of 370 MBq (18)F-FDG, and image acquisition with a PET/CT scanner for 4 min per bed position). RESULTS.: (18)F-FDG-PET/CT detected the occult primary cancer in 20 cases (53%), showing higher sensitivity than that reported for any other imaging modality, including PET. CONCLUSIONS.: The encouraging results, if validated by larger series, support the use of PET/CT in patients with carcinoma of unknown primary origin and negative conventional imaging results.
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2-Deoxy-2-[F-18]Fluoro-D-glucose Positron Emission Tomography Illustrates Two Visceral Tumors in a Post Kidney Transplant Patient with Multiple Cutaneous Malignancies.

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The success of renal transplantation brings with it the dilemma of managing patients with complications from lifelong immunosuppressive therapy. Immunosuppressed transplant recipients are a special population with significantly increased risk for development of skin cancers. Because malignant tumors are increasing as demonstrated on 2-deoxy-2-[F-18]fluoro-d-glucose (FDG) positron emission tomography (PET) image, we report the unusual coincidence of multiple cutaneous cancers and two visceral malignancies 20 years after renal transplantation. The malignancies include basal cell and squamous cell carcinomas and malignant fibrous histiocytoma. FDG-PET images show, in this case, visceral masses with increased metabolism: one in the left upper lung and one in the abdomen, corresponding to individual mass lesions observed on computed tomography (CT) images of the chest and abdomen. A fine-needle biopsy of the nodule of the left upper lung lobe yielded a diagnosis of a sarcoma. The mass lesion of the abdomen had caused bowel obstruction, requiring exploratory laparotomy; histopathological findings from the resected mass from the abdomen confirmed the diagnosis malignant fibrous histiocytoma. This long-term immune suppressed transplant recipient developed viscerally located malignant lesions demonstrated by FDG-PET imaging and three types of cutaneous malignancies (skin cancers).


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OBJECTIVES: To investigate the existence of quantum metabolic values in various subtypes of non-Hodgkin's lymphoma (NHL).

METHODS: Fifty-eight patients with newly diagnosed NHL and positron emission tomography (PET) performed within three months of biopsy were included. The standardized uptake value (SUV) from PET over the area of biopsy and serum glucose [Glc] were recorded. The group glucose sensitivity (G) for indolent and aggressive NHL was obtained by linear regression with ln(SUV) = G*ln[Glc] + C, where C is a constant for the group. Finally, the individual's glucose sensitivity (g) was obtained by g = {ln(SUV)-C}/ln[Glc], along with their means in various subtypes of NHL. To further investigate the influence of extreme [Glc] conditions, the SUVs corrected by the individually calculated g at various glucose levels, [Glc] using SUV = SUV ([Glc]'/[Glc]) (g), were compared to the original SUVs for both indolent and aggressive NHL.

RESULTS: The averaged g (=G) for aggressive was significantly different from that for indolent NHL (-0.94 +/- 0.51 vs. +0.13 +/- 0.10, respectively, p < 0.00005). There were significant differences in SUV for [Glc] < 80 or >110 mg/dl for both types of NHL. Unlike overlap among SUVs between NHL subtypes, the g value clearly categorized them into two distinct groups with positive (near-zero) and negative g values (around -1) for the indolent and aggressive NHLs, respectively.

CONCLUSIONS: Distinct quantum metabolic values of -1 and 0 were noted in NHL. Aggressive NHL has a more negative value (or higher glucose sensitivity) than that of indolent and, thus, is more susceptible to extreme glucose variation.

Multiple Myeloma: Molecular Imaging with 11C-Methionine PET/CT--Initial Experience.


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Purpose: To prospectively assess molecular imaging of multiple myeloma (MM) by using the radiolabeled amino acid carbon 11 ([11]C) methionine and positron emission tomography (PET)/computed tomography (CT). Materials and Methods: The study was approved by the institutional local ethics committee and the national radiation protection authorities. All patients with MM and control patients gave written informed consent. Nineteen patients with MM (11 women, eight men; age range, 42-64 years) and 10 control patients with hyperparathyroidism without hematologic diseases (six women, four men; age range, 43-75 years) underwent PET/CT 20 minutes after injection of a mean of 1.0 GBq +/- 0.2 (standard deviation) ([11]C-methionine. Presence and extent of CT-assessed tumor manifestations and ([11]C-methionine bone marrow (BM) uptake were determined on the basis of maximum standardized uptake value (SUV(max)). MM imaging patterns, normal BM, and maximal lesion ([11]C-methionine uptake in patients with MM were compared with those in control patients. In two patients with MM, sulfur 35 ([35]S) methionine uptake in freshly isolated BM plasma cells was measured. Values for SUV(max) of groups were compared by using the Mann-Whitney test on a per-patient basis. Results: ([35]S) methionine uptake of plasma cells was five- to sixfold higher than in normal BM cells. ([11]C-methionine BM uptake in control patients was homogeneous and low. All patients with MM except one with exclusively extramedullary myeloma had ([11]C-methionine-positive lesions. Maximal lesion and normal BM ([11]C-methionine mean SUV(max) were 10.2 +/- 3.5 and 4.3 +/- 2.0, respectively, and thus were significantly higher than that of BM in the control group (mean, 1.8 +/- 0.3; P < .001). Extramedullary MM was clearly visible in three patients (mean SUV(max), 7.2 +/- 2.4). Additional ([11]C-methionine-positive lesions in normal cancellous bone were found in nearly all patients with MM. In pretreated patients with MM, a moderate fraction of osteolytic lesions had no ([11]C-methionine uptake. Conclusion: On the basis of increased methionine uptake in plasma cells, active MM can be imaged with ([11]C-methionine PET/CT. (c) RSNA, 2006.
PET-Oncology

Multimodality imaging features in a case of bronchial carcinoid including FDG PET.


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Background: Pulmonary carcinoid tumors are rare, low-grade neuroendocrine malignancies which comprise 1-2% of all lung neoplasms. Approximately 80% of carcinoid tumors occur in the central airways and present clinically as obstructive pneumonia or hemoptysis. Experience with F18 FDG PET to image pulmonary carcinoid tumors is limited. Case Report: A 67 year old woman presented with two episodes of hemoptysis within one month. A whole body FDG PET scan was performed in addition to a contrast enhanced chest CT, a whole body In111 octreotide scan, and quantitative lung perfusion scan during the diagnostic evaluation. An endobronchial lesion was discovered and the patient underwent a successful resection of the right middle and lower lobes. The histopathology of the lesion was consistent with a typical carcinoid tumor. Conclusions: We describe multimodality imaging findings along with the histopathology and a review of the literature, focusing on the role of FDG PET in the management of patients with bronchial carcinoid tumors.

Positron emission tomography in oncology.

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dagger Department of Radiology.

Increasing access to positron emission tomography-computed tomography (PET-CT) has resulted in a shift towards functional imaging, being the primary tool in the assessment of viable tumour in oncology patients. In this review, we discuss the basic principles of this evolving technology and the radio-isotopes it employs. The main clinical applications of PET-CT are reviewed and some of the limitations of the technique are highlighted. Finally, we offer insight into possible future developments and how these modify current practice.

The role of 2-deoxy-2-[F-18]fluoro-D-glucose positron emission tomography in disseminated carcinoma of unknown primary site.

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BACKGROUND.: The authors conducted a comprehensive review of the efficacy of 2-deoxy-2-[F-18]fluoro-D-glucose positron emission tomography (FDG-PET) in the detection of primary tumors in patients with disseminated carcinoma of unknown primary site. METHODS.: Ten studies (involving a total of 221 patients) that were published between 1998 and 2006 were reviewed. Each study evaluated the role of FDG-PET in the detection of unknown primary tumors after a conventional diagnostic workup. Although 94% of patients had a single site of metastases, the studies otherwise were very heterogeneous in the studied population, study design, and additional diagnostic workup. RESULTS.: In 41% of patients, FDG-PET detected primary tumors that were not apparent after conventional workup. In this group of patients, the overall sensitivity, specificity, and accuracy rates of FDG-PET in detecting unknown primary tumors were 91.9%, 81.9%, and 80.5%, respectively. FDG-PET imaging also led to the detection of previously unrecognized metastases in 37% of patients. Lung cancers represented 59% of the detected tumors. FDG-PET had a notably high false-positive rate (58.3%) in tumors of the lower digestive tract. FDG-PET altered the clinical management in 34.7% of patients. Most of those patients (53%) received specific chemotherapy for lung and pancreatic cancers; whereas 12% received specific therapy for breast, ovarian, and prostate cancers; and 14% underwent surgery with curative intent. CONCLUSIONS.: FDG-PET was an efficient method for detecting primary tumors that were undetected by other modalities and was sensitive for the detection of previously unrecognized metastases. FDG-PET significantly changed clinical management in approximately one-third of the patients studied. Cancer 2007. (c) 2006 American Cancer Society.

A comparative study on the value of FDG-PET and sentinel node biopsy to identify occult axillary metastases.


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BACKGROUND: Sentinel node biopsy (SNB) has become a standard treatment in staging axillary lymph nodes in early breast cancer. SNB, however, is an invasive procedure and is time-consuming when the sentinel node is analysed intra-operatively. Breast cancer is frequently characterised by increased 2-fluoro-2-deoxy-D-glucose uptake and many studies have shown encouraging results in detecting axillary lymph node metastases. The aim of this study was to compare SNB and -positron emission tomography (-PET) imaging, to assess their values in detecting occult axillary metastases. PATIENTS AND METHODS: In all, 236 patients with breast cancer and clinically negative axilla were enrolled in the study. 18-FDG-PET was carried out before surgery, using a positron emission tomography (PET)computed tomography scanner. In all patients, SNB was carried out after identification through lymphoscintigraphy. Patients
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underwent axillary lymph nodes dissection (ALND) in cases of positive FDG-PET or positive SNB. The results of PET scan were compared with histopathology of SNB and ALND. RESULTS: In all, 103 out of the 236 patients (44%) had metastases in axillary nodes. Sensitivity of FDG-PET scan for detection of axillary lymph node metastases in this series was low (37%); however, specificity and positive predictive values were acceptable (96% and 88%, respectively). CONCLUSIONS: The high specificity of PET imaging indicates that patients who have a PET-positive axilla should have an ALND rather than an SNB for axillary staging. In contrast, FDG-PET showed poor sensitivity in the detection of axillary metastases, confirming the need for SNB in cases where PET is negative in the axilla.

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Objective: Therapeutic decision-making in metastatic renal cell carcinoma (MRCC) is based on conventional radiological evaluation. Fluorodeoxyglucose positron emission tomography (FDG-PET) scans may modify this strategy. Methods: Patients with MRCC for whom a therapeutic decision had been made underwent an FDG-PET scan in order to complete the standard radiological evaluation. Results: Twenty-four patients and 26 FDG-PET scans were eligible. In 18 patients, metastatic disease was evaluable on the computed tomography (CT) scan; the FDG-PET scan was positive in 16 patients and negative in 10. In 2 patients, the FDG-PET scan was positive while they were considered disease free on radiological evaluation. In 5 patients (20.8%), the previous therapeutic decision was changed. Thirteen patients had a pathological evaluation for 19 sites. One patient out of 13 had a false-positive FDG-PET scan, while 4 sites out of 6 were false-negative. The sensitivity was 75% (95% CI: 47.6-92.7) and the predictive positive value was 92.3% (95% CI: 64-99.8). With a median follow-up of 24 months, 3 patients developed new metastatic sites. Conclusion: Our data suggest that, when positive, an FDG-PET scan may modify the decision made: when negative, it should not modify decision-making especially for surgery, owing to its sensitivity. Copyright (c) 2006 S. Karger AG, Basel.

Distributions of positron-emitting nuclei in proton and carbon-ion therapy studied with GEANT4.

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Depth distributions of positron-emitting nuclei in PMMA phantoms are calculated within a Monte Carlo model for heavy-ion therapy (MCHIT) based on the GEANT4 toolkit (version 8.0). The calculated total production rates of (11)C, (10)C and (15)O nuclei are compared with experimental data and with corresponding results of the FLUKA and POSGEN codes. The distributions of e(+) annihilation points are obtained by simulating radioactive decay of unstable nuclei and transporting positrons in the surrounding medium. A finite spatial resolution of the positron emission tomography (PET) is taken into account in a simplified way. Depth distributions of beta(+) activity as seen by a PET scanner are calculated and compared to available data for PMMA phantoms. The obtained beta(+) activity profiles are in good agreement with PET data for proton and (12)C beams at energies suitable for particle therapy. The MCHIT capability to predict the beta(+) activity and dose distributions in tissue-like materials of different chemical composition is demonstrated.

Diagnostic accuracy of colorectal cancer staging with whole-body PET/CT colonography.


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CONTEXT: Staging of patients with colorectal cancer often requires a multimodality, multistep imaging approach. Colonography composed of a combined modality of positron emission tomography (PET) and computed tomography (CT) provides whole-body tumor staging in a single session. OBJECTIVES: To determine the staging accuracy of whole-body PET/CT colonography compared with the staging accuracies of CT followed by PET (CT + PET) and CT alone and to evaluate the effect of PET/CT colonography on therapy planning compared with conventional staging (CT of the abdomen and thorax and optical colonoscopy). DESIGN, SETTING, AND PATIENTS: Prospective study of 47 patients enrolled between May 2004 and June 2006 with clinical findings and optical colonoscopy that suggested primary colorectal cancer (mean [SD] age, 71 [11] years; range, 47-92 years). Patients underwent whole-body PET/CT colonography 1 day after colonoscopy. The study was conducted at a university hospital with a mean (SD) follow-up of 447 (140) days (range, 232-653 days). MAIN OUTCOME MEASURES: Correct classification of overall TNM stage using PET/CT colonography compared with CT + PET and CT alone. Secondary outcome measures were the accurate assessment of T-stage, N-stage, and M-stage by PET/CT colonography compared with CT + PET and CT alone and the effect of PET/CT colonography on therapy planning. RESULTS: Of the 47 patients with a total of 50 lesions, the overall TNM stage was correctly determined for 37 lesions with PET/CT colonography (74%; 95% confidence interval [CI], 60%-85%), 32 lesions with CT + PET (64%; 95% CI, 49%-77%), and 26 lesions with CT alone with a threshold of 0.7 cm for malignant nodes but were detected with a threshold of 1 cm. Differences were not detected in defining M-stage
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separately or when comparing the accuracies of PET/CT colonography with CT + PET. PET/CT colonography affected consecutive therapy decisions in 4 patients (9%; 95% CI, 2.4%-20.4%) compared with conventional staging (CT alone and colonoscopy).

CONCLUSIONS: In this preliminary study, PET/CT colonography is at least equivalent to CT + PET for tumor staging in patients with colorectal cancer. Thus, PET/CT colonography in conjunction with optical colonoscopy may be a suitable concept of tumor staging for patients with colorectal cancer.


1-{[11C]-acetate PET imaging in head and neck cancer-a comparison with (18)F-FDG-PET: implications for staging and radiotherapy planning.


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PURPOSE: The aim of this study was to evaluate the feasibility of using 1-{[11C]-acetate positron emission tomography (ACE-PET) to detect and delineate the gross tumour volume of head and neck cancer before radiotherapy, and to compare the results with those obtained using (18)F-fluoro-2-deoxy-D-glucose (FDG) PET. METHODS: Ten patients with histologically verified squamous cell carcinoma were investigated by FDG-PET and dynamic ACE-PET prior to radiotherapy. The two scans were performed on the same day or on consecutive days, except in one patient in whom they were done 5 days apart. Diagnostic CT or MRI was performed in all patients. The image data sets were analysed both visually and semi-quantitatively. All primary tumours and metastases were delineated automatically by using the 50% threshold of maximum radioactivity corrected for background. The mean standardised uptake value (SUV) and the tumour volumes were evaluated and compared. RESULTS: All ten primary tumours were detected by ACE-PET, while nine primaries were detected by FDG-PET and CT and/or MRI. The ACE SUV tended to be lower than the FDG SUV (5.3+/-2.7 vs 9.6+/-7.0, p=0.07). The tumour volumes delineated with ACE were on average 51% larger than the FDG volumes (p<0.05). ACE-PET identified 20/21 lymph node metastases, while only 13/21 lesions were detected by FDG-PET and 16/21 lesions by CT or MRI. CONCLUSION: ACE-PET appears promising for the staging of head and neck cancer. The biological information provided by both FDG and ACE-PET, especially in radiotherapy.

Gynecol Oncol. 2006 Dec 5

The positron emission tomography with F18 17beta-estradiol has the potential to benefit diagnosis and treatment of endometrial cancer.

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BACKGROUND: The positron emission tomography (PET) with F18 17beta-estradiol (FES) has good imaging for assessment of estrogen receptor in breast cancer. CASE.: We report on a 30-year-old woman who desired to preserve her fertility with well-differentiated endometrial adenocarcinoma. Before hormone treatment was started, FES-PET showed increased uptake of endometrium, magnetic resonance imaging (MRI) showed thickness and F-18 fluorodeoxyglucose (FDG)-PET showed increased uptake. FES-PET after 3 months showed remaining FES uptake, but there were no abnormal findings on MRI and FDG-PET. Hysteroscopy showed remaining adenocarcinoma. After additional treatment, FES-PET showed a therapeutic response, and hysteroscopy showed no abnormal finding. CONCLUSIONS: To our knowledge, this is the first report that FES-PET has the potential to provide more useful information than did FDG-PET about the hormone therapy.


18F-choline PET/CT for initial staging of advanced prostate cancer.

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18F-Fluoro-deoxy-glucose positron emission tomography in lymphoma of mucosa-associated lymphoid tissue: histology makes the difference.

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BACKGROUND: The usefulness of 2-[fluorine-18]fluoro-2-deoxy-D-glucose Positron emission tomography (18F-FDG-PET) in lymphoma of mucosa-associated lymphoid tissue (MALT lymphoma) is still a matter of debate, and conflicting results have been reported. We have evaluated whether the histological feature of plasmacytic differentiation (PD) might explain the heterogeneous behavior of MALT lymphoma regarding 18F-FDG uptake. PATIENTS AND METHODS: A total of 35 patients with a diagnosis of MALT lymphoma referred to our PET unit were studied. Whole-body 18F-FDG-PET scans were carried out on a General Electrics advanced PET scanner 40 min after i.v. injection of 300-380 MBq 18F-FDG. Images were reconstructed iteratively. In areas with focally elevated FDG uptake, standard uptake values (SUVs) were calculated. RESULTS: A total of 19 patients had MALT lymphoma with
plasmacytic differentiation (pMALT), while MALT lymphoma without plasmacytic features was diagnosed in 16 patients. Sixteen of 19 patients with PD showed significant 18F-FDG uptake in involved sites (SUV: 3.5-11.7). By contrast, 13 of 16 patients with normal MALT lymphoma showed a false-negative 18F-FDG-PET result. Two of these patients disclosed no tracer uptake in the majority of involved sites apart from one single lesion, while three had a true-positive 18F-FDG-PET scan (SUV: 3.4-6.0). CONCLUSIONS: 18F-FDG-PET visualizes pMALT in a high proportion of patients, whereas FDG-PET results are significantly less reliable in typical MALT (P = 0.001). This finding may partly account for the heterogeneous results of 18F-FDG-PET-studies in MALT lymphoma.

Arch Surg. 2006 Dec;141(12):1220-6; discussion 1227.

Preoperative positron emission tomography to evaluate potentially resectable hepatic colorectal metastases.

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HYPOTHESIS: Positron emission tomography (PET) influences clinical management in the preoperative evaluation of patients with hepatic metastases from colorectal cancer. DESIGN: Prospective cohort study. SETTING: Academic tertiary care center. PATIENTS: From January 1, 2000, through December 31, 2002, 71 consecutive patients referred with potentially resectable hepatic metastases based on conventional imaging findings underwent PET or PET with computed tomography in the subsequent preoperative evaluation. INTERVENTION: Performance of hepatic resection was based on the results of the overall preoperative evaluation. MAIN OUTCOME MEASURES: Concordance with conventional imaging findings, identification of additional findings, and change in clinical management were analyzed. RESULTS: The PET findings confirmed the lesions identified by conventional imaging techniques in 64 (90%) of the patients. Additional lesions were identified on PET in 23 patients (32%). The information obtained by PET resulted in a change in clinical management in 17 cases (24%). False-positive PET findings occurred in 6 patients (8%), whereas false understaging occurred in 11 (15%). In no cases did PET findings have an adverse impact on patient outcome. CONCLUSIONS: Positron emission tomography provides useful information in the selection of patients with hepatic metastases from colorectal cancer being considered for surgical therapy. Such improved selection may serve to reduce the number of unnecessary surgical explorations and result in improved long-term survival in patients undergoing resection. Positron emission tomography should be integrated into the routine preoperative evaluation of patients being considered for hepatic resection of colorectal metastases.


Sarcomatoid renal cell carcinoma: rapid dissemination detected on FDG PET-CT.

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We present the FDG PET-CT findings in a patient with persistent pain 7 weeks after a nephrectomy and lymph node dissection for a sarcomatoid renal cell carcinoma. Although conventional imaging was unable to detect evidence of metastatic spread outside the para-aortic nodes, a PET-CT scan showed unexpected extensive dissemination. Currently, there are no reports in the literature of the PET-CT findings in sarcomatoid renal cell carcinomas.


FDG-PET after 1 cycle of therapy predicts outcome in diffuse large cell lymphoma and classic Hodgkin disease.


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BACKGROUND: Early prediction of response to therapy may offer the potential to identify patients who will benefit from standard conventional therapy. The objective of this study was to determine the predictive value of FDG-PET as an early response indicator after 1 cycle of chemotherapy for progression-free survival (PFS) in diffuse large cell lymphoma (DLCL) and classic Hodgkin disease (HD). METHODS: FDG-PET was performed before, after 1 cycle, and after completion of chemotherapy in 47 patients. The patients were followed with a median follow-up of 21 months (range, 3-47 months). PFS was compared between PET-positive and PET-negative patients after 1 cycle and after completion of therapy. RESULTS: All PET-negative patients after 1 cycle (n = 31) had sustained complete remission with a median follow-up of 28 months. Fourteen of 16 PET-positive patients after 1 cycle had refractory disease or relapsed (median PFS, 5.5 months). There were 2 false-positive results, 1 with an active infection at the biopsy site and the other in a patient who had been in remission after radiation therapy. There was good agreement between the results obtained after 1 cycle and at completion of therapy (kappa, 0.80); however, the negative predictive value was higher for FDG-PET after 1 cycle than after completion of chemotherapy (100% vs 91.4%), although not statistically different (P = .40). CONCLUSIONS: FDG-PET had a high prognostic value after 1 cycle of chemotherapy, thus it can be a valid alternative for posttreatment evaluation of DLCL and HD and may offer the potential for change in treatment paradigms. (c) 2006 American Cancer Society.
In an effort to develop a peptide-based radiopharmaceutical for the detection of tumors overexpressed vasoactive intestinal peptide receptors with positron emission tomography, we have prepared a novel [R(8,15,21), L(17)]-VIP peptide for (18)F-labeling. This peptide inhibited (125I)-VIP binding to rat lungs membranes with high affinity (half-maximal inhibitory concentrations (IC(50)) of 0.12 nm). Additionally, [R(8,15,21), L(17)]-VIP showed higher stability than native vasoactive intestinal peptide in vivo of mice. With N-succinimidyl 4-[(18)F] fluorobenzoate as labeling prosthetic group, [(18)F]FB-[R(8,15,21), L(17)]-VIP was obtained in >99% radiochemical purity within 100 min in decay-for-corrected radiochemical yield of 33.6 +/- 3% (n = 5) and a specific radioactivity 255 GBq/mumol at the end of synthesis. Stability of [(18)F]FB-[R(8,15,21), L(17)]-VIP in vitro and in vivo were investigated. Biodistribution of this trace was carried out in mice with induced C26 colorectal tumor. Fast clearance of [(18)F]FB-[R(8,15,21), L(17)]-VIP from non-target tissues and specific uptakes by tumors realized higher tumor-to-muscle ratio (3.55) and tumor-to-blood ratio (2.37) 60 min postinjection. Changes in further management based on PET/CT were recorded. RESULTS: Thirty (65%) patients had tumor recurrence, and 16 (35%) patients showed no further evidence of disease. Thirty-one patients had 32 abnormal PET/CT studies, and 15 patients had normal studies with an overall sensitivity, specificity, and accuracy of 90%, 71%, and 83%, respectively. In 37 patients, PET/CT was compared with contrast-enhanced CT and had a higher sensitivity (85% vs 70%), specificity (76% vs 47%), and accuracy (81% vs 59%). PET/CT had an impact on the management of 24 (51%) patients. Of these, chemotherapy or radiotherapy was started in 16 patients, treatment was modified in 2 patients, and 6 patients were referred to biopsy, followed by referral to surgery for 2 patients. CONCLUSIONS: In patients with breast cancer and rising tumor markers, FDG-PET/CT had high performance indices and was superior to CT for diagnosis of tumor recurrence, which led to changes in the subsequent clinical management of 51% of these patients. (c) 2006 American Cancer Society. Cancer Sci. 2006 Dec;97(12):1291-7.

Present role and future prospects of positron emission tomography in clinical oncology.

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Positron emission tomography (PET) has emerged as a significant molecular imaging technique in clinical oncology and cancer research. PET with (18)F-fluorodeoxyglucose ((18)F-FDG) demonstrates elevated glucose consumption by tumor cells, and is used clinically for the accurate staging and restaging of cancer, planning of radiotherapy, and predicting response or lack of response in the early stages of treatment. Combined PET and computed tomography (PET/CT) provides both functional and morphological information of the disease to allow accurate diagnosis of cancer. PET with new radiotracers such as protein synthesis markers and proliferation markers, as well as hypoxia and receptor-binding agents, will offer patient-specific images in order to yield tailored diagnostic and prognostic information.

Radiolabeling and in vitro and in vivo Characterization of [(18)F]FB-[R(8,15,21), L(17)]-VIP as a PET Imaging Agent for Tumor Overexpressed VIP Receptors.


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In an effort to develop a peptide-based radiopharmaceutical for the detection of tumors overexpressed vasoactive intestinal peptide receptors with positron emission tomography, we have prepared a novel [R(8,15,21), L(17)]-VIP peptide for (18)F-labeling. This peptide inhibited (125I)-VIP binding to rats lungs membranes with high affinity (half-maximal inhibitory concentrations (IC(50)) of 0.12 nm). Additionally, [R(8,15,21), L(17)]-VIP showed higher stability than native vasoactive intestinal peptide in vivo of mice. With N-succinimidyl 4-[(18)F] fluorobenzoate as labeling prosthetic group, [(18)F]FB-[R(8,15,21), L(17)]-VIP was obtained in >99% radiochemical purity within 100 min in decay-for-corrected radiochemical yield of 33.6 +/- 3% (n = 5) and a specific radioactivity 255 GBq/mumol at the end of synthesis. Stability of [(18)F]FB-[R(8,15,21), L(17)]-VIP in vitro and in vivo were investigated. Biodistribution of this trace was carried out in mice with induced C26 colorectal tumor. Fast clearance of [(18)F]FB-[R(8,15,21), L(17)]-VIP from non-target tissues and specific uptakes by tumors realized higher tumor-to-muscle ratio (3.55) and tumor-to-blood ratio (2.37) 60 min postinjection. Clear difference was observed between the blocking and unblocking experiments in biodistribution and whole body radioautography. [(18)F]FB-[R(8,15,21), L(17)]-VIP has demonstrated its potential for diagnosing tumors overexpressed vasoactive intestinal peptide receptors both in vitro and in vivo.

Combined positron emission tomography/computed tomography for evaluation of presumed choroidal metastases.


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Abstract Background: Choroidal metastases are the most common intraocular malignancy and are the first sign of systemic malignancy in approximately one-third of patients. Of patients with no previous diagnosis of cancer, oncological evaluation fails to find the primary lesion in approximately 50% of cases. Newer imaging modalities such as combined positron emission tomography/computed tomography (PET/CT) may improve the yield of the systemic work-up. Methods: Consecutive patients presenting with presumed...
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choroidal metastases were evaluated with whole body combined PET/CT scanning. Results: Four patients presenting to a tertiary referral hospital with choroidal metastases as the first sign of systemic malignancy were evaluated. In all four cases, PET/CT demonstrated the ocular lesion, and the primary malignancy which was confirmed by tissue biopsy. False-negative results were seen in two cases of cerebral metastases. PET/CT demonstrated lesions not visible on CT or magnetic resonance imaging in two cases. Conclusions:

Combined PET/CT is a useful addition to the work-up of patients with choroidal metastases. It provides the opportunity to detect lesions not visible with other imaging modalities and the ability to image patients with contraindications to magnetic resonance imaging. It is essential to correlate PET images with clinical information and the results of other imaging modalities and tissue biopsy remains the gold standard in the diagnosis of malignancy. False positives and negatives can occur with PET/CT, and further research is needed before this promising technology becomes a routine part of the evaluation of patients with choroidal metastases.


Focal F-18 FDG uptake mimicking malignant gastric localizations disappearing after water ingestion on PET/CT images.

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Diffuse, increased gastric wall F-18 FDG uptake is widely observed during PET/CT examinations, frequently unrelated to malignant findings, but simply caused by inflammatory disease, physiological emptying, or visceral thickening. Hence, elevated F-18 FDG gastric uptake can lead to equivocal misinterpretation, especially in patients with known gastric malignant disease, at posttherapy reevaluation. Gastric wall contraction can increase F-18 FDG uptake, especially for a remnant stomach, increasing the percentage of false-positive results with a direct impact on therapeutic management. One field PET/CT acquisition centered on the hypochondrial regions a few minutes after water ingestion should be performed routinely if standard images are doubtful (increased tracer uptake and visceral thickening) to differentiate benign from malignant uptake.


F-18 FDG PET scan findings in a case of carcinoma of the breast with a rare site of metastases to the gingival region.

Malhotra G, Nair N, Awasare S.

Malignant tumors of the breast have an inherent potential to metastasize more often to the regional lymph nodes. It is rare to find a metastasis to the oral region from a primary in the breast, but when this does occur, it usually involves the jawbones rather than the soft tissues. A 33-year-old premenopausal woman, a diagnosed case of locally advanced right breast carcinoma, underwent right modified radical mastectomy followed by chemotherapy as per the institutional protocol. She presented after 2 years with an exophytic growth on the right side of the lung, and an area of intense hypermetabolic activity in the left acetabular and ischial region. The present case demonstrates a rare site of metastasis in the oral region from carcinoma of the breast.


Gallbladder metastasis from malignant melanoma: diagnosis with FDG PET/CT.

Rehani B, Strohmeyer P, Jacobs M, Mantil J.

Melanoma with metastasis to the gallbladder is sometimes seen on autopsy but is rarely seen in living patients, in part because it is often asymptomatic. A 67-year-old man with a history of malignant melanoma in situ underwent an F-18 FDG PET/CT scan, which showed a gallbladder focus (SUV 16.9). Four months later, on the repeat FDG PET/CT scan, a new lesion in the gallbladder was noted. Laparoscopic cholecystectomy was done and histopathologic findings were consistent with gallbladder metastasis of melanoma. PET/CT detects metastasis at unusual sites accurately and is helpful in correct staging and management of patients with melanoma.


Multiple metastases to skeletal muscle from carcinoma of the esophagus detected by FDG PET-CT imaging.

Heffernan E, Fennelly D, Collins CD.

A 67-year-old woman was treated with neoadjuvant chemotherapy, esophagectomy, and subsequent radiotherapy for T3N1 poorly differentiated adenocarcinoma of the esophagus. Five months after surgery, a routine follow-up CT demonstrated a 1.2-cm soft tissue mass in the posterior mediastinum suspicious for local recurrence. An FDG-PET/CT study confirmed tumor in the posterior mediastinum and also showed focal areas of increased tracer uptake within several muscles. Skeletal muscle is one of the most unusual sites of
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metastatic disease, although it is probable that the more frequent use of FDG-PET imaging will lead to an increase in the detection of such lesions.


FDG PET/CT flip flop phenomenon in treated lymphoma of bone.

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A 47-year-old man with primary large B-cell lymphoma of bone underwent an F-18 fluorodeoxyglucose positron emission tomography/computed tomography (FDG PET/CT) scan for staging. The study demonstrated multiple areas of uptake consistent with osseous lymphoma. After multiple cycles of chemotherapy, a follow-up study demonstrated a dramatic flip flop appearance in which the previously noted areas of osseous lymphoma were photopenic and normal marrow appeared to have increased activity. This flip flop appearance could incorrectly suggest lymphomatous infiltration of normal marrow.


Fluorine-18 fluorothymidine: a new positron emission radioisotope for renal tumors.

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Fluorine-18 fluorothymidine (F-18 FLT) is a radioisotope based on the nucleic acid thymidine and has emerged as an important tracer that mirrors cellular proliferation in positron emission tomography (PET) studies. Early studies in human tumors have been promising. However, imaging of renal tumors using F-18 FLT PET studies has not previously been described. In this report, a difficult case of renal transitional cell carcinoma in a longstanding cyst was clearly delineated using F-18 FLT. Importantly, the study was able to guide clinicians toward appropriate surgical management. The use of such tracers may herald a new era in renal tumor imaging.


F-18 FDG PET/CT evaluation of osseous and soft tissue sarcomas.

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INTRODUCTION: Osseous and soft tissue sarcomas (OSTS) represent a histologic heterogeneous group of malignant tumors. Most of the current clinical data on the role of F-18 FDG PET in sarcomas come from patients studied with dedicated PET and less frequently with hardware fusion PET/CT. Therefore, we were prompted to review our experience with F-18 FDG PET/CT in OSTS. METHODS: This is a retrospective study (January 2003-December 2005) of 44 patients with histologic diagnoses of OSTS who had F-18 FDG PET/CT at our institution. The group included 22 men and 22 women with an age range of 2 of 84 years (average, 37 +/- 20.2 years). The administered doses of F-18 FDG range 4.1 to 19.5 mCi (average, 14.3 +/- 3 mCi). Reinterpretation of the imaging studies for accuracy and data analysis from medical records was performed. RESULTS: The sensitivity and specificity of combined F-18 FDG PET/CT were 100% (95% confidence interval [CI] = 75.7-100) and 93.3% (95% CI = 78.7-98.1) for the primary OSTS, and 80% (95% CI = 58.4-91.9) and 86.4% (95% CI = 66.7-95.2) for metastases. When interpreted separately, CT outperformed PET for pulmonary metastases detection: CT was 76.5% sensitive and 88% specific, whereas PET was only 57.1% sensitive but 96.4% specific. For detection of other metastases, CT was 82.3% sensitive and 76% specific, with PET demonstrating 78.6% sensitivity and 92.8% specificity. CONCLUSION: Relatively similar results (except better specificity for PET and PET/CT) were noted when examining the rate of metastases detection, excluding pulmonary lesions. However, CT had a better detection rate for pulmonary metastases when compared with PET alone. A negative PET scan in the presence of suspicious CT findings in the chest cannot reliably exclude pulmonary metastases from OSTS.


Correlation of GLUT-1 Overexpression, Tumor Size, and Depth of Invasion with 18F-2-fluoro-2-deoxy-D-glucose Uptake by Positron Emission Tomography in Colorectal Cancer.


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We investigated the wide variability of 18F-2-fluoro-2-deoxy-D-glucose (FDG) uptake, semiquantified as standardized uptake value (SUV), in positron emission tomography (PET) scanning, in 20 patients with colorectal cancer (CRC), including 1 with synchronous hepatic metastasis. The sensitivity of PET in CRC diagnosis was 100%, with a mean SUV of 8.0 (3.1-11.9). Tumor size and depth of invasion were associated with higher SUVs (P=.004, .042, respectively). Strong glucose transporter-1 (GLUT-1) expression had significantly positive correlation with the SUV (r=.619, P=.003). GLUT-1 expression revealed positive staining in 17 (85%) of the 20 primary lesions. The central part of the tumor, thought to be relatively hypoxic, had stronger GLUT-1 expression and a higher SUV than the periphery, in both the primary tumor and hepatic metastatic foci. Our data suggest that the SUVs of FDG uptake in PET may be a noninvasive biomarker for advanced CRC, indicative of a large hypoxic tumor with deep invasion.
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Computed tomography (CT) and positron emission tomography with [(18)F]fluoro-2-deoxy-d-glucose (FDG-PET) images of pulmonary cryptococcosis mimicking lung cancer.

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Background: The objective of this study was to clarify the clinical features of pulmonary cryptococcosis using chest computed tomography (CT) and positron emission tomography with [(18)F]fluoro-2-deoxy-d-glucose (FDG-PET), with a view to developing appropriate treatment. Methods: We analyzed the clinical features, and chest CT and FDG-PET characteristics of six cases of pulmonary cryptococcosis that were treated by surgery. The patients comprised four males and two females, ranging in age from 28 to 79 years. Results: All the patients were asymptomatic and had no extrapulmonary involvement. In all cases, chest CT showed nodular shadows. Spiculation and convergence of peripheral vessels were demonstrated in three cases, and pleural indentation in two cases. FDG-PET was performed in four of the cases, and showed accumulation of FDG in all of them. The standard uptake value (SUV) ranged from 0.93 to 4.85. Chest CT findings and accumulation of FDG made it difficult to distinguish pulmonary cryptococcosis from malignancies. Segmentectomy or wedge resection was performed in all cases for pathological diagnosis, and this revealed Cryptococcus fungal bodies. After surgical resection, no sign of relapse has been seen in any of the patients. Conclusions: Surgical resection is recommended for both diagnosis and treatment of pulmonary cryptococcosis.


Incidental finding of an ([11]C)-choline PET-positive solitary plasmacytoma lesion.


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[(18)F]Fluorocholine PET/CT imaging for the detection of recurrent prostate cancer at PSA relapse: experience in 100 consecutive patients.


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PURPOSE: We evaluated the potential of PET/CT and [(18)F]fluoromethylcholine (FCH) in the assessment of suspected recurrence of prostate cancer after treatment. METHODS: One hundred consecutive prostate cancer patients with a persistent increase in serum PSA (>0.1 ng/ml) after radical prostatectomy (58 cases), radiotherapy (21 cases) or hormonal therapy alone (21 cases) were investigated. After injection of 3.7-4.07 MBq/kg of FCH, both early (at <15 min) and delayed (at >60 min) PET/CT scans were performed in 43 patients, delayed PET/CT scans in 53 patients and early PET/CT scans in four patients. RESULTS: Of the 100 patients, 54 (PSA 0.22-511.79 ng/ml) showed positive FCH PET/CT scans. Thirty-seven patients had bone and/or abdominal lymph node uptake, while 17 showed pelvic activity. Malignant disease was confirmed in all but one. Delayed SUV(max) of bone metastases was significantly higher (p<0.0001 by paired t-test) than that measured at <15 min, whereas no differences were observed between early and delayed SUVs of malignant lymph nodes or pelvic disease. Forty-six patients (PSA 0.12-14.3 ng/ml) showed negative FCH PET/CT scans. Of the negative PET/CT scans, 89% were obtained in patients with serum PSA <4 ng/ml and 87% in patients with a Gleason score <8. In none of these cases could recurrent tumour be proven clinically during a follow-up of 6 months. CONCLUSION: FCH PET/CT is not likely to have a significant impact on the care of prostate cancer patients with biochemical recurrence until PSA increases to above 4 ng/ml. However, in selected patients, FCH PET/CT helps to exclude distant metastases when salvage local treatment is intended.


Value of PET/CT versus PET and CT performed as separate investigations in patients with Hodgkin's disease and non-Hodgkin's lymphoma.


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PURPOSE: The aim of this study was to assess the clinical benefit of combined [(18)F]FDG PET/CT in patients with malignant lymphoma as compared to separately performed PET and CT. METHODS: Overall, 100 patients with Hodgkin's disease (HD) or non-Hodgkin's lymphoma (NHL) were included in this study. Co-registered PET/CT with [(18)F]FDG and contrast medium was performed in 50 consecutive patients with NHL (n=38) or HD (n=12) for initial staging (IS) (n=12) or re-treatment staging (RS) (n=38). Another 50 patients with NHL (n=32) or HD (n=18) underwent separate PET and CT investigations within a time frame of 10 days for IS (n=22) or RS (n=28). Lymphoma involvement was separately evaluated for seven different regions in each patient. Each patient had clinical follow-up evaluation for >6 months. PET and CT data were analysed separately as well as side-by-side or in fused mode. RESULTS: In the PET/CT group, region-based evaluation for lymphoma involvement suggested a sensitivity/specificity of 85%/91% for CT, 98%/99% for PET and 98%/99% for PET/CT. In the PET and CT group, region-based evaluation showed a sensitivity/specificity of 87%/80% for CT, 98%/99% for PET and 98%/100% for PET and CT read side by side. CONCLUSION: PET was superior to CT alone and was
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**Comparative benefits and limitations of (18)F-FDG PET and CT-MRI in documented or suspected recurrent cervical cancer.**

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**PURPOSE:** The purpose of this study was to assess the comparative benefits and limitations of (18)F-fluorodeoxyglucose (FDG) PET and CT-MRI in documented or suspected recurrence of cervical cancer after primary treatment. **METHODS:** Three patient groups were enrolled. Group A patients had biopsy-documented recurrent or persistent cervical cancer. Group B patients had suspicion of recurrent tumour on CT-MRI without biopsy proof and were potentially curable. Group C patients were in complete remission after previous definitive treatment for histologically confirmed cervical carcinoma but had elevated serum squamous cell carcinoma antigen (tumour marker) levels despite negative CT-MRI. Clinical management decisions were recorded with CT-MRI alone and with additional FDG PET. Discordances and concordances between CT-MRI and FDG PET results were identified and related to final diagnosis as based on histopathology or follow-up. **RESULTS:** A total of 150 patients (ten regions per patient) were eligible for analysis, with 58 in group A, 52 in group B and 40 in group C. For the 149 discordant regions, 126 (84.6%) had final diagnoses. Of these final diagnoses, there was additional benefit from FDG PET over CT-MRI in 73.8% (93/126), with FDG PET correcting false negatives (FNs) on CT-MRI in 74.2% (69/93) and correcting false positives (FPs) on CT-MRI in 25.8% (24/93). Among lesions confirmed by FDG PET, 75.4% (52/69) were extra-pelvic. There was additional benefit of CT-MRI compared with FDG PET in 26.2% (33/126): in nine (27.3%) CT-MRI results were shown to be true positive (TP) whereas FDG PET yielded FN results, while in 24 (72.7%) CT-MRI corrected FP results on FDG PET. Among the nine FNs on FDG PET that were identified by CT-MRI, four were extra-pelvic. Among the FPs on FDG PET that were excluded by CT-MRI, 79.2% (19/24) were extra-pelvic. **CONCLUSION:** For recurrent cervical cancer, the benefits of FDG PET exceed those of CT-MRI owing to the ability of FDG PET to identify extra-pelvic metastases and its higher sensitivity and specificity.


**Microvessel density and p53 in detecting cervical cancer by FDG PET in cases of suspected recurrence.**

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**PURPOSE:** Cervical cancer is the second most frequently diagnosed cancer in women worldwide. About one-third of patients experience recurrent disease. A better chance of survival might be achieved by the early detection of recurrent cervical cancer. [(18)F]fluoro-2-deoxy-D-glucose (FDG) PET could be a promising imaging modality for this purpose, given that FDG PET has high diagnostic efficacy. Ideally, pre-selection of patients should be performed before considering FDG PET. The purpose of this study was to investigate parameters of primary cervical cancer associated with recurrence as a basis for pre-selection of patients in whom FDG PET should be performed. **METHODS:** Thirty-eight cervical cancer patients, clinically suspected of having recurrent disease, underwent FDG PET. Tissue from primary tumours and nine histologically confirmed metastases was analysed for biomarkers possibly related to glucose metabolism and prognosis (vascular endothelial growth factor, CD31 for microvessel density, glucose transporter-1, hexokinases I, II and III, Ki67, p53, hypoxia-inducible factor alphalpalpha, and degree of infiltration by lymphocytes and macrophages). **RESULTS:** Based on clinical outcome, sensitivity and specificity of FDG PET were 96% and 100%, respectively. Cox regression revealed microvessel density and p53 (tumour suppressor protein) to be the two most important biomarkers for prediction of recurrence (hazard ratios 2.54 and 2.28, respectively). By combining these two biomarkers in a parallel test, sensitivity and specificity in predicting recurrence were 87% and 71%, respectively. Leave-one-out cross-validation demonstrated predictive validity of a model based on microvessel density and p53. **CONCLUSION:** In this first study of its kind, we have demonstrated that microvessel density and p53 profiles could be important in pre-selecting cervical cancer patients for detection of recurrence by FDG PET.


**FDG-a marker of tumour hypoxia? A comparison with [(18)F]fluoromisonidazole and pO (2)-polarography in metastatic head and neck cancer.**


Department of Nuclear Medicine, University Hospital Aachen, Aachen, Germany.

**PURPOSE:** Experimental data suggest that the accumulation of [(18)F]fluorodeoxyglucose (FDG) in malignant tumours is related to regional hypoxia. The aim of this study was to evaluate the clinical potential of FDG positron emission tomography (PET) to assess tumour hypoxia in comparison with [(18)F]fluoromisonidazole (FMISO) PET and pO(2)-polarography. **METHODS:** Twenty-four patients with head and neck malignancies underwent FDG PET, FMISO PET, and pO(2)-polarography within 1 week. Parameters of pO(2)-polarography were the relative frequency of pO(2) readings /i<=2.5 mmHg, /i<5 mmHg and /i<10 mmHg, respectively, as well as the mean and median pO(2). **RESULTS:** We observed a moderate correlation of the maximum standardised uptake value (SUV) of FDG with the tumour to blood ratio of FMISO at 2 h (R=0.53, p<0.05). However, SUV of FDG was similar in hypoxic and normoxic tumours as defined by pO(2)-polarography (6.9+/−3.2 vs 6.2+/−3.0, NS), and the FDG uptake was not correlated with the results of pO(2)-
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polarography. The retention of FMISO was significantly higher in hypoxic tumours than in normoxic tumours (tumour to muscle ratio at 2 h: 1.8±0.4 vs 1.4±0.1, p<0.05), and the FMISO tumour to muscle ratio showed a strong correlation with the frequency of pO(2) readings <5 mmHg (R=0.80, p<0.001). CONCLUSION: These results support the hypothesis that tumour hypoxia has an effect on glucose metabolism. However, other factors affecting FDG uptake may be more predominant in chronic hypoxia, and thus FDG PET cannot reliably differentiate hypoxic from normoxic tumours.

Haematologica. 2006 Dec;91(12 Suppl):ECR54.

PET-imaging as a useful tool for early detection of the relapse site in the management of primary myeloid sarcoma.

Karlin L, Itti E, Pautas C, Rachid M, Bories D, Cordonnier C, Maury S.

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PET-imaging as a useful tool for early detection of the relapse site in the management of primary myeloid sarcoma.


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Dynamic FDG-PET is useful for detection of cholangiocarcinoma in patients with PSC listed for liver transplantation.


J Clin Oncol. 2006 Dec 1;24(34):54-5.

Positron emission tomography scans in postchemotherapy seminoma patients with residual masses: a retrospective review from Indiana University Hospital.

Lewis DA, Tann M, Kesler K, McCool A, Foster RS, Einhorn LH.


Monitoring of early response to neoadjuvant chemotherapy in stage II and III breast cancer by [18F]fluorodeoxyglucose positron emission tomography.


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PURPOSE: This study aimed to assess prospectively the efficacy of sequential [18F]fluorodeoxyglucose positron emission tomography (FDG PET) to evaluate early response to neoadjuvant chemotherapy in stage II and III breast cancer patients. PATIENTS AND METHODS: Images were acquired with a PET/computed tomography scanner in 64 patients after administration of FDG (5 MBq/kg) at baseline and after the first, second, third, and sixth course of chemotherapy. Ultrasound and mammography were used to assess tumor size. Decrease in the standardized uptake value (SUV) with PET was compared with the pathologic response. RESULTS: Surgery was performed after six courses of chemotherapy and pathologic analysis revealed gross residual disease in 28 patients and minimal residual disease in 36 patients. Although SUV data did not vary much in nonresponders (based on pathology findings), they decreased markedly to background levels in 94% (34 of 36) of responders. When using 60% of SUV at baseline as the cutoff value, the sensitivity, specificity, and negative predictive value of FDG PET were 61%, 96%, and 68% after one course of chemotherapy, 89%, 95%, and 85% after two courses, and 88%, 73%, and 83% after three courses, respectively. The same parameters with ultrasound (US) and mammography were 64%, 43%, and 55%, and 31%, 56%, and 45%, respectively. Assessment of tumor response with US or mammography was never significant whatever the cutoff. CONCLUSION: Pathologic response to neoadjuvant chemotherapy in stage II and III breast cancer can be predicted accurately by FDG PET after two courses of chemotherapy.


The Utility of F-18 Fluorodeoxyglucose Whole Body PET Imaging for Determining Malignancy in Cystic Lesions of the Pancreas.

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Previous studies have suggested that whole body positron-emission tomography (PET) can distinguish between benign and malignant cysts of the pancreas. Patients were identified (n = 68) who had undergone whole body PET imaging for a cystic lesion of the pancreas between Jan. 1997 and May 2005. Cross-sectional imaging studies were reviewed by a single blinded radiologist, and positive PET studies were reviewed by a blinded nuclear medicine physician. Operative resection was performed in 21 patients (31%), and 47 patients were managed with radiographic follow-up. F-18 Fluorodeoxyglucose (FDG)-avid lesions were identified in eight of the 68 patients (12%). Within the resected group of patients (n = 21), four of the seven patients (57%) with either in situ or invasive malignancy (adenocarcinoma: 3 of 5, papillary mucinous carcinoma: 1 of 2) had positive PET imaging (mean SUV, 5.9; range 2.5-8.0), and 2 of the 14 patients (14%) with benign lesions had positive PET imaging (serous cystadenoma, n = 1, SUV = 3.3; pseudocyst n = 1, SUV = 2.7). All lesions proven to be malignant with increased FDG uptake had highly suspicious findings on cross-sectional imaging. Within the group of resected patients, the sensitivity of PET for identifying malignant pathology was 57%, and the specificity was 85%. The sensitivity and specificity of PET for malignancy in this study was lower than previously reported, and PET findings did not identify otherwise occult malignant cysts. We do not believe whole body FDG-PET to be essential in the evaluation of cystic lesions of the pancreas.

CONCLUSIONS: (18)F-fluorodeoxyglucose PET/CT imaging improves accurate localization of metabolic activity and thus the pancreas.

Use of integrated FDG PET/CT imaging in pulmonary carcinoid tumours.

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BACKGROUND: Integrated positron emission tomography (PET)/computed tomography (CT) scanners have been recently introduced in the diagnostic work-up of suspected pulmonary malignancy and demonstrate encouraging results in the staging of non-small-cell lung cancer. OBJECTIVE: To evaluate the usefulness of integrated FDG PET/CT in pulmonary carcinoid tumours. SETTING: University hospital. METHODS: We studied 13 patients (mean age +/- 1 SD, 57 +/- 11 years) with pulmonary carcinoid tumours. All patients demonstrated a single pulmonary lesion. Integrated PET/CT scan and surgical resection were performed in all patients. RESULTS: The pulmonary lesion size ranged from 1.1 to 5.0 cm. Final histological diagnosis confirmed 12 typical and one atypical pulmonary carcinoid. Mean proliferation rate of the typical carcinoids was 1.7 +/- 1.4%. None of the patients had recurrent carcinoid disease or died during follow-up (864 +/- 218 days). Mean standardized uptake value (SUV) of (18)F-fluorodeoxyglucose (FDG) in typical carcinoids was 3.0 +/- 1.5 (range 1.2 - 6.6); SUV in the atypical carcinoid was remarkably high with a value of 8.5. The SUV was lower than 2.5 in 6 of 12 patients (50%). Mediastinal lymph node metastases or extrathoracic metastases were not detected in any patient. CONCLUSIONS: (18)F-fluorodeoxyglucose PET/CT imaging improves accurate localization of metabolic activity and thus the interpretation of pulmonary lesions on CT. FDG uptake in pulmonary carcinoid tumours is often lower than expected for malignant tumours. Therefore, surgical resection or biopsy of lesions suspected to be carcinoids should be mandatory, even if they show no hypermetabolism on FDG PET images.

Paraneoplastic cerebellar degeneration: Yo-expressing tumor revealed after a 5-year follow-up with FDG-PET.

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We report a patient with anti-Yo associated paraneoplastic cerebellar degeneration (PCD) whose tumor was demonstrated 5 years after developing PCD and had strong expression of Yo (cdr2) antigen. Review of this case along with clinical series and studies of tumor growth rates question the effectiveness of the anti-tumor immune response. These studies and similar cases suggest that the tumor may trigger the anti-Yo immune response at microscopic stages of development. An overwhelming majority of anti-Yo positive patients eventually develop a detectable malignancy, which argues in favor of a poorly effective or non-sustained anti-tumor immune response.

PET of Vascular Endothelial Growth Factor Receptor Expression.

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For solid tumors and metastatic lesions, tumor vascularity is a critical factor in assessing response to therapy. Here we report the first example, to our knowledge, of (64)Cu-labeled vascular endothelial growth factor 121 (VEGF(121)) for PET of VEGF receptor (VEGFR) expression in vivo. METHODS: VEGF(121) was conjugated with 1,4,7,10-tetraazadodecane-N,N,N',N''-tetraacetic acid (DOTA) and then labeled with (64)Cu for small-animal PET of mice bearing different sized U87MG human glioblastoma xenografts. Blocking experiments and ex vivo histopathology were performed to confirm the in vivo results. RESULTS: There were 4.3 +/- 0.2 DOTA molecules per VEGF(121), and the VEGFR2 binding affinity of DOTA-VEGF(121) was comparable to VEGF(121). (64)Cu labeling of DOTA-VEGF(121) was achieved in 90 +/- 10 min and the radiolabeling yield was 87.4% +/- 3.2%. The specific activity of (64)Cu-DOTA-VEGF(121) was 3.2 +/- 0.1 GBq/mg with a radiochemical purity of >98%. Small-animal PET revealed rapid, specific, and
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prominent uptake of (64)Cu-DOTA-VEGF(121) in small U87MG tumors (high VEGFR2 expression) but significantly lower and sporadic uptake in large U87MG tumors (low VEGFR2 expression). No appreciable renal clearance of (64)Cu-DOTA-VEGF(121) was observed, although the kidney uptake was relatively high likely due to VEGFR1 expression. Blocking experiments, immunofluorescence staining, and western blot confirmed the VEGFR specificity of (64)Cu-DOTA-VEGF(121). CONCLUSION: Successful demonstration of the ability of (64)Cu-DOTA-VEGF(121) to visualize VEGFR expression in vivo may allow for clinical translation of this radiopharmaceutical for imaging tumor angiogenesis and guiding antiangiogenic treatment, especially patient selection and treatment monitoring of VEGFR-targeted cancer therapy.


64Cu-Azabicyclo[3.2.2]Nonane Thiosemicarbazone Complexes: Radiopharmaceuticals for PET of Topoisomerase II Expression in Tumors.

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Topoisomerase II (Topo-II) is an essential enzyme in the DNA replication process and is the primary cellular target for many of the most widely used and effective anticancer agents. It has been reported that thiosemicarbazones (TSCs) are potent antitumor agents that inhibit Topo-II. The aim of this study was to investigate the relationship between the in vitro and in vivo behavior of novel (64)Cu-TSC complexes and the expression of Topo-II activity. METHODS: Four (4)N-azabicyclo[3.2.2]nonane TSC derivatives (EPH142, EPH143, EPH144, and EPH270) were successfully radiolabeled with (64)Cu, to form lipophilic cations of the general formula [(64)CuL][Cl] and the partition coefficient (logP) values were determined. One agent [(64)Cu-EPH270](+) was observed in vitro in cultured cell studies. The kinetics of 2 compounds, [(64)Cu-EPH144](+) and [(64)Cu-EPH270](+), were examined in mice bearing L1210 tumors and small-animal PET was conducted in mice bearing L1210 and PC-3 tumors, which expressed high and low levels of Topo-II, respectively. All data were compared with the activity and levels of Topo-II, as determined by a commercially available assay kit and western blot analysis. RESULTS: The 4 complexes were radiolabeled by incubation of (64)CuCl(2) with the ligand in ethanol solution. The complexes were isolated in high radiochemical purity, as determined by radio-thin-layer chromatography and radio-high-performance liquid chromatography. The compounds were shown to be lipophilic with logP values ranging from 1.34 to 1.92. In biodistribution studies, good L1210 tumor uptake was noted [(64)Cu-EPH144](+) at 1 h, 4.70 %ID/g (percentage injected dose per gram); 4 h, 8.80 %ID/g; 24 h, 6.64 %ID/g; and [(64)Cu-EPH270](+) at 1 h, 2.58 %ID/g; 4 h, 6.00 %ID/g; 24 h, 6.80 %ID/g. Small-animal PET of animals with L1210 tumors (high Topo-II expressing) showed excellent tumor accumulation compared with that of animals with PC-3 tumors (low Topo-II expression), and the L1210 tumor uptake was significantly reduced by coadministration of a Topo-II poison. CONCLUSION: Here we describe the characterization of a new class of copper-radiolabeled TSC analogs. We demonstrate that the accumulation of the (64)Cu-compounds is related to the expression levels of Topo-II in tumor tissue.


Predicting Chemotherapy Response to Paclitaxel with 18F-Fluoropaclitaxel and PET.

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Paclitaxel is used as a chemotherapy drug for the treatment of various malignancies, including breast, ovarian, and lung cancers. To evaluate the potential of a noninvasive prognostic tool for specifically predicting the resistance of tumors to paclitaxel therapy, we examined the tumoral uptake of (18)F-Fluoropaclitaxel ((18)F-FPAC) in mice bearing human breast cancer xenografts by using small-animal-dedicated PET and compared (18)F-FPAC uptake with the tumor response to paclitaxel treatment. METHODS: PET data were acquired after tail vein injection of approximately 9 MBq of (18)F-FPAC in anesthetized nude mice bearing breast cancer xenografts. Tracer uptake in reconstructed images was quantified by region-of-interest analyses and compared with the tumor response, as measured by changes in tumor volume, after treatment with paclitaxel. RESULTS: Mice with tumors that progressed demonstrated lower tumoral uptake of (18)F-FPAC than mice with tumors that did not progress or that regressed (r = 0.55, P < 0.02; n = 19), indicating that low (18)F-FPAC uptake was a significant predictor of chemoresistance. Conversely, high (18)F-FPAC uptake predicted tumor regression. This relationship was found for mice bearing xenografts from cell lines selected to be either sensitive or intrinsically resistant to paclitaxel in vitro. CONCLUSION: PET data acquired with (18)F-FPAC suggest that this tracer holds promise for the noninvasive quantification of its distribution in vivo in a straightforward manner. In combination with approaches for examining other aspects of resistance, such quantification could prove useful in helping to predict subsequent resistance to paclitaxel chemotherapy of breast cancer.


Lack of Correlation of Hypoxic Cell Fraction and Angiogenesis with Glucose Metabolic Rate in Non-Small Cell Lung Cancer Assessed by 18F-Fluoromisonidazole and 18F-FDG PET.

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PET offers a noninvasive means to assess neoplasms, in view of its sensitivity and accuracy in staging tumors and potentially in monitoring treatment response. The aim of this study was to evaluate newly diagnosed non-small cell lung cancer (NSCLC) for the presence of hypoxia, as indicated by the uptake of (18)F-fluoromisonidazole ((18)F-FMISO), and to examine the relationship of hypoxia to the uptake of (18)F-FDG, microvessel density, and other molecular markers of hypoxia. METHODS: Twenty-one patients with suspected or biopsy-proven NSCLC were enrolled prospectively in this study. All patients had PET studies with (18)F-FMISO and (18)F-FDG. Seventeen patients subsequently underwent surgery, with analysis performed for tumor markers of angiogenesis and hypoxia. RESULTS: In the 17 patients with resectable NSCLC (13 men, 4 women; age range, 51-77 y), the mean (18)F-FMISO uptake in tumor was significantly lower than that of (18)F-FDG uptake (P < 0.0001) and showed no correlation with (18)F-FDG uptake (r = 0.26). The mean (95% confidence interval [CI]) (18)F-FMISO SUV(max) (maximum standardized uptake value) was 1.20 [0.95-1.45] compared with the mean [95% CI] (18)F-FDG SUV(max) of 5.99 [4.62-7.35]. The correlation between (18)F-FMISO uptake, (18)F-FDG uptake, and tumor markers of hypoxia and angiogenesis was poor. A weakly positive correlation between (18)F-FMISO and (18)F-FDG uptake and Ki67 was found. CONCLUSION: The hypoxic cell fraction of primary NSCLC is consistently low, and there is no significant correlation in NSCLC between hypoxia and glucose metabolism in NSCLC assessed by (18)F-FDG. These findings have direct implications in understanding the role of angiogenesis and hypoxia in NSCLC biology.


**Intravenous Furosemide Injection During 18F-FDG PET Acquisition.**

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Urinary-system elimination of (18)F-FDG can be mistaken for pathologic uptake. Furosemide helps eliminate this artifact. Unnecessary administration should be avoided. Our approach obviates furosemide administration and other invasive procedures in many cases. METHODS: Thirty-seven cancer patients referred for PET to evaluate treatment response or suspected recurrence were prospectively studied using whole-body scanning, with (18)F-FDG injected via dorsal hand catheter beforehand. The catheter was left in place to enable injection of furosemide while the patient was inside the scanner. After abdominopelvic scanning, physicians evaluated the need to inject furosemide. Thirty minutes after furosemide injection, another abdominopelvic scan was obtained to detect postinjection urinary tract changes. RESULTS: Postfurosemide images showed effects due to physiologic elimination in 24 patients (64.9%), of whom 11 patients (45.8%) had more than one inconclusive pre furosemide finding. In 13 patients (35.1%), delayed images confirmed persistent lymph node uptake, including 3 patients (23.1%) with 1 lesion. CONCLUSION: Furosemide injection during scanning reduces artifacts, shortens examinations, and helps avoid invasive procedures.


**Lessons from the old masters: pragmatism or purity, FDG PET SUV, serum glucose and prediction of nodal status in non-small cell lung cancer.**

Akhurst T.


**Consideration of serum glucose levels during malignant mediastinal lymph node detection in non-small-cell lung cancer by FDG-PET.**

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BACKGROUND AND OBJECTIVE: Glucose and FDG compete for uptake by cancers. Here, we undertook to improve diagnostic accuracy of FDG-PET for determining mediastinal lymph node (LN) status in NSCLC by considering serum glucose level. METHODS: NSCLC patients (n = 70) who underwent curative lung resection and mediastinal LN dissection within 1 month of FDG-PET were enrolled. MaxSUV was calculated using lean body weight and used to determine a new parameter (maxSUV x serum glucose level; maxSUV-GL). Histopathologic LN results were compared with maxSUV and maxSUV-GL values. RESULTS: Of 71 LN stations whose FDG uptake could be measured, 21 were malignant and 50 benign. MaxSUV of LN had AUC of 0.729 (95% CI: 0.610-0.827) by ROC analysis with sensitivity of 47.6% (10/21), specificity of 94.0% (47/50), and a cutoff value of 3. Using maxSUV-GL the corresponding values were; AUC 0.825 (95% CI: 0.716-0.905) and sensitivity 76.2% (16/21), with a cutoff value of 290.4, which represented a significant improvement (P < 0.01) without compromising specificity 88.0% (44/50) (P > 0.05). The exclusion of neo-adjuvant chemotherapeutic and diabetic patients resulted in a similar improvement in diagnostic accuracy. CONCLUSION: By considering serum glucose level during FDG-PET using the new parameter maxSUV-GL, sensitivity for malignant mediastinal LN detection is improved.

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**The clinical stage of non-small cell lung cancer as assessed by means of fluorodeoxyglucose-positron emission tomographic/computed tomographic scanning is less accurate in cigarette smokers.**

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OBJECTIVE: The treatment of non-small cell lung cancer depends on the stage, and this is clinically best determined by using fluorodeoxyglucose-positron emission tomography/computed tomography. We evaluated the effect smoking has on the accuracy of this
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Can [18F]-fluorodeoxyglucose standardized uptake values of PET imaging predict pathologic extrathyroid invasion of thyroid papillary microcarcinomas?

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OBJECTIVE: To evaluate the hypothesis that the [F]-fluorodeoxyglucose (FDG) standardized uptake values (SUVs) of positron emission tomographic (PET) imaging can predict pathologic extrathyroid invasion of thyroid papillary microcarcinomas (TPMC) onset. METHODS: Prospective clinical study. From 2004 to 2005, 44 consecutive patients with TPMC (< 1 cm), confirmed by ultrasonography and aspiration cytology, had FDG PET scans performed. Among them, 66 tumor foci in 41 patients were confirmed to be of less than 1 cm in diameter by the final surgical pathology report. According to the microcarcinoma tumor focus, prediction of pathologic extrathyroid invasion, by clinical variables including sonographic findings and SUVs from PET imaging, was evaluated by the univariate and multivariate logistic regression analysis. RESULTS: Univariate analysis showed that the tumor site attached to the thyroid capsule and the SUVs of PET imaging could predict pathologic extrathyroid invasion. However, the tumor site attached to the thyroid capsule and an age older than 45 were significant predictors by multivariate analysis (P < 0.001 and P = 0.036). SUVs from PET imaging were only correlated with the size of tumor (P < 0.001). CONCLUSION: The SUVs from FDG PET imaging alone cannot predict the pathologic extrathyroid invasion in patients with TPMC. However, the ultrasonographic findings, such as tumor site, provide better information about the extrathyroid invasion of TPMC tumor foci.


Preliminary experience of 18F-fluorodeoxyglucose positron emission tomography in Castleman’s disease.

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Departments of Haematology.

The prognostic value of fluorodeoxyglucose positron emission tomography (FDG-PET) and gallium-67 scan (GS) performed early after chemotherapy was assessed in 40 patients with newly diagnosed aggressive lymphoma. FDG-PET and GS were performed before and after three cycles of CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) or two cycles of ACVBp (doxorubicin, cyclophosphamide, vindesine, bleomycin, prednisone), with or without rituximab. Thirty-five patients had diffuse large B-cell lymphoma (DLBCL), two had mantle-cell lymphoma and three had T-cell lymphoma. Four patients relapsed despite early negative FDG-PET and GS including all three patients with T-cell lymphoma. Nine patients stayed in remission despite positive FDG-PET and/or GS of whom five showed moderate intensity residual bone uptake. Seven of these nine early false positives had a negative exam at the end of treatment. In patients with DLBCL, the 2-year event-free survival was 85% for negative versus 30% for positive FDG-PET patients (P = 0.003) whereas it was 78% for negative versus 33% for positive GS patients (P = 0.018). Sensitivity, specificity and diagnostic accuracy of FDG-PET and GS were not significantly different: 90% versus 70%, 76 versus 80% and 80 versus 77%, respectively. We conclude that both FDG-PET and GS are valuable tools to early predict outcome in patients with DLBCL.


Quantitative micro positron emission tomography (PET) imaging for the in vivo determination of pancreatic islet graft survival.

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Islet transplantation is an attractive approach for treating type-1 diabetes, but there is a massive loss of transplanted islets. It is currently only possible to estimate islet mass indirectly, through measurement of circulating C-peptide and insulin levels. This type of estimation, however, is not sufficiently sensitive or reproducible for follow-up of individuals who have undergone islet transplantation. Here we show that islet graft survival could be assessed for 1 month in diabetic NOD mice using 9-(4-([18]F)-fluoro-3-hydroxymethylbutyl)guanine ([18]F)FHBG)-positron emission tomography (PET) technology, the PET signal reflecting insulin secretory capacity of transplanted islets. Expression of the gene encoding viral interleukin-10 (vIL-10), was measurable in real time with PET scanning. Additionally, we addressed the clinical potential of this approach by visualizing transplanted islets in the liver, the preferred clinical transplantation site. We conclude that quantitative in vivo PET imaging is a valid method for facilitating the development of protocols for prolonging islet survival, with the potential for tracking human transplants.


**18F-FDG PET imaging in assessing exudative pleural effusions.**


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**BACKGROUND:** This study evaluates the accuracy of [F]fluorodeoxyglucose positron emission tomography (F-FDG PET) imaging with semi-quantitative analysis for differentiating benign from malignant pleural exudates and for guiding the search for the primary tumour of pleural metastases. **METHODS:** Whole-body 18F-FDG PET was performed in 79 patients with exudative pleurisy. Standard uptake values were normalized for body weight, body surface area, lean body mass (SUVbw, SUVbsa, SUVlbm) with and without correction for blood glucose levels. Thoracoscopy was systematically performed to reveal pathological diagnosis. **RESULTS:** All SUVs were significantly higher in all malignant pleural diseases (n = 51) than in benign (n = 28) (P < 0.001). Moreover SUVs were greater in the pleural metastases from pulmonary primaries (n = 25) and in mesotheliomas (n = 8) than in extrathoracic primaries (n = 18) (P < 0.01) with no significant difference between lung cancers and mesotheliomas. Receiver operating curve (ROC) analysis between benign and malignant lesions showed areas under the curves that ranged from 0.803 (SUVbsa g) to 0.863 (SUVbw). The cut-off value for SUVbw which gave the best accuracy (82.3%) was 2.2. When comparing thoracic with extrathoracic primaries the highest accuracy (80.4%) was found for a cut-off value of 2.6. **CONCLUSION:** Semi-quantitative analysis of 18F-FDG PET imaging helps to differentiate malignant from benign pleural exudates and to distinguish between thoracic or extrathoracic primaries.


**Positron emission tomography in the detection and staging of ocular adnexal lymphoproliferative disease.**


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**PURPOSE:** To evaluate the role of fluorine 18 deoxyglucose positron emission tomography (FDG PET) in the initial staging of ocular adnexal lymphoma (OAL). **DESIGN:** Retrospective nonrandomized case series. **PARTICIPANTS:** Eleven patients with OAL who underwent FDG PET at initial staging. **METHODS:** Retrospective review of all the clinical and imaging records, including computed tomography (CT) and FDG PET. **MAIN OUTCOME MEASURES:** The ability of PET studies to detect OAL and distant disease was compared with CT. **RESULTS:** Eleven patients with OAL who underwent FDG PET at initial staging were retrospectively reviewed having full access to their clinical and imaging data. Fluorine 18 deoxyglucose PET found distant disease in 5 of 6 lymphoma patients with systemic disease; 4 of these patients (66%) were upstaged, changing the clinical management. Orbital lesions were demonstrated in 3 of 11 patients, giving PET a sensitivity of 27% in the orbit and 83% systemically for detection of lymphoma. **CONCLUSION:** The ability of FDG PET to find systemic extranodal lymphomatous sites not detected with conventional imaging provides valuable information in OAL patients, which may result in important changes in staging and management. The technique does have limitations in detecting OAL compared with conventional imaging, possibly owing to background physiologic activity in the extraocular muscles in the orbit and the small volume of some orbital deposits.

Semin Oncol. 2006 Dec;33 Suppl 11:99-103.

**Functional Imaging for Early Prediction of Response to Chemoradiotherapy: 3'-deoxy-3'-[18]F-fluorothymidine Positron Emission Tomography - A Clinical Application Model of Esophageal Cancer.**

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Pathologic complete response after neoadjuvant chemoradiation therapy is associated with increased survival in esophageal cancer. Early detection of response or nonresponse to neoadjuvant chemoradiation might allow individualization of treatment strategies and avoidance of unnecessary treatment. Positron emission tomography (PET) with [18]Ffluorodeoxyglucose (FDG) permits detection of changes in tumor proliferation before any change in tumor size occurs, and FDG-PET findings have been correlated with outcomes in esophageal cancer. However, FDG-PET may fail to distinguish between residual tumor and inflammation and between complete response and partial...
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response with substantial residual tumor burden. PET with the nucleoside analogue 3'-deoxy-3'-(18)F-fluorothymidine (FLT) has been found to be more accurate than FDG-PET in visualizing early changes in tumor proliferation. In a recent study in experimental models of esophageal cancer, FLT-PET was more accurate than FDG-PET in detecting early changes in proliferation following docetaxel and radiation therapy in human SEG-1 cells and mouse SEG-1 xenografts, including having a much stronger correlation with histologic findings. Clinical studies are needed to determine if FLT-PET can distinguish among degrees of response to neoadjuvant chemoradiation in patients with esophageal cancer.

Ann Surg Oncol. 2006 Nov 29; [Epub ahead of print]

Comparison of Multiphase CT, FDG-PET and Intra-Operative Ultrasound in Patients with Colorectal Liver Metastases Selected for Surgery.

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BACKGROUND: For patients with colorectal liver metastases, resection is the treatment of choice. Careful selection of these patients is crucial in order to reduce the chance of unexpected findings at laparotomy and abandoning further surgical intervention. Here, we evaluate the predictive value of CT and FDG-PET of the liver and extrahepatic findings compared to findings during laparotomy and 6 months follow-up. METHODS: 131 consecutive patients, selected for hepatic surgery for colorectal liver metastases by CT and FDG-PET, were evaluated prospectively. During surgery, the liver was assessed by intra-operative ultrasound, palpation and histology. RESULTS: In 127 patients (97%), CT was true-positive for liver metastases. In 3 patients, CT was false-positive and in 1 patient false-negative. In 126 patients (96%), FDG-PET was true-positive for liver metastases, in 2 patients FDG-PET was false-negative, in 3 patients true-negative (negative FDG-PET, false-negative CT). At laparotomy a total of 363 liver metastases were identified: 63 lesions <10 mm [10 (16%) detected by both CT and FDG-PET], 172 lesions of 10-20 mm [123 (72%) CT-positive, 129 (75%) by FDG-PET-positive], and 28 lesions >20 mm [124 (97%) CT-positive, 121 (95%) FDG-PET-positive]. CT and FDG-PET missed approximately 30% of the smaller liver lesions, resulting in a significant change in clinical management during surgery in only nine patients. CONCLUSIONS: CT and FDG-PET have a similar diagnostic yield for the identification of liver metastases; both modalities being adequate on a patient-basis but inadequate to detect the smallest of liver lesions. However, the clinical relevance of the latter is limited.

Br J Haematol. 2006 Nov 27; [Epub ahead of print]

(18)F-Fluorodeoxyglucose positron emission tomography for evaluation of intravascular large B-cell lymphoma.

Odawara J, Asada N, Aoki T, Yamakura M, Takeuchi M, Ohuchi T, Matsue K.

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Lung Cancer. 2006 Nov 25; [Epub ahead of print]

Repeat (18)F-FDG PET for monitoring neoadjuvant chemotherapy in patients with stage III non-small cell lung cancer.


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PURPOSE: The relevance of (18)F-FDG PET for staging non-small cell lung cancer (NSCLC), in particular for the detection of lymph node or distant metastases, has been shown in several studies. The value of FDG-PET for therapy monitoring in NSCLC, in contrast, has not yet been sufficiently analysed. Aim of this study was to evaluate FDG-PET for monitoring treatment response during and after neoadjuvant radiochemotherapy (NARCT) in advanced NSCLC. METHODS: Sixty-five patients with histologically proven NSCLC stage III initially underwent three FDG-PET investigations, during NARCT prior to initiating radiation, and post-NARCT. Changes of FDG-uptake in the primary tumour at two time-points during NARCT were analysed concerning their impact on long-term survival. RESULTS: The mean maximum FDG uptake (standardized uptake value, SUVmax) of the whole group decreased significantly during NARCT (SUVmax PET 1: 14.9+/−4.0, SUVmax PET 3: 5.5+/−2.4, p=0.004). The difference between initial FDG uptake (PET 1) and uptake after induction chemotherapy (PET 2) was found to be highly predictive for long-term survival patients which had a greater than 60% decreases in their SUV change had a significantly longer survival than those below this threshold (5-year-survival 60% versus 15%, p=0.0007). Patients who had a decrease of less than 25% in their SUV change had a 5-years-survival lower than 5%. Furthermore, the difference between initial FDG uptake (PET 1) and uptake after completion of the whole NARCT (PET 3) was predictive for survival when 75% was applied as cut-off (p=0.02). However, the level of significance was considerably lower. CONCLUSION: FDG-PET is suitable for therapy monitoring in patients with stage III NSCLC. The decrease of FDG uptake during induction chemotherapy is highly predictive for patient outcome.

Gynecol Oncol. 2006 Nov 24; [Epub ahead of print]

Positron emission tomography and leiomyomas: Clinicopathologic analysis of 3 cases of PET scan-positive leiomyomas and literature review.

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INTRONDUCTION: Studies have suggested that PET scans can differentiate between leiomyomas and leiomyosarcomas. Our experience, however, shows that PET scan-positive smooth muscle tumors are not necessarily malignant. CASE REPORTS: Three patients with cancer underwent PET imaging. In all three, the most worrisome finding was a PET scan-positive uterine tumor. After surgical extirpation, all three uterine tumors were found to be benign smooth muscle neoplasms. DISCUSSION: To explore the potential reason these tumors were positive on PET imaging, we performed a detailed histopathologic and immunohistochemical study of all specimens. Pathologic evaluation revealed a leiomyoma, a cellular leiomyoma, and a stromal tumor. There was no association between an increased Ki67 (proliferative) index and positivity on PET imaging. Increased vascularity, however, appeared to be a feature common to the leiomyomas that were PET-positive.

**Respiration. 2006 Nov 24**

**Intramuscular Tumor Detected by FDG Positron Emission Tomography Scanning following Postoperative Lung Cancer.**

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**AIM:** In patients with colorectal cancer an accurate diagnostic work-up is mandatory in order to perform the most specific treatment. At this moment 18F-fluoro-deoxy-glucose positron emission tomography (FDG-PET) is considered an accurate imaging technique in staging/restaging several malignancies. The aim of this paper is to review the scientific literature available about the role of FDG-PET in the management of patients with colorectal cancer. METHODS: An overview on Medline of scientific literature concerning FDG-PET and colorectal cancer was performed. The most relevant studies are reported. Advantages, limitations and new chances in using FDG-PET in these subsets of patients are summarized. RESULTS: FDG-PET is a useful tool in the evaluation of colorectal cancer. In surgical extirpation, all three uterine tumors were found to be benign smooth muscle neoplasms. DISCUSSION.: To explore the potential reason these tumors were positive on PET imaging, we performed a detailed histopathologic and immunohistochemical study of all specimens. Pathologic evaluation revealed a leiomyoma, a cellular leiomyoma, and a stromal tumor. There was no association between an increased Ki67 (proliferative) index and positivity on PET imaging. Increased vascularity, however, appeared to be a feature common to the leiomyomas that were PET-positive.

**Eur J Surg Oncol. 2006 Nov 22; [Epub ahead of print]**

**The role of 18F-fluoro-deoxy-glucose positron emission tomography (FDG-PET) in the management of patients with colorectal cancer.**

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**AIM:** In patients with colorectal cancer an accurate diagnostic work-up is mandatory in order to perform the most specific treatment. At this moment 18F-fluoro-deoxy-glucose positron emission tomography (FDG-PET) is considered an accurate imaging technique in staging/restaging several malignancies. The aim of this paper is to review the scientific literature available about the role of FDG-PET in the management of patients with colorectal cancer. METHODS: An overview on Medline of scientific literature concerning FDG-PET and colorectal cancer was performed. The most relevant studies are reported. Advantages, limitations and new chances in using FDG-PET in these subsets of patients are summarized. RESULTS: FDG-PET is a useful tool in the evaluation of colorectal cancer. In comparison to conventional imaging technique, FDG-PET has an additional diagnostic value because it allows to metabolically characterize undetermined lesions suspected for recurrence of disease, to perform a complete pre-surgical staging and to identify occult metastatic disease. In clinical practice its use leads to a change in therapeutic choices in a high percentage of cases. CONCLUSIONS: FDG-PET should be considered an essential diagnostic tool in the management of patients with colorectal cancer, especially in recurrent disease evaluation.

**Eur J Nucl Med Mol Imaging. 2006 Nov 21; [Epub ahead of print]**

**Juvenile fibroadenoma of the breast demonstrated on (111)In-octreotide SPECT and (18)F-FDG PET/CT.**

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**A model to simulate tumour oxygenation and dynamic [18F]-Fmiso PET data.**

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The microenvironment of a tumour, in particular its hypoxic status, is a crucial factor in its response to radiotherapy. Conventional techniques for measuring hypoxia are either invasive or follow surgical intervention, and thus not ideal. Positron emission tomography allows the non-invasive pre-surgical assessment of oxygen status by measuring the spatiotemporal distribution of hypoxia-specific tracers. However, the relationship between levels of uptake and the underlying oxygen tension are yet to be elucidated. Furthermore, it is not fully understood how changes in the underlying physiology affect the appearance of uptake. This paper presents a modular simulation of the tumour microenvironment, underpinned by a probability density function (PDF) to model the vasculature. The model is solved numerically, to simulate both the steady-state oxygenation of a tumour and the spatiotemporal distribution of the hypoxia-specific tracer, [18F]-fluoromisonidazole (Fmiso), in a 2D environment. The results show that using a PDF to represent the vasculature effectively captures the 'hypoxic island' appearance of oxygen-deficient tissues seen ex vivo. Simulated tissue activity curves (TACs) demonstrate the general two-stage trend of empirical data, with an initial perfusion-dominated uptake, followed by hypoxia-specific binding. In well-perfused tissue, activity follows plasma levels in early stages, with binding of Fmiso only becoming apparent at a later stage. In structurally hypoxic tissue, a more gradual initial increase in activity is observed, followed by the same accumulation slope. We demonstrate the utility of theoretical modelling of tracer uptake, by quantifying the changes in TAC structure that arise as a result of altering key physiological characteristics. For example, by decreasing either the proximity of tissue to the vasculature, or the effective diffusion coefficient of Fmiso, we can observe a shift of TAC structure from corresponding to well-perfused to avascular regions, despite wholly different underlying causes.
A method for dose delivery monitoring after high energy photon therapy has been investigated based on positron emission tomography (PET). The technique is based on the activation of body tissues by high energy bremsstrahlung beams, preferably with energies well above 20 MeV, resulting primarily in 11C and 15O but also 13N, all positron-emitting radionuclides produced by photoneutron reactions in the nuclei of 12C, 16O and 14N. A PMMA phantom and animal tissue, a frozen hind leg of a pig, were irradiated to 10 Gy and the induced positron activity distributions were measured off-line in a PET camera a couple of minutes after irradiation. The accelerator used was a Racetrack Microtron at the Karolinska University Hospital using 50 MV scanned photon beams. From photonuclear cross-section data integrated over the 50 MV photon fluence spectrum the predicted PET signal was calculated and compared with experimental measurements. Since measured PET images change with time post irradiation, as a result of the different decay times of the radionuclides, the signals from activated 12C, 16O and 14N within the irradiated volume could be separated from each other. Most information is obtained from the carbon and oxygen radionuclides which are the most abundant elements in soft tissue. The predicted and measured overall positron activities are almost equal (-3%) while the predicted activity originating from nitrogen is overestimated by almost a factor of two, possibly due to experimental noise. Based on the results obtained in this first feasibility study the great value of a combined radiotherapy-PET-CT unit is indicated in order to fully exploit the high activity signal from oxygen immediately after treatment and to avoid patient repositioning. With an RT-PET-CT unit a high signal could be collected even at a dose level of 2 Gy and the acquisition time for the PET could be reduced considerably. Real patient dose delivery verification by means of PET imaging seems to be applicable provided that biological transport processes such as capillary blood flow containing mobile 15O and 11C in the activated tissue volume can be accounted for.

The Role of Positron Emission Tomography in the Management of Recurrent Colorectal Cancer: A Review.

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PURPOSE: Surgery remains the only option for potential cure in patients with recurrent colorectal cancer. Accurate staging modalities aid in the avoidance of futile surgery, which may result in considerable morbidity in patients with incurable disease. Current imaging techniques used in disease staging often are not sensitive enough to identify low-volume metastatic disease. This study reviews the role of positron emission tomography in the assessment of patients with suspected recurrent colorectal cancer. METHODS: A literature search using the PubMed, MEDLINE, and Embase database was performed, locating English language articles on positron emission tomography, positron emission tomography, recurrent colon, and/or rectal cancer. The references of these papers were searched manually for further references. RESULTS: Positron emission tomography is more sensitive and more specific than conventional diagnostic imaging for metastatic disease and local recurrence respectively. Studies confirm the superior ability of positron emission tomography scans compared with conventional diagnostic imaging in differentiating between scar tissue and invasive tumor. Positron emission tomography scanning is more sensitive and specific for the assessment of liver metastases (and probably in patients with lung metastasis) than conventional diagnostic imaging. Positron emission tomography is superior to conventional diagnostic imaging in the investigation of raised carcinoembryonic antigen in the postoperative patient and alters management in approximately 37 percent of patients with recurrent colorectal cancer. The limitations and cost effectiveness of positron emission tomography are discussed. CONCLUSIONS: Positron emission tomography scanning is emerging as the imaging modality of choice for patients being considered for surgery for locally recurrent colorectal cancer. Positron emission tomography has the greatest impact by detecting unresectable disease and thereby averting inappropriate surgery. Despite the high set-up costs, its use seems to be cost effective.

POST-therapy surveillance of patients with uterine cancers: value of integrated FDG PET/CT in the detection of recurrence.


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PURPOSE: The purpose of this study was to prospectively determine the diagnostic accuracy of PET/CT in the detection of recurrence in patients with treated uterine cancers. METHODS: Twenty-five women, ranging in age from 37 to 79 years (mean 58.9 years), who
Use of integrated (18)F-FDG PET/CT to improve the accuracy of initial cervical nodal evaluation in patients with head and neck squamous cell carcinoma.

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BACKGROUND: We investigated the accuracy of performing cervical nodal evaluation with using integrated (18)F-fluorodeoxyglucose positron emission tomography (PET/CT) for squamous cell carcinoma (SCC) of the head and neck as compared with using PET and contrast-enhanced CT (CECT) alone. METHODS: The presence of metastatic lymphadenopathy in each cervical nodal group (level I-VI) and the nodal (N) classification of 47 patients with SCC of the head and neck were determined by using PET, CECT, and PET/CT, respectively, and the results were verified according to the histopathologic findings. RESULTS: Among the 91 foci that had abnormal uptake on PET, the combined PET/CT images provided additional information over PET for the anatomical localization and lesion characterization of 18 sites (19.8%) in 17 patients (36.2%). PET/CT also showed the best results among the three imaging modalities for the sensitivity, specificity, and accuracy (91.8, 98.9, and 97.1%, respectively) for predicting metastatic nodes on a level-by-level analysis, and PET/CT had a higher accuracy (85.1%) for the pathologic nodal classification over the clinical examinations (68.1%) or PET (70.2%). CONCLUSIONS: Combined PET/CT images are more accurate than the PET or CECT images alone for conducting cervical node evaluation in the patients suffering with head and neck SCC. (c) 2006 Wiley Periodicals, Inc. Head Neck, 2007.


Prognostic significance of [(18)F]fluorodeoxyglucose uptake on positron emission tomography in patients with pathologic stage I lung adenocarcinoma.

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BACKGROUND: [(18)F]Fluor-2-deoxyglucose uptake on positron emission tomography (FDG-PET) has been frequently used for diagnosis and staging of lung cancer. The prognostic significance of FDG uptake on PET was evaluated in patients with pathologic Stage I lung adenocarcinoma (tumor stages were based on the TNM classification of the International Union Against Cancer). METHODS: Disease-free survival of 98 patients with pathologic Stage I lung adenocarcinoma who were treated by curative resection was examined in relation to sex, age, histologic grade of differentiation, surgical procedure, tumor stage, and FDG uptake measured as the maximum standardized uptake value (SUV). RESULTS: Sixty-three patients were had Stage IA disease and 35 patients had Stage IB disease. Six patients each with Stage IA and Stage IB disease developed disease recurrence after a mean postsurgical follow-up period of 31 months. Ten (23%) of the 43 patients with SUV > or = 3.3 developed a recurrence compared with 2 (4%) of the 55 patients with SUV < 3.3 (P = .020). Ten (20%) of the 51 patients with moderately or poorly differentiated adenocarcinoma developed disease recurrence, compared with 2 (4%) of the 47 patients with well-differentiated adenocarcinoma (P = .056). Multivariate analysis demonstrated that histologic grade of differentiation was not correlated with the frequency of tumor recurrence (P = .286), whereas SUV was found to be marginally correlated (P = .079). CONCLUSIONS: FDG uptake appears to be predictive of disease-free survival in patients with Stage I lung adenocarcinoma. FDG uptake could yield important information for determining the likely value of postoperative adjuvant chemotherapy in such patients.


Molecular imaging of proliferation in malignant lymphoma.


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We have determined the ability of positron emission tomography (PET) with the thymidine analogue 3'-deoxy-3'-[(18)F]fluorothymidine (FLT) to detect manifestation sites of malignant lymphoma, to assess proliferative activity, and to differentiate aggressive from indolent tumors. In this prospective study, FLT-PET was done additionally to routine staging procedures in 34 patients with malignant lymphoma. Sixty minutes after i.v. injection of approximately 330 MBq FLT, emission and transmission scanning was done. Tracer uptake in lymphoma was evaluated semiquantitatively by calculation of standardized uptake values (SUV) and correlated to tumor grading and proliferation fraction as determined by Ki-67 immunohistochemistry. FLT-PET detected a total of 490 lesions compared with 420 lesions revealed by routine staging. In 11 patients with indolent lymphoma, mean FLT-SUV in biopsied lesions was 2.3 (range, 1.2-4.5). In 21
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patients with aggressive lymphoma, a significantly higher FLT uptake was observed (mean FLT-SUV, 5.9; range, 3.2-9.2; P < 0.0001) and a cutoff value of SUV = 3 accurately discriminated between indolent and aggressive lymphoma. Linear regression analysis indicated significant correlation of FLT uptake in biopsied lesions and proliferation fraction (r = 0.84; P < 0.0001). In this clinical study, FLT-PET was suitable for imaging malignant lymphoma and noninvasive assessment of tumor grading. Due to specific imaging of proliferation, FLT may be a superior PET tracer for detection of malignant lymphoma in organs with high physiologic fluorodeoxyglucose uptake and early detection of progression to a more aggressive histology or potential transformation.

Value of PET restaging after chemotherapy for non-Hodgkin's lymphoma: Implications for consolidation radiotherapy.

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Purpose/Objective: Patients treated for non-Hodgkin's Lymphoma (NHL) frequently are restaged for response using positron emission tomography (PET) scanning. This study investigates the role of subsequent consolidation radiation therapy (CRT) based on PET response to chemotherapy. Materials/Methods: An IRB-approved database was queried for patients who underwent PET scans after chemotherapy for NHL between 1995 and 2004; 77 patients were identified. To determine benefit of CRT, overall survival and local control were assessed with median follow-up of 39.8 months (range, 2-125 months). Results: Median age of patients was 53 (range, 18-82 years). Multivariate analysis adjusted for age, indolent vs. aggressive histology, and time from chemotherapy to PET revealed FLT positive scans (RR = 30.5; 95%CI = 5.9, 156.4), lack of RT (RR = 5.25; 95%CI = 1.26, 21.79), and Stage III/IV presentation (RR = 4.35; 95%CI = 1.03, 20) predicted increased likelihood of recurrence. Patients with positive PET scans after chemotherapy had significantly higher risk of relapse than those with negative scans (58.1% vs. 15.2%; p < 0.0001), although not everyone with positive scans recurred. Patients with positive PET scans receiving RT were not protected from relapse (63.2% relapse with RT, 50% relapse without RT; p = 0.71); in fact, over half the relapses in patients receiving RT for persistently positive PET scans were in-field. Crude 2 year OS was significantly different between PET positive and PET negative cohorts (p < 0.01). Conclusions: While RT may control relapse in PET negative patients, NHL patients who remain PET positive after chemotherapy are not well managed by RT alone.

Oral Oncol. 2006 Nov 15

F-18 FDG-PET as a routine surveillance tool for the detection of recurrent head and neck squamous cell carcinoma.

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In order to determine the efficacy and proper timing of routine PET scans for surveillance of recurrent head and neck squamous cell carcinoma (HNSCC), we evaluated the diagnostic performance of routine PET scans in relation to time interval from completion of treatment. Amongst 206 retrospectively evaluated post-treatment PET scans of 159 patients with HNSCC, 156 were performed for routine surveillance in subclinical cases. Diagnostic performance of PET scan and follow-up outcome were evaluated in relation to the time interval (2-6months, 6-12months, 12-24months, and >24months) of PET scan from the completion of treatment. Overall sensitivity and NPV of these PET scans for recurrence were 92.5% and 94.8%, compared with 55.0% and 76.9% for conventional evaluation methods. In the 156 routine scans, the diagnostic sensitivity, specificity, and NPV for locoregional recurrence were 90%, 91% and 97%, respectively, and the values for distant metastases and second primary cancers were 100%, 97% and 100%, respectively. The diagnostic accuracy of routine PET scans was not significantly altered by the time interval. Most (97%) of true negative cases on routine PET scans had no recurrence during a median 14months follow-up. PET scan may be a useful tool in routine surveillance for detection of recurrence in subclinical patients. For routine surveillance, the initial PET scan should be performed within 6months after completion of treatment and the proper timing of next routine PET scan for subclinical patient with initial negative PET result might be 1year after initial PET scan.

Oral Oncol. 2006 Nov 15

Clinical significance of intrathoracic lesions detected by (18)F-fluorodeoxyglucose positron emission tomography in the management of patients with head and neck cancer.

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Few studies have used positron emission tomography (PET) to identify metastases or simultaneous thoracic malignancies in patients with head and neck cancer (HNC). We retrospectively investigated the role of (18)F-fluorodeoxyglucose (FDG) positron emission tomography (PET) in detecting thoracic malignancies in patients with previously untreated HNC. Patients (n=86) with HNC and intrathoracic lesions on PET were divided into those who had abnormal FDG uptake in the mediastinum (n=29), lungs (n=34), or both (n=23). Whole body PET and chest computed tomography (CT) results were blindly reviewed and scored by two observers. The accuracy of FDG PET and CT were drawn from patients in whom diagnosis was confirmed, by histopathology or follow-up imaging, and risk factors for thoracic malignancy were analyzed. Malignancy was suspected in 23 of 86 patients (27%) with FDG uptake. Most of the lesions (83%) with abnormal FDG uptake were benign, with thoracic malignancy confirmed in 15 patients (17%). The overall sensitivity, specificity, and accuracy of FDG PET for intrathoracic malignancy in these patients were 80%, 85%, and 84%, respectively. The
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likelihood of thoracic malignancy in the HNC patients was associated with high FDG uptake of thoracic lesions. FDG PET may reveal lung and mediastinal malignancies with high accuracy in patients with HNC. The thoracic staging by FDG PET may be helpful in therapeutic planning for these patients.


(18)F-FDG PET for assessment of therapy response and preoperative re-evaluation after neoadjuvant radio-chemotherapy in stage III non-small cell lung cancer.


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PURPOSE: The aim of this study was to evaluate FDG-PET for assessment of therapy response and for prediction of patient outcome after neo-adjuvant radio-chemotherapy (NARCT) of advanced non-small cell lung cancer (NSCLC). METHODS: Seventy patients with histologically proven stage III NSCLC underwent FDG-PET investigations before and after NARCT. Changes in FDG uptake and PET findings after completion of NARCT were compared with (1) the histology of tumour samples obtained at surgery or repeat mediastinoscopy, and (2) treatment results in terms of achieved operability and long-term survival. RESULTS: The mean average FDG uptake of the primary tumours in the patient group decreased significantly during NARCT (p = 0.004). Sensitivity, specificity and overall accuracy of FDG-PET were 94.5%, 80% and 91%, respectively, for the detection of residual viable primary tumour, and 77%, 68% and 73%, respectively, for the presence of lymph node metastases. A negative PET scan or a reduction in the standardised uptake value (SUV) of more than 80% was the best predictive factor for a favourable outcome of further treatment. Progressive disease according to PET (new tumour manifestations or increasing SUV) was significantly correlated with an unfavourable outcome (p = 0.005). In this subgroup, survival of patients who underwent surgery was not significantly different from survival among those who did not undergo surgery, whereas for the whole patient group, complete tumour resection had a significant influence on outcome. CONCLUSION: FDG-PET is suitable to assess response to NARCT in patients with stage III NSCLC accurately. It was highly predictive for treatment outcome and patient survival. PET may be helpful in improving restaging after NARCT by allowing reliable assessment of residual tumour viability.


Combined PET/CT in the follow-up of differentiated thyroid carcinoma: what is the impact of each modality?

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PURPOSE: (18)F-fluorodeoxyglucose (FDG) positron emission tomography (PET) is a well-established method in the follow-up of patients with differentiated thyroid carcinoma (DTC), elevated thyroglobulin (Tg) and negative [131]I scans. This retrospective clinical study was designed to evaluate the impact of computed tomography (CT) and that of FDG-PET in combined FDG-PET/CT examinations on the restaging of DTC patients. METHODS: Forty-seven FDG-PET/CT scans of 33 patients with a history of DTC, elevated Tg levels and negative [131]I uptake or additionally suspected [131]I-negative lesions were studied. PET and CT images were analysed independently by an experienced nuclear medicine specialist and a radiologist. Afterwards a final consensus interpretation, the gold standard in our department, was provided for the fused PET/CT images and, if available, for supplementary investigations. RESULTS: Thirty-five investigations (74%) revealed pathological FDG-PET/CT findings. In summary, 25 local recurrences, 62 lymph node metastases and 122 organ metastases (41 lung, 60 bone, 21 other organs) were diagnosed. In 36 out of 47 examinations (77%), the original PET diagnoses were modified in the final consensus interpretation owing to the CT assessments. In 8 of the 35 pathological FDG-PET/CT examinations (23%), the final consensus interpretation of the PET/CT images led to an alteration in the treatment plan. CONCLUSION: PET/CT is a powerful fusion of two pre-existing imaging modalities, which not only improves the diagnostic value in restaging DTC patients with elevated Tg and negative [131]I scan, but also provides accurate information regarding subsequent treatment options and may lead to a change in treatment management.

Pancreatology. 2006 Nov 13;6(6):512-519


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Background: This study assessed the value of image fusion with (18)F-fluorodeoxyglucose-positron emission tomography (FDG-PET) and magnetic resonance imaging (MRI) in patients suspected of having pancreatic cancer. Methods: 32 patients (12 women, 20 men; age 24-79 years; mean 56.6 years) were included. All patients underwent whole-body FDG-PET examinations and contrast-enhanced MRI. Image fusion used a semiautomatic voxel-based algorithm. Separate reading, side-by-side analysis and evaluation of fused PET/MRI images were performed. Results were correlated to histopathology (n = 30), or clinical follow-up (n = 2). Results: 15/32 patients had pancreas cancer and 17/32 patients benign disease. The sensitivity and specificity for cancer detection by FDG-PET were 93 and 41% for visual and 86 and 58% for semiquantitative analysis whereas MRI achieved 100 and 76% respectively. Topographical assignment of PET foci by image fusion was superior to side-by-side analysis in 11/39 (28%) foci (in 8/32 patients). However, a true impact on therapeutic strategy was observed only in 1/8 patients as the presence of multiple metastases, irresistible primaries or medical reasons for inoperability prevented a curative setting. Conclusion: Compared to side-by-side analysis, PET/MRI image fusion improves the
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PET scanning in the detection of occult gastric metastases from lung carcinoma.

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Role of [(18)F]FDG PET/CT in the assessment of suspected recurrent ovarian cancer: correlation with clinical or histological findings.


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PURPOSE: To evaluate the accuracy of integrated positron emission tomography (PET) and computed tomography (CT) for depiction of suspected recurrent ovarian carcinoma after treatment, with use of clinical or histological findings as the reference standard. METHODS: Seventy-seven women (median age, 51 years) with ovarian carcinoma treated with primary cytoreductive surgery followed by platinum-based combination chemotherapy were included, and [(18)F]fluorodeoxyglucose (FDG) PET/CT was performed for suspected recurrence. In all patients, imaging findings were compared with results of histological examination after surgical exploration or clinical follow-up to determine the diagnostic accuracy of PET/CT in the evaluation of disease status. Fisher's exact test was used to measure the ability of PET/CT to predict recurrent lesions. RESULTS: Forty-five (58.4%) of the 77 patients had documented recurrence during surgical exploration or clinical follow-up, while 32 (41.6%) had no evidence of recurrent tumour. Of the 45 patients with recurrent disease, 27 (60%) were confirmed to have recurrence by surgical biopsy. A correlation was found between PET/CT and histological or clinical analyses (kappa = 0.894). The overall sensitivity, specificity, accuracy, positive predictive value and negative predictive value of PET/CT were 93.3%, 96.9%, 94.8%, 97.7% and 91.2%, respectively. PET/CT modified the diagnostic or treatment plan in 19 (24.7%) patients, by leading to the use of previously unplanned therapeutic procedures in 11 (57.9%) patients and the avoidance of previously planned diagnostic procedures in eight (42.1%) patients. CONCLUSION: Integrated FDG PET/CT is a sensitive post-therapy surveillance modality for the detection of recurrent ovarian cancer; it aids decisions on treatment plans and may ultimately have a favourable impact on prognosis.

PET/CT imaging in response evaluation of SCLC patients.

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(18)FDG uptake during induction chemoradiation for oesophageal cancer fails to predict histomorphological tumour response.


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To determine whether [(18)F]-fluorodeoxyglucose-positron emission tomography (FDG-PET) could predict the pathological response in oesophageal cancer after only the first week of neoadjuvant chemoradiation. Thirty-two patients with localised oesophageal cancer had a pretreatment PET scan and a repeat after the first week of chemoradiation. The change in mean maximum standardised uptake value (SUV) and volume of metabolically active tissue (MTV) was compared with the tumour regression grade (TRG) in the final histology. Those who achieved a TRG of 1 and 2 were deemed responders and 3-5 nonresponders. In the responders (28%), the SUV fell from 12.6 (+/-6.3) to 8.1 (+/-2.9) after 1 week of chemoradiation (P=0.070). In nonresponders (72%), the results were 9.7 (+/-5.4) and 7.1 (+/-3.8), respectively (P=0.003). The MTV in responders fell from 36.6 (+/-22.7) to 22.3 (+/-10.4) cm(3) (P=0.180), while in nonresponders, this fell from 35.9 (+/-36.7) to 31.9 (+/-52.7) cm(3) (P=0.405). There were no significant differences between responders and nonresponders. The hypothesis that early repeat FDG-PET scanning may predict histomorphologic response was not proven. This may reflect an inflammatory effect of radiation that obscures tumour-specific metabolic changes at this time. This assessment may have limited application in predicting response to multimodal regimens for oesophageal cancer.


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PET-Oncology

Epithelial-myoepithelial carcinoma (EMC) is a rare low-grade malignant salivary gland neoplasm typically found in the parotid gland. This report describes a case of EMC that arose from the submandibular gland, and gives special emphasis to the preoperative diagnostic value of positron emission tomography (PET) in combination with computed tomography (CT) and magnetic resonance imaging (MRI). Although a preoperative diagnostically specific image of EMC could not be established, the malignant nature of this tumor was detected by these combined examinations.

Ann Surg Oncol. 2006 Nov 5

The Role of FDG-PET in the Selection of Patients with Colorectal Liver Metastases.

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BACKGROUND: Selection of patients for hepatic resection of colorectal liver metastases is still limited. After conventional work up by computed tomography (CT) scan, 60% of patients will develop recurrent disease in the early years after resection. The aim of the present study was to evaluate whether an additional fluorine-18-deoxyglucose positron emission tomography (FDG-PET) improves patient selection and therefore adds value to select patients for curative liver resection. METHODS: Data from 203 patients selected for surgical treatment of colorectal liver metastases between 1995 and 2003 were collected in a prospective database. Group A consisted of 100 consecutive patients selected for hepatic surgery by conventional diagnostic imaging (CT chest and abdomen) only. Group B consisted of 103 consecutive patients selected for hepatic surgery by conventional diagnostic methods plus an additional FDG-PET. RESULTS: The number of patients with futile surgery, in which further treatment was considered inappropriate at laparotomy, was 28.0% in group A and 19.4% in group B. The reason for unresectable disease differed between groups. In group A, 10/100 (10.0%) patients showed extrahepatic abdominal disease versus 2/103 patients (1.9%) in group B (P = .017). In all other cases, resection was not performed because liver disease proved too extensive at laparotomy. For patients ultimately undergoing surgical treatment of the metastases, survival was comparable between groups. Overall survival at 3 years was 57.1% in group A versus 60.1% in group B. Disease-free survival at 3 years was 23.0% in group A and 31.4% in group B. CONCLUSIONS: In patients with colorectal liver metastases, FDG-PET may reduce the number of negative laparotomies. However, the effect size on the selection of these patients seems not sufficient enough to affect the overall and disease-free survival after treatment.

Lung Cancer. 2006 Nov 2

FDG-PET maximum standardised uptake value is associated with variation in survival: Analysis of 498 lung cancer patients.

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We sought to establish the extent to which tumour uptake of [18F]-fluoro2-deoxy-glucose is associated with survival in patients with primary lung cancer. From our analysis of data concerning 498 lung cancer patients, including surgical and non-surgical cases, we conclude that there is a clear association between higher tumour uptake of glucose and worse survival.


Metachronous, multicentric giant cell tumor of the sphenoid bone with histologic, CT, MR imaging, and positron-emission tomography/CT correlation.

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Giant cell tumor (GCT) of the sphenoid bone is a relatively rare entity and metachronous multicentric GCT of the sphenoid is even rarer; we are aware of only 3 previous cases in the literature. We describe here a tumor of the sphenoid bone that was identified 15 years after multiple resections of a GCT of the left inferior pubic ramus. Correlation is made between the histopathologic findings, MR imaging of the brain, CT of the head, and fusion positron-emission tomography (PET)/CT scan performed with fluorine-18 fluorour-2-deoxy-D-glucose (18F-FDG). This report is the first to describe the appearance of a GCT of the sphenoid bone on a fusion PET/CT examination. High metabolic activity in the base of the skull adjacent to the middle cranial fossa was demonstrated in a fashion similar to that of the known pelvic lesion. This case also demonstrates that the increased metabolic activity seen in a GCT of the sphenoid bone may be partially obscured by the adjacent physiologic high metabolic activity of the brain.
PET-Oncology

Characterization of the solitary pulmonary nodule: 18F-FDG PET versus nodule-enhancement CT.

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OBJECTIVE: The purpose of this study was to directly compare nodule-enhancement CT and 18F-FDG PET in the characterization of indeterminate solitary pulmonary nodules (SPNs) greater than 7 mm in size. MATERIALS AND METHODS: Examinations from patients undergoing both nodule-enhancement CT and 18F-FDG PET to characterize the same indeterminate SPN were reviewed. For nodule-enhancement CT, an SPN was considered malignant when it showed an unenhanced to peak-contrast-enhanced increase in attenuation greater than 15 H. Fluorine-18-FDG PET studies were blindly reinterpreted by two qualified nuclear radiologists. SPNs qualitatively showing hypermetabolic activity greater than the mediastinal blood pool were interpreted as malignant. These interpretations were compared with the original prospective clinical readings and to semiquantitative standardized uptake value (SUV) analysis. Results were compared with pathologic and clinical follow-up. RESULTS: Forty-two pulmonary nodules were examined. Twenty-five (60%) were malignant, and 17 (40%) were benign. Nodule-enhancement CT was positive in all 25 malignant nodules and in 12 benign nodules, with sensitivity and specificity of 100% and 29%, respectively, and with a positive predictive value (PPV) and negative predictive value (NPV) of 68% and 100%, respectively. Qualitative 18F-FDG PET interpretations were positive in 24 of the 25 malignant nodules and in four benign nodules. Fluorine-18-FDG PET was considered negative in one malignant nodule and in 13 of the 17 benign nodules. This correlates with a sensitivity and specificity of 96% and 76%, respectively, and with a PPV and NPV of 86% and 93%, respectively. Original prospective 18F-FDG PET and semiquantitative SUV analysis showed sensitivity, specificity, PPV, and NPV of 88%, 76%, 85%, and 81% and 84%, 82%, 88%, and 78%, respectively. CONCLUSION: Due to its much higher specificity and only slightly reduced sensitivity, 18F-FDG PET is preferable to nodule-enhancement CT in evaluating indeterminate pulmonary nodules. However, nodule-enhancement CT remains useful due to its high NPV, convenience, and lower cost. Qualitative 18F-FDG PET interpretation provided the best balance of sensitivity and specificity when compared with original prospective interpretation or SUV analysis.


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Early therapy response assessment with metabolic imaging is potentially useful to determine prognosis in aggressive lymphoma and, thus, can guide first-line therapy. Forty-eight patients with aggressive lymphoma [24 Hodgkin's disease (HD); 24 non-Hodgkin's lymphoma (NHL)] underwent fluorodeoxyglucose positron emission tomography (FDG-PET) before chemotherapy (PET1) and at mid-treatment (PET2). Therapeutic response was evaluated using conventional methods at mid-treatment. PET2 results were related to event-free survival (EFS) and overall survival (OS) using Kaplan-Meier analyses. PET1 was positive in all patients. PET2 was negative in 38 patients (18 NHL–20 HD) and positive in 10 (6 NHL–4 HD). Of the PET-negative patients, 61 and 65% achieved complete remission, and only 50 and 25% of PET-positive patients, respectively, for NHL and HD, achieved complete remission. Significant associations were found between PET2 and EFS (p=0.0006) and OS (p=0.04) for NHL, and EFS (p<0.0001) for HD (but not for OS, because no HD patient died). FDG-PET at mid-treatment can predict the outcome of patients with aggressive lymphoma and should be a useful tool to modify an ineffective therapy.

FDG-PET for prediction of survival of patients with metastatic colorectal carcinoma.

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BACKGROUND: The current study focuses on the prognostic value of pretreatment metabolic activity in metastases as measured with [(18)F]fluorodeoxyglucose positron emission tomography (FDG-PET), as an indicator of survival in colorectal cancer. PATIENTS AND METHODS: In a prospective series of 152 patients with metastatic colorectal cancer, of whom 67 were treated with resection of metastases and 85 with chemotherapy, standardized uptake values (SUV) as measured with FDG-PET, were calculated prior to treatment. Survival probabilities were estimated by Cox proportional regression analysis. For Kaplan-Meier analysis SUV was stratified by the median value. Survival differences were assessed using the log-rank test. RESULTS: SUV in metastases was a significant predictor for overall survival (hazard ratio 1.17, 95% confidence interval 1.06–1.30, P = 0.002), independent of the subsequent treatment. According to the median value of the patient population a low (SUV < 4.26) and high uptake group (SUV > 4.26) was defined. The median survival and the 2- and 3-year survival rates were 32 months, 59% and 45%, respectively, in the low-uptake group and 19 months, 37% and 28%, respectively, in the high-uptake group (P = 0.017). CONCLUSION: A significant survival benefit was observed in patients with low FDG uptake in metastases of colorectal cancer.
PET-Oncology

**[Positron emission tomography in head and neck squamous cell carcinomas]**

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18F-Fluorodeoxyglucose positron emission tomography (PET) is an imaging modality which is becoming increasingly essential in oncology, especially in the management of head and neck squamous cell carcinomas (SCC). The most common uses of the PET are listed in this thematic study: initial staging, cervical lymph node metastases from an unknown primary tumor and post-therapeutic follow-up. The advantages and drawbacks of this imaging tool are weighed here according to both our experience and data from the literature. Decision schemes are suggested for each use so as to optimize the use of this imaging modality in the management of these SCC. Other fields of application for the PET are mentioned, such as the in-progress evaluation of response to chemotherapy, the interest of this imaging tool in radiotherapy as well as current biochemical developments concerning new tracers.

**18F-FDG PET/CT fusion imaging in paediatric solid extracranial tumours.**


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This paper aims at discussing the utility of 18F-FDG PET/CT in the evaluation of paediatric solid extracranial tumours. Following a brief discussion of the basic principles and methodology of PET/CT system, it reviews the main characteristics of the tumours that can be visualised with 18F-FDG PET and presents examples of cases where the combined use of 18F-FDG PET/CT fusion imaging helped in the management of patients. It will also discuss the physiologic biodistribution of 18F-FDG, outlining the normal variants in the paediatric patients that may lead to misinterpretation.

**Positron emission tomography/computed tomography: diagnostic accuracy in lymphoma.**


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An accurate initial staging of patients with non-Hodgkin lymphoma (NHL) and Hodgkin lymphoma (HL) is critical for the selection of an appropriate treatment. Computed tomography (CT) remains the standard imaging technique, although it is based on anatomic criteria. Positron emission tomography (PET) with 2-deoxy-2-[fluorine-18]fluoro-d-glucose (FDG) provides useful functional information but requires anatomical correlation to localise lesions accurately. We have prospectively compared the accuracy of combined PET/CT with that of CT and PET alone at initial staging in lymphoma patients. Forty-seven newly diagnosed patients were evaluated. PET/CT was superior compared with CT and PET in nodal evaluation and detection of extranodal disease. Using a staging algorithm with PET/CT resulted in the disease stage being increased in 11 of 47 patients (10 NHL and 1 HL) (McNemar test \( P = 0.012 \)). Therefore, a different treatment strategy based on PET/CT findings was suggested for seven patients (14.8%). PET/CT markedly improves accuracy in the diagnostic work-up of patients with lymphoma.

**Sequential positron emission tomography using [18F]fluorodeoxyglucose for monitoring response to chemotherapy in metastatic breast cancer.**

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PURPOSE: To evaluate the clinical value of positron emission tomography (PET) for monitoring chemotherapy in metastatic breast cancer. EXPERIMENTAL DESIGN: Twenty patients with hormonorefractory or hormonoreceptor-negative multimeetastatic breast
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cancer were prospectively included. PET studies were done at baseline, at day 21 after the first cycle and at day 21 after the third cycle of chemotherapy. Metabolic response was defined based on visual and various modes of standardized uptake value (SUV) analysis of sequential PET studies. RESULTS: After one cycle, PET indicated a partial response in 12 patients, stable disease in 7 patients, and progressive disease in 1 patient, according to the visual analysis. After three cycles, PET showed a complete response in 5 patients, partial response in 11 patients, stable disease in 3 patients, and progressive disease in 1 patient. Seventy-five percent of the patients showing a metabolic response on visual analysis effectively responded to the treatment. The average SUV decreased on both the second and the third PET study, but only changes measured after three cycles of chemotherapy predicted the clinical response to chemotherapy and the overall survival. All methods for calculating the SUV (normalized for body weight, body surface area, or lean body mass) provided similar results. CONCLUSION: Semi-quantitative analysis of [18F]fluorodeoxyglucose-PET studies done after three cycles of chemotherapy is useful for monitoring the response to chemotherapy in metastatic breast cancer.


False-positive axillary lymph node on FDG-PET/CT scan resulting from immunization.

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An initial CT of a 59-year-old man with increasing back pain and weight loss showed lymphadenopathy in multiple nodal beds. A biopsy showed diffuse, large B-cell lymphoma (DLBCL). After initial chemotherapy, residual disease prompted an autologous stem cell transplant. After a follow-up FDG-PET/CT scan showed no FDG-avid disease, a subsequent study showed FDG uptake in a nonenlarged left axillary lymph node. Questioning elicited a recent immunization history. A follow-up PET/CT scan showed no uptake in this lymph node and no disease recurrence. Without this history, an unnecessary biopsy or treatment may have ensued. Methods to avoid such occurrences are discussed.


Attenuation artifact from sclerotic bone can mimic active bone metastasis on PET-CT.

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We report the PET-CT appearance of sclerotic bone mimicking active bone metastasis in a 57-year-old woman with right breast cancer and bone and hepatic metastases. Hybrid PET-CT was performed 1 month after completion of surgery and chemoradiation treatment. PET-CT demonstrated hypermetabolic foci in the right pulmonary hilum and liver. Increased hypermetabolic activity in L1 and L3 vertebral bodies was also seen corresponding to sclerotic vertebral bodies on CT study. The activity in L1 and L3 vertebral bodies was not visualized on nonattenuation-corrected images, consistent with an attenuation correction artifact resulting from extensive sclerosis in these regions.


Diffuse bone marrow uptake on F-18 FDG PET in patients with myelodysplastic syndromes.


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It is well known that hematopoietic cytokine stimulation can cause diffuse increase of FDG accumulation in bone marrow on PET imaging, which simulates that seen in patients with bone marrow metastases. However, diffuse bone marrow FDG uptake can be caused by other etiologies. We report 2 patients who did not have a history of hematopoietic cytokine stimulation. The FDG PET images showed diffuse bone marrow FDG uptake, and the patients were diagnosed as having myelodysplastic syndromes. These cases demonstrate that diffuse FDG uptake by bone marrow can suggest neoplastic disease of the hematopoietic tissues.


Tear of plantar fascia and tibiocalcaneal ligament with positive F-18 FDG PET findings.

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Although PET/CT imaging provides the most comprehensive evaluation of cancer, coexisting hypermetabolic benign processes may interfere with the staging of aggressive malignancy such as melanoma and extranodal non-Hodgkin lymphoma. Acute and subacute skeletal injuries have been reported as false-positive PET findings. The authors present additional mimickers of high metabolic malignancy with a case of stage III recurrent melanoma featuring F-18 FDG accumulation at partially torn medial plantar fascia and tibiocalcaneal ligament of the left foot.


FDG PET/CT demonstrates the effectiveness of isolated limb infusion for malignant melanoma.

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PET-Oncology

A 43-year-old woman presented with a nodular melanoma treated with wide excision, split skin graft, and sentinel node biopsy. At 2-year follow up, she was noted to have clinical recurrence at the excision site. FDG PET/CT demonstrated in-transit metastasis in her left thigh in addition to disease at the site of the sentinel node biopsy. Isolated limb infusion was performed with melphalan and dactinomycin. PET/CT at 5 weeks demonstrated resolution of the in-transit metastasis and the disease at the excision site. This report of PET/CT demonstrates the effectiveness of chemotherapy for malignant melanoma delivered by isolated limb infusion.


Pulmonary lymphangitic carcinomatosis (PLC): spectrum of FDG-PET findings.

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The lungs are among the most common sites for metastases from a multitude of cancers. The majority of pulmonary metastases appear nodular on radiologic images. Interstitial spread of tumor through pulmonary lymphatics, also known as pulmonary lymphangitic carcinomatosis (PLC), is not uncommon and constitutes approximately 7% of pulmonary metastases. PLC is most often seen with adenocarcinoma of a variety of histologies such as thyroid carcinoma, and melanoma. It is usually noted in late stages of malignancy and therefore is indicative of a poor prognosis. Diagnosis of PLC is usually based on a combination of clinical and radiologic findings. However, the diagnosis is difficult when patients have limited clinical findings or have a history of or the possibility of other interstitial lung diseases. High-resolution computed tomography (HRCT) has been the modality of choice in the radiologic diagnosis of PLC. Imaging features of PLC on HRCT include thickening of interlobular septa, fissures, and bronchovascular bundles. Distribution of PLC may be focal or diffuse, unilateral or bilateral, and symmetric or asymmetric. Although FDG-PET has been extensively used in primary or secondary lung malignancies, its role and appearance in PLC have not been well determined in the literature. In this communication, we describe a spectrum of FDG-PET and CT findings in 5 cases with PLC. Similar to CT, the distribution of PLC can be extensive or limited on the FDG-PET. Diffuse, lobar, or segmental FDG uptake in the lungs is seen in extensive PLC. In limited PLC, a linear or a hazy area of FDG uptake extending from the tumor can be seen. Recognition of various patterns related to PLC on FDG-PET may allow accurate diagnosis of disease and could potentially influence the management of these patients.


Delayed [(18)F]FDG PET imaging of central nervous system lymphoma: is PET better than MRI?


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Preparation and evaluation of (89)Zr-Zevalin for monitoring of (90)Y-Zevalin biodistribution with positron emission tomography.


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PURPOSE: To evaluate whether (89)Zr can be used as a PET surrogate label for quantification of (90)Y-ibritumomab tiuxetan ((90)Y-Zevalin) biodistribution and dosimetry before myeloablative radioimmunotherapy. METHODS: Zevalin was labelled with (89)Zr by introducing N-succinyl desferal (N-sucDf) as a second chelate. For comparison of the in vitro stability of (89)Zr-Zevalin and (88)Y-Zevalin (as a substitute for (90)Y), samples were incubated in human serum at 37 degrees C up to 6 days. Biodistribution of (89)Zr-Zevalin and (88)Y-Zevalin was assessed at 24, 48, 72 and 144 h p.i. by co-injection in nude mice bearing the non-Hodgkin’s lymphoma (NHL) xenograft line Ramos. The clinical performance of (89)Zr-Zevalin-PET was evaluated via a pilot imaging study in a patient with NHL, who had undergone [(18)F]FDG-PET 2 weeks previously. RESULTS: Modification of Zevalin with N-sucDf resulted in an N-sucDf-to-antibody molar ratio of 0.83+/-0.04. After radiolabelling and purification, the radiochemical purity and immunoreactivity of (89)Zr-Zevalin always exceeded 95% and 80%, respectively. (89)Zr-Zevalin showed the same stability in serum as (88)Y-Zevalin, with a radiochemical purity >95% during a period of 6 days. The co-injected (89)Zr-Zevalin and (88)Y-Zevalin conjugates showed a very similar biodistribution, except for liver and bone accumulation at 72 and 144 h p.i., which was significantly higher for (89)Zr than for (88)Y. PET images obtained after injection of (89)Zr-Zevalin showed clear targeting of all known tumour lesions. CONCLUSION: (89)Zr-Zevalin and (88)Y-Zevalin showed a very similar biodistribution in mice, implying that (89)Zr-Zevalin-PET might be well suited for prediction of (90)Y-Zevalin biodistribution in a myeloablative setting.


Risk assessment in liposarcoma patients based on FDG PET imaging.


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**PET-Oncology**

PURPOSE: Tumor grade and subtype are considered standard parameters for risk assessment in patients with liposarcoma. The aim of this study was to assess the clinical value of [(18)F]fluorodeoxyglucose (FDG) PET-derived maximum standardized uptake value (SUV(max)) for prediction of outcome in liposarcoma patients. METHODS: (18)F-FDG PET was performed in 54 patients with liposarcoma prior to therapy. SUV(max) was calculated for each tumor and results were correlated with tumor grade, subtype, and relapse-free survival. RESULTS: SUV(max) ranged from 0.4 to 15.9 (mean 3.6) and was significantly lower in grade I than in grade II and grade III tumors. SUV(max) was 2.3 +/- 1.7, 3.5 +/- 1.5, 4.8 +/- 2.5, and 5.6 +/- 5.8 in well-differentiated, myxoid/round cell, dedifferentiated, and pleomorphic subtypes, respectively. Borderline differences (p=0.059) were found between tumor SUV(max) in patients with and without relapse. Using a SUV of 3.6 as cut-off, the accuracy in predicting a relapse was 75%. Tumor grade yielded a lower accuracy for predicting relapse (50%), as did tumor subtype (35%). In Kaplan-Meier survival analysis, patients with a SUV(max) >3.6 had a significantly shorter disease-free survival of 21 months compared with 44 months in patients with a SUV(max) <3.6. Tumor grading and tumor subtype did not yield significant differences. CONCLUSION: Pretherapy tumor SUV obtained by FDG PET imaging was a more useful parameter for risk assessment in liposarcoma than tumor grade or subtype. A SUV(max) of more than 3.6 resulted in a significantly reduced disease-free survival and identified patients at high risk for developing early local recurrences or metastatic disease.

**PET/CT in patients with hepatocellular carcinoma using [(18)F]fluorocholine: preliminary comparison with [ (18)F]FDG PET/CT.**

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PURPOSE: The diagnostic accuracy of [(18)F]fluorodeoxyglucose (FDG) PET is insufficient to characterise hepatocellular carcinoma (HCC) in liver masses and to diagnose all cases of recurrent HCC. HCC has been reported to take up [(11)C]acetate, but routine use of this tracer is difficult. Choline is another tracer of lipid metabolism, present in large amounts in HCC. In a proof-of-concept study, we evaluated [(18)F]fluorocholine (FCH) uptake by HCC and compared FCH PET/CT with FDG PET/CT. METHODS: Twelve patients with newly diagnosed (n=8) or recurrent HCC (n=4) were prospectively enrolled. HCC was assessed by histology in eight cases and by American Association for the Study of Liver Diseases (AASLD) criteria in four cases. All patients underwent whole-body PET/CT 10 min after injection of 4 MBq/kg FCH. Within 1 week, 9 of the 12 patients also underwent whole-body FDG PET/CT 1 h after injection of 5 MBq/kg FDG. RESULTS: The per-patient analysis showed a detection rate of 12/12 using FCH PET/CT for both newly diagnosed and recurrent HCC. The median signal to noise ratio was 1.5 +/- 0.38. There was a trend towards a higher FCH SUV(max) in well-differentiated HCC (15.6 +/- 7.9 vs 11.9 +/- 0.9, NS). Of the nine patients who underwent FCH and FDG PET/CT, all nine were positive with FCH whereas only five were positive with FDG. CONCLUSION: FCH provides a high detection rate for HCC, making it potentially useful in the initial evaluation of HCC or in the detection of recurrent disease. The favourable result of this proof-of-concept study opens the way to a phase III prospective study.

**FDG-PET and CT patterns of bone metastases and their relationship to previously administered anti-cancer therapy.**


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PURPOSE: To assess [(18)F]fluorodeoxyglucose (FDG) uptake in bone metastases in patients with and without previous treatment, and compare positive positron emission tomography (PET) with osteolytic or osteoblastic changes on computed tomography (CT). METHODS: One hundred and thirty-one FDG-PET/CT studies were reviewed for bone metastases. A total of 294 lesions were found in 76 patients, 81 in untreated patients and 213 in previously treated patients. PET was assessed for abnormal FDG uptake localised by PET/CT to the skeleton. CT was evaluated for bone metastases and for blastic or lytic pattern. The relationship between the presence and pattern of bone metastases on PET and CT, and prior treatment was statistically analysed using the chi-square test. RESULTS: PET identified 174 (59%) metastases, while CT detected 280 (95%). FDG-avid metastases included 74/81 (91%) untreated and 100/213 (95%) treated lesions (p<0.001). On CT there were 76/81 (94%) untreated and 204/213 (96%) treated metastases (p NS). In untreated patients, 85% of lesions were seen on both PET and CT (26 blastic, 43 lytic). In treated patients, 53% of lesions were seen only on CT (95 blastic, 18 lytic). Of the osteoblastic metastases, 65/174 (37%) were PET positive and 98/120 (82%), PET negative (p<0.001). CONCLUSION: The results of the present study indicate that when imaging bone metastases, prior treatment may alter the relationship between PET and CT findings. Most untreated bone metastases are PET positive and lytic on CT, while in previously treated patients most lesions are PET negative and blastic on CT. PET and CT therefore appear to be complementary in the assessment of bone metastases.

**FDG uptake and glucose transporter type 1 expression in lymph nodes of non-small cell lung cancer.**

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AIMS: FDG uptake in NSCLC is related to glucose transporter type 1 (Glut-1) expression. Here, we investigated the direct causal relationship between FDG uptake and Glut-1 expression to determine the role of Glut-1 in FDG uptake by malignant and benign lymph nodes.
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nodes (LNs). METHODS: Fifty-five curative lung resections in 53 NSCLC patients (male:female=36:17, age=62.0±11.8 years) were included. Maximum standardized uptake values (maxSUVs) of LNs in preoperative whole body FDG-PET and Glut-1 immunostaining results were compared. RESULTS: Of 316 pathologically confirmed LNs, 12.3% (39/316) were malignant, and in malignant LNs, FDG positive LNs were no different from FDG negative LNs in terms of size (15.0±6.7 mm vs 10.0±6.1 mm, p>0.05), or in terms of the proportion of LNs occupied by tumor (60.0±28.8% vs 39.2±38.4%, p>0.05), but had greater percentages of Glut-1 positive cells in tumors (74.1±31.8% vs 22.7±18.7%, p<0.01), and Glut-1 staining intensities (3.4±0.9 vs 1.8±1.3, p<0.01). FDG negative malignant LNs featured cytoplasmic Glut-1 expression and adenocarcinoma. Glut-1 staining intensities were found to be significantly correlated with the maxSUVs of malignant LNs (r=0.516, p<0.05), but the percentages of Glut-1 positive cells in tumors were not (r=0.2072, p>0.05). Analysis of FDG positive benign LNs showed that maxSUV was not correlated with degree of follicular hyperplasia, or Glut-1 expression (p>0.05). CONCLUSIONS: Intense Glut-1 immunoreactivity was found to be proportionally related to the degree of FDG uptake by malignant LNs in NSCLC. However, the finding that Glut-1 expression in lymphoid hyperplasia showed no correlation with FDG uptake in benign LNs requires further investigation.


Efficacy of PET/CT in the accurate evaluation of primary colorectal carcinoma.

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AIM: This study was performed to assess in the accurate evaluation of primary colorectal carcinoma using PET/CT. METHODS: One hundred patients with primary colorectal carcinoma were evaluated during 2004. All patients underwent PET/CT when their preoperative serum carcinoembryonic antigen was >or=10 ng/mL or when CT showed equivocal findings. The appropriateness of PET/CT-induced changes was noted by subsequent operative findings and follow-up. RESULTS: PET/CT more detected 15 intra-abdominal metastatic lesions than abdomino-pelvic CT scan. PET/CT showed true negative findings in 13 patients and false positive or negative findings in 10. Changes was noted by subsequent operative findings and follow-up. RESULTS: PET/CT altered management plan in 24% of patients with primary colorectal carcinoma in correct direction. These findings suggest that PET/CT should be considered a part of standard work up for preoperative evaluation in a subset of patients with colorectal carcinoma.


Pathologic, radiologic and PET scan response of gastrointestinal stromal tumors after neoadjuvant treatment with imatinib mesylate.

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AIM: The aim of this study is to review the radiologic, PET scan and pathologic response and the outcome of patients with advanced GIST treated with neoadjuvant IM followed by surgical resection. MATERIALS AND METHODS: We report a case and review 36 patients reported in MEDLINE with advanced GIST treated with neoadjuvant IM followed by surgical resection. RESULTS: Thirty-seven patients with a median age of 56 years (range, 32-76 years) at presentation were treated with neoadjuvant IM. Radiologic response accurately predicted pathological response in 31/36 patients, whereas PET scan was accurate in predicting treatment response in only 6/23 patients. CONCLUSION: This study demonstrates that the pathologic response of GIST to IM is usually incomplete and does not correlate with the complete response seen on PET scan. This finding suggests that surgical resection will continue to play a vital role in the treatment of patients with advanced disease responding to IM treatment.


Choline metabolism in cancer: implications for diagnosis and therapy.

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Magnetic resonance studies from the last 10 years have conclusively demonstrated that choline metabolism is altered in a wide variety of cancers. In cancer, the choline metabolite profile is characterized by an elevation of phosphocholine and total choline-containing compounds. This elevation is increasingly being used as an endogenous biomarker of cancer. Importantly, the enzymes and pathways resulting in these distinct alterations in phosphocholine and total choline may provide novel molecular targets for specific, targeted anticancer therapies. In this article, we have summarized some of the magnetic resonance spectroscopy and positron emission tomography techniques that are currently available, or will be in the near future, for choline metabolism-based diagnosis, staging and therapy assessment in cancer patients. This review also outlines currently known molecular alterations that cause the aberrant choline metabolite profile in cancers and concludes with a summary of recent research findings that may, in the future, lead to novel anticancer therapies targeting choline metabolism.
Role of \([18F]\)fluoro-2-deoxy-D-glucose positron emission tomography in re-locally recurrent cervical cancer.

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Cervical cancer patients with histologically documented recurrence after curative salvage therapy or unexplained tumor marker elevation (negative computed tomography and/or magnetic resonance imaging [CT-MRI]) proven to be a re-recurrence when a further attempt for cure (or control of cancer) appeared feasible were enrolled. Lesion status was determined from pathology or clinical follow-up for at least 12 months. Management decisions were recorded with CT-MRI alone and incorporating \([18F]\)fluoro-2-deoxy-D-glucose positron emission tomography (FDG-PET), respectively. The benefits calculated were based on clinical impact because of the FDG-PET findings. Cox proportional hazards model was used to select independent prognostic covariates. Of the 26 patients who were eligible for analysis, 12 (46.2%) patients had positive impacts due to PET. Squamous cell carcinoma (SCC, P = 0.029), re-recurrence at distant metastasis only (P = 0.012), and level of SCC antigen < or = 4 ng/mL (P = 0.005) were significantly associated with better survival. A scoring system using these covariates defined three distinct prognostic groups (P = 0.0001). Patients with score 0 had a 36-month cumulative survival rate of 80%. Using this prognostic scoring system, FDG-PET may facilitate selecting appropriate management for the individual patient with re-recurrent cervical cancer.


The clinical usefulness of \(18F\)-fluorodeoxyglucose positron emission tomography in the differential diagnosis, staging, and response evaluation after concurrent chemoradiotherapy for pancreatic cancer.

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GOALS: The aims of this study were to determine the clinical use of \(18F\)-fluorodeoxyglucose positron emission tomography (FDG-PET) in the differential diagnosis of patients with suspected pancreatic cancer and in the determination of tumor response after concurrent chemoradiotherapy for pancreatic cancer. BACKGROUND: Despite advances in diagnostic tools for pancreatic cancer, it is difficult to differentiate pancreatic cancer from mass-forming pancreatitis. Even with current imaging modalities, it is also difficult to assess tumor response to therapeutic intervention. STUDY: One hundred two patients with suspected pancreatic cancer were selected for this study. Dynamic computerized tomography (CT) scan and FDG-PET were used sequentially to diagnose pancreatic cancer. After diagnostic confirmation their diagnostic yields were compared. We also evaluated the treatment response in 15 patients who underwent chemoradiation therapy with dynamic CT scan and FDG-PET and compared their results. RESULTS: In 93 out of 102 patients, pancreatic cancer was confirmed. FDG-PET showed higher diagnostic accuracy than CT scan (95.1% vs. 76.5%). FDG-PET was also superior to CT in the detection of liver metastasis. FDG-PET detected treatment response in 5 out of 15 cases after chemoradiation therapy, whereas CT could not detect any treatment response. Comparing responder and nonresponder, FDG-PET was able to predict significantly different prognosis (399 vs. 233 d, P < 0.05). CONCLUSIONS: FDG-PET is a very useful tool in diagnosing pancreatic cancer. FDG-PET may be also used as an adjunct for determining the treatment modality of pancreatic cancer and evaluating tumor response to chemoradiation therapy.


A case of neurolymphomatosis involving cranial nerves: MRI and fusion PET-CT findings.

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\(18F\)-FDG PET definition of gross tumor volume for radiotherapy of non-small cell lung cancer: is a single standardized uptake value threshold approach appropriate?

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PET with \(18F\)-FDG has been used in radiation treatment planning for non-small cell lung cancer (NSCLC). Thresholds of 15%-50% the maximum standardized uptake value (SUV(max)) have been used for gross tumor volume (GTV) delineation by PET (PET(GTV)), with 40% being the most commonly used value. Recent studies indicated that 15%-20% may be more appropriate. The purposes of this study were to determine which threshold generates the best volumetric match to GTV delineation by CT (CT(GTV)) for peripheral NSCLC and to determine whether that threshold can be generalized to tumors of various sizes. METHODS: Data for patients who had peripheral NSCLC with well-defined borders on CT and SUV(max) of greater than 2.5 were reviewed. PET/CT datasets were reviewed, and a volume of interest was determined to represent the GTV. The CT(GTV) was delineated by using standard lung windows and reviewed by a radiation oncologist. The PET(GTV) was delineated automatically by use of various percentages of the SUV(max). The PET(GTV)-to-CT(GTV) ratios were compared at various thresholds, and a ratio of 1 was considered the best match, or the optimal threshold. RESULTS: Twenty peripheral NSCLCs with volumes easily defined on CT were evaluated. The SUV(max) (mean +/- SD) was 12 +/- 8, and the mean CT(GTV) was 198 cm(3) (97.5% confidence interval, 5-1,008). The SUV(max) were 16 +/- 5, 13 +/- 9, and
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3.0 +/- 0.4 for tumors measuring greater than 5 cm, 3-5 cm, and less than 3 cm, respectively. The optimal thresholds (mean +/- SD) for the best match were 15% +/- 6% for tumors measuring greater than 5 cm, 24% +/- 9% for tumors measuring 3-5 cm, 42% +/- 2% for tumors measuring less than 3 cm, and 24% +/- 13% for all tumors. The PET(GTV) at the 40% and 20% thresholds underestimated the CT(GTV) for 16 of 20 and 14 of 20 lesions, respectively. The mean difference in the volumes (PET(GTV) minus CT(GTV)) [PET(GTV) - CT(GTV)] at the 20% threshold was 79 cm(3) (97.5% confidence interval, -922 to 178). The PET(GTV) at the 20% threshold overestimated the CT(GTV) for all 4 tumors measuring less than 3 cm and underestimated the CT(GTV) for all 6 tumors measuring greater than 5 cm. The CT(GTV) was inversely correlated with the PET(GTV) - CT(GTV) at the 20% threshold (R(2) = 0.90, P < 0.0001). The optimal threshold was inversely correlated with the CT(GTV) (R(2) = 0.79, P < 0.0001). CONCLUSION: No single threshold delineating the PET(GTV) provides accurate volume definition, compared with that provided by the CT(GTV), for the majority of NSCLCs. The strong correlation of the optimal threshold with the CT(GTV) warrants further investigation.


Forced diuresis improves the diagnostic accuracy of 18F-FDG PET in abdominopelvic malignancies.


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Our aim was to evaluate the role of forced diuresis in improving the diagnostic accuracy of abdominopelvic (18)F-FDG PET.

METHODS: Thirty-two patients were enrolled. Besides the presence of known intravesical tumors or undefined renal lesions on the initial PET scan, the inclusion criterion was the appearance of indeterminate or equivocal (18)F-FDG foci that extended along the course of the urinary tract and could not confidently be separated from urinary activity. For each patient, a second abdominopelvic PET study was performed after intravenous injection of 0.5 mg of furosemide per kilogram of body weight (maximum, 40 mg) coupled with parenteral infusion of physiologic saline. RESULTS: Forced diuresis coupled with parenteral hydration eliminated any significant (18)F-FDG in characterizing 3 renal-space-occupying lesions could not be improved by our protocol. CONCLUSION: Furosemide challenge has the potential to noninvasively resolve the inherent (18)F-FDG contrast handicap in the lower urinary tract.
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Metastasis detection with 18 FDG-positron emission tomography/computed tomography in gestational trophoblastic neoplasia: a report of 2 cases.

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BACKGROUND: The imaging methods proposed by the International Consensus for the Diagnosis of Metastases in Trophoblastic Neoplasia are sufficient to stage the disease in most cases. However, there are 2 circumstances in which a more accurate imaging method is necessary: to demonstrate fusing images in conventional studies and persistent low 18 FDG-PET/CT human chorionic gonadotropin (hCG) values. Eighteen-fluoro-2-deoxyglucose-positron emission tomography/computed tomography (18 FDG-PET/CT) can be helpful in these cases. CASES: Case 1. A 51-year-old woman was referred to the Hospital Universitario de Caracas from another hospital with a diagnosis of cervical adenosquamous carcinoma. She complained of vaginal bleeding; clinical and sonographic evaluation demonstrated a tumor in the uterus and lower third of the vagina. A new histopathologic study was performed, and choriocarcinoma (CC) was diagnosed and staged as International Federation of Gynecologists and Obstetricians (FIGO) II:12 The imaging studies were confusing, so an 18 FDG-PET/CT was performed, showing multiple nodules in the lungs. Case 2. A 25-year-old woman was admitted with symptoms that mimicked those of ectopic pregnancy; a left salpingectomy was performed, with a histopathologic report of CC. It was so an 18 FDG-PET/CT was performed, showing multiple nodules in the lungs. Case 2. A 25-year-old woman was admitted with symptoms that mimicked those of ectopic pregnancy; a left salpingectomy was performed, with a histopathologic report of CC. It was classified as FIGO stage 11:4. Treatment consisted of chemotherapy, hysterectomy and 1 pelvic tumor resection. Two years after discontinuing therapy, persistent low hCG values were detected without evident metastatic disease demonstrated by CT. Eighteen FDG-PET/CT showed multiple pulmonary nodules. CONCLUSION: Eighteen FDG-PET/CT reveals metastases that are either confusing or not detected by other imaging techniques currently accepted in most gestational trophoblastic neoplasia protocols.


Value of whole body 18FDG-PET to identify the active site of gestational trophoblastic neoplasia.

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OBJECTIVE: To evaluate the usefulness of positron emission tomography with 18-fluorodeoxyglucose (18FDG-PET) in locating residual or relapsed gestational trophoblastic neoplasia (GTN). STUDY DESIGN: The Charing Cross GTN database was screened, and 11 patients who had undergone 18FDG-PET were identified. A retrospective analysis was conducted to determine the value of this investigation as compared with other imaging modalities in clinical care. RESULTS: All patients had elevated beta-human chorionic gonadotropin (beta-hCG) at the time of the investigation; none were false positive. In 7 patients the 18FDG-PET scans correctly confirmed the presence (4 of 7 cases) or absence (3 of 7 cases) of disease sites defined by other imaging investigations. In 2 patients positive PET-guided appropriate surgical resection of lung lesions that appeared of equivocal significance on computed tomography (CT) resulted in hCG normalization. One patient had a pulmonary metastasis on CT not considered positive on 18FDG-PET (false negative). One patient with enlarged mediastinal lymph nodes on CT that were 18FDG-PET positive also had a vascular uterus on magnetic resonance imaging/Doppler ultrasound that was negative on PET (false negative). Hysterectomy led to hCG normalization and cure. The mediastinal lymph nodes were positive on CT and PET due to sarcoidosis (false positive). Patients with serum hCG levels <10 IU/L could have positive PET scans; that can contribute to patient care. CONCLUSION: 18FDG-PET can aid in identifying residual disease sites in women relapsing from previously treated GTN. However, careful evaluation in combination with other imaging modalities is required to reduce the risk of false positive and negative results.


Tumor fluoro-2-deoxy-D-glucose avidity on positron emission tomographic scan predicts mortality in patients with early-stage pure and mixed bronchioloalveolar carcinoma.

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OBJECTIVE: Bronchioloalveolar carcinoma is a clinically heterogeneous subtype of non-small cell lung carcinoma that frequently has low 2-[18F]fluoro-D-glucose (FDG) uptake on positron emission tomographic scanning. We investigated whether tumor FDG avidity was associated with worse survival among patients with completely resected node-negative pure and mixed bronchioloalveolar carcinoma. METHODS: We performed a cohort study of 36 patients who had completely resected pure and mixed bronchioloalveolar carcinoma between 1998 and 2004, who had no hilar or mediastinal lymph node metastases, and who had undergone a preoperative positron emission tomographic scan. Tumor FDG avidity was defined as a standardized uptake value of 2.5 or greater. Survival analysis was performed with a proportional hazards model. RESULTS: Of 36 patients studied, 26 patients (72%) were alive and 10 patients (28%) were dead after a median follow-up of 31 months (interquartile range 17-41 months). Seventeen patients (47%) had FDG-avid tumors, and 19 patients (53%) had non-avid tumors. Three-year survival was 49% in the FDG-avid group and 95% in the non-avid group (P = .005). FDG avidity had a hazard ratio of death of 8.6 (95% confidence interval 1.4-244.7, P = .02) after adjusting for tumor size, the presence of multifocal bronchioloalveolar carcinoma, and the presence of histologically mixed bronchioloalveolar carcinoma. CONCLUSIONS: Preoperative tumor FDG standardized uptake value of 2.5 or greater on positron emission tomography is a powerful predictor of long-term mortality in patients with lymph node-negative pure and mixed bronchioloalveolar carcinoma who undergo complete surgical resection. Patients with a high level of FDG uptake (standardized uptake value > or = 2.5) may benefit from adjuvant chemotherapy or more frequent clinical follow-up.

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PURPOSE: Accurate detection of lymph node metastases in prostate cancer has important implications for prognosis and approach to treatment. We investigated whether preoperative [18F]fluorocholine combined in-line positron emission tomography-computerized tomography and intraoperative laparoscopic radioisotope guided sentinel pelvic lymph node dissection can detect pelvic lymph node metastases in patients with clinically localized prostate cancer as reliably as extended pelvic lymph node dissection. MATERIALS AND METHODS: A total of 20 patients (mean age 63.9 +/- 6.7 years, range 52 to 75) with clinically localized prostate cancer, prostate specific antigen greater than 10 ng/ml, and/or a Gleason score sum of 7 or greater and negative bone scan were enrolled in the study. [18F]fluorocholine combined in-line positron emission tomography-computerized tomography was performed before surgery. Sentinel pelvic lymph node dissection preceded extended pelvic lymph node dissection including the area of the obturator fossa, external iliac artery/vein and internal iliac artery/vein up to the bifurcation of the common iliac artery. Laparoscopic radical prostatectomy was performed afterward. RESULTS: In 10 of the 20 patients (50%) lymph node metastases were detected, and were exclusively found outside the obturator fossa in 62%. These metastases would not have been identified with standard lymph node dissection of the obturator fossa only. [18F]fluorocholine combined in-line positron emission tomography-computerized tomography was true positive in 1, false-positive in 2, false-negative in 9 and true negative in 8 patients. The largest lymph node metastasis not seen with [18F]fluorocholine combined in-line positron emission tomography-computerized tomography was 8 mm. Laparoscopic sentinel guided lymph node dissection revealed lymph node metastases in 8 of 10 patients. In the other 2 patients sentinel lymph node dissection was not conclusive. In 1 patient normal nodal tissue was completely replaced by cancer and, therefore, there was no tracer uptake in the involved pelvic sidewall/node, and the other patient had no tracer activity at all in the involved pelvic sidewall. Extended pelvic lymph node dissection missed 1 lymph node metastasis (2 mm diameter near pudendal artery) which was detected by sentinel pelvic lymph node dissection only. CONCLUSIONS: Extended pelvic lymph node dissection reveals a higher number of lymph node metastases as described for obturator fossa dissection only. [18F]fluorocholine combined in-line positron emission tomography-computerized tomography is not useful in searching for occult lymph node metastases in clinically localized prostate cancer. Sentinel guided pelvic lymph node dissection allows the detection of even small lymph node metastases. The accuracy of sentinel pelvic lymph node dissection is comparable to that of extended pelvic lymph node dissection when the limitations of the method are taken into consideration.

Indolent enterococcal abscess mimicking recurrent renal cell carcinoma on MR imaging and PET/CT after radiofrequency ablation.

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A case of asymptomatic enterococcal abscess was found to mimic recurrent renal cell carcinoma (RCC) on gadolinium-enhanced magnetic resonance (MR) imaging and positron emission tomography/computed tomography (CT) 15 months after radiofrequency ablation for RCC. This case illustrates that indolent infection can closely mimic recurrent neoplasm on imaging. The authors suggest that if bacterial and fungal cultures had been performed during the CT-guided biopsy, the subsequent open surgical procedure might have been avoided.

Characteristics of Advantages of Positron Emission Tomography over Computed Tomography for N-staging in Lung Cancer Patients.

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OBJECTIVE: We analyzed the characteristics of advantages of positron emission tomography (PET) over computed tomography (CT) for N-staging in lung cancer patients. METHODS: Preoperative PET and CT scans were performed for 2057 lymph node stations in 205 patients with peripheral-type lung cancer. The advantages of PET over CT for N-staging were analyzed among lymph node locations and histological subtypes. RESULTS: The pathological N-stages were N0 in 143 patients, N1 in 31, N2 in 24 and N3 in 7. PET was able to diagnose N0, N2 and N3 diseases more accurately than CT (P=0.03, 0.01 and 0.02, respectively), but there was no significant difference between the two modalities for N1 disease. In the upper mediastinal lymph node stations, both false-negative and false-positive were significantly less frequent with PET than with CT (P=0.001). In the lower mediastinal and supra clavicle lymph nodes, PET showed a lower frequency of false-negative than CT (P=0.04 and 0.003, respectively), but there was no significant difference in the frequency of false-positive between the two modalities. Among histological types, PET could stage adenocarcinoma with less frequent false-negative and squamous cell carcinoma with less frequent false-positive than CT (P=0.02 and 0.005, respectively). CONCLUSION: For N-staging, PET was superior to CT for the following: (1) more accurate for N0, N2 and N3 diseases but not for N1; (2) lower frequency of false-
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positive in the upper mediastinal nodes; and (3) lower frequencies of false-negative in adenocarcinoma and false-positive in squamous cell carcinoma. Recognizing these advantages of PET could make the N-staging of lung cancer more accurate.


[Significance of PET and Integrated PET/CT in the Diagnostics of Occult Primary Tumors.]

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BACKGROUND: In the last years (18)F-FDG-positron-emission-tomography (PET) worked satisfactorily as helpful auxiliary method in order to verify recurrency of head and neck tumors and to detect primary tumors in case of CUP syndrome especially when CT and MR imaging failed to identify the tumor accurately. Fusion of FDG hypermetabolism in PET scan and anatomical structures is achieved by integrating positron emission tomography with CT and provides improvement also in case of CUP syndrome. This retrospective study shows 47 patients with neck metastases where PET or PET/CT helped to detect primary tumor site. PATIENTS: In a retrospective investigation 49 PET studies of 47 patients with CUP syndrome were analyzed. RESULTS: 9 cases had positive PET findings, 1 case false-positive. 5 cases were false-negative. In 40 PET studies there couldn't be found any sign of suspicious FDG hypermetabolism. CONCLUSION: PET and PET/CT deliver a certain improvement in localization of primary tumor site and therapeutical strategy.


The role of (18)F-FDG-PET imaging for the selection of liver transplantation candidates among hepatocellular carcinoma patients.


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Positron emission tomography (PET) using F-18 fluoro-2-deoxy-d-glucose ((18)F-FDG) is now well established as a noninvasive diagnostic tool for the detection of a variety of malignant tumors. However, in the case of hepatocellular carcinoma (HCC), several investigators have reported controversial conclusions and an inadequate sensitivity for PET (50-55%). Nevertheless, a high positive rate of (18)F-FDG accumulation has been reported in patients with high-grade HCC and in those with markedly elevated alpha-fetoprotein (AFP) levels. Here, we retrospectively reviewed 38 HCC cases that received liver transplantation (LT) at our center between November 2000 and July 2004 and underwent whole-body PET imaging. (18)F-FDG uptake was measured in the liver, and its prognostic significance was investigated. Of 38 patients enrolled, 13 patients had positive PET scans for a liver tumor. When we analyzed the association between tumor factors and PET+ (greater PET lesion uptake) in the liver, preoperative AFP level and vascular invasion were found to be significantly associated with PET+ (P = 0.003 and P < 0.001, respectively). However, the association between histological grade and PET+ findings did not reach statistical significant difference (P = 0.074). Moreover, the 2-year recurrence-free survival rate of PET- patients was significantly higher than that of PET+ patients (85.1% vs. 46.1%) (P = 0.0005). Of 6 PET+ patients who met the Milan criteria, 4 patients (66.7%) had recurrence, but all 20 PET- patients who met the Milan criteria were recurrence free. Thus, PET imaging could be a good preoperative tool for estimating the post-LT risk of tumor recurrence. Because PET imaging failed to identify the tumor accurately. PET-based tumors are a sensitive function of threshold contour level for all patients and phantom data sets. A 5% change in threshold contour level can translate into a 200% increase in volume. Phantom data indicate that I(V100) can be set as a fraction, i.e. the maximum measured uptake. Fractional threshold values in the cylindrical water phantom range from 0.23 to 0.51. Both the fractional threshold and the threshold-volume curve are dependent on lesion size, with lesions smaller than approximately 5 cm3 displaying a more pronounced sensitivity and larger fractional threshold values. The threshold-volume curves and fractional threshold values also depend on the reconstruction algorithm and smoothing filter with more smoothing requiring a higher fractional threshold contour level. The threshold contour level affects the tumor size, and therefore the ultimate boost dose that is achievable with IMRT. In an example head and neck IMRT plan, the D95 of the planning target volume decreased from 7770 to 7230 cGy for 42% vs. 55% contour threshold levels.
PET-based tumor volumes are strongly affected by the choice of threshold level. This can have a significant dosimetric impact. The appropriate threshold level depends on lesion size and image reconstruction parameters. These effects should be carefully considered when using PET contour and/or volume information for radiotherapy applications.

**Dose-volume delivery guided proton therapy using beam on-line PET system.**

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Proton therapy is one form of radiotherapy in which the irradiation can be concentrated on a tumor using a scanned or modulated Bragg peak. Therefore, it is very important to evaluate the proton-irradiated volume accurately. The proton-irradiated volume can be confirmed by detection of pair annihilation gamma rays from positron emitter nuclei generated by the target nuclear fragment reaction of irradiated proton nuclei and nuclei in the irradiation target using a positron emission tomography (PET) apparatus, and dose-volume delivery guided proton therapy (DGPT) can thereby be achieved using PET images. In the proton treatment room, a beam ON-LINE PET system (BOLPs) was constructed so that a PET apparatus of the planar-type with a high spatial resolution of about 2 mm was mounted with the field of view covering the isocenter of the beam irradiation system. The position and intensity of activity were measured using the BOLPs immediately after the proton irradiation of a gelatinous water target containing 160 nuclei at different proton irradiation energy levels. The change of the activity-distribution range against the change of the physical range was observed within 2 mm. The experiments of proton irradiation to a rabbit and the imaging of the activity were performed. In addition, the proton beam energy used to irradiate the rabbit was changed. When the beam condition was changed, the difference between the two images acquired from the measurement of the BOLPs was confirmed to clearly identify the proton-irradiated volume.

**Improved quantitation for PET/CT image reconstruction with system modeling and anatomical priors.**

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Accurate quantitation of positron emission tomography (PET) tracer uptake levels in tumors is important for staging and monitoring response to treatment. Quantitative accuracy in PET is particularly poor for small tumors because of system partial volume errors and smoothing operations. This work proposes a reconstruction algorithm to reduce the quantitative errors due to limited system resolution and due to necessary image noise reduction. We propose a method for finding and using the detection system response in the projection matrix of a statistical reconstruction algorithm. In addition, we use aligned anatomical information, available in PET/CT scanners, to govern the penalty term applied during each image update. These improvements are combined with Fourier rebinning in a clinically feasible algorithm for reconstructing fully three-dimensional PET data. Results from simulation and measured studies show improved quantitation of tumor values in terms of bias and variance across multiple tumor sizes and activity levels with the proposed method. At common clinical image noise levels for the detection task, the proposed method reduces the error in maximum tumor values by 11% compared to filtered back-projection and 5% compared to conventional iterative methods.


**Standardized uptake values of normal breast tissue with 2-deoxy-2-[F-18]fluoro-D: -glucose positron emission tomography: variations with age, breast density, and menopausal status.**

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OBJECTIVE: This study was conducted to assess the effect of breast density, age, and menopausal status on the 2-deoxy-2-[F-18]fluoro-D: -glucose (FDG) uptake in normal breast tissue by quantitative standardized uptake values (SUV). METHODS: A total of 96 patients (premenopausal 54; postmenopausal 42) with histologically proven unilateral breast cancer who underwent FDG-posietron emission tomography (PET) scans for staging were included in this study. The median age was 52+/−11 years (range 32-79 years). Fifty-nine patients had grade III or IV mammographic density (dense breast), whereas 37 patients had grade I or II breast density (nondense) according to the ACR Lexicon criteria. In the present study, we analyzed maximum and average SUVs for contralateral normal breast. RESULTS: Maximum and average SUVs for normal dense breasts were 1.02+/−0.30 and 0.84+/−0.27, respectively. Similar values for the nondense breasts were 0.66+/−0.24 and 0.53+/−0.23, respectively. Both maximum and average SUVs of dense breasts were significantly higher than those of nondense breasts (p<0.001). There was no significant difference in SUVs of nipple in patients with dense and nondense breasts. There was no significant effect of age and menopausal status on SUVs of normal breast. However, there were trends of negative relationship, i.e., decreasing SUVs with increasing age. CONCLUSION: There was a significant difference in SUVs between the dense and nondense normal breast. However, the maximum SUVs in the dense breasts were well below the threshold of 2.5, a widely used cutoff value for malignancy. Menopausal status and age do not significantly affect the uptake of FDG.
### Integrated PET-CT for the characterization of adrenal gland lesions in cancer patients: diagnostic efficacy and interpretation pitfalls.

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Integrated fluorine-18 fluorodeoxyglucose positron emission tomography (PET)-computed tomography (CT) for adrenal gland imaging in cancer patients allows early detection and accurate localization of adrenal lesions and differentiation of metastatic nodules from benign lesions, thereby facilitating treatment planning. However, false-positive findings are encountered at integrated PET-CT in approximately 5% of adrenal lesions identified as positive at PET, including adrenal adenomas, adrenal endothelial cysts, and infectious lesions. Moreover, false-negative findings may be seen in adrenal metastatic lesions with hemorrhage or necrosis, small-sized (≤10-mm) metastatic nodules, and metastases from pulmonary bronchioalveolar carcinoma or carcinoid tumors. An awareness of the potential pitfalls of integrated PET-CT enhances the diagnostic efficacy of this modality by allowing differentiation of metastatic adrenal lesions from other abnormalities. RSNA, 2006

### Stage T1 non-small cell lung cancer: preoperative mediastinal nodal staging with integrated FDG PET/CT--a prospective study.


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PurPOSE: To prospectively evaluate the sensitivity and specificity of integrated fluorine 18 fluorodeoxyglucose (FDG) positron emission tomography (PET) and computed tomography (CT) (PET/CT) for the preoperative diagnosis of mediastinal nodal metastasis in stage T1 non-small cell lung cancer (NSCLC), with surgical and histologic results as reference standards. MATERIALS AND METHODS: Institutional review board approval and informed consent were obtained. From June 2003 to February 2005, 150 patients (89 men and 61 women; mean age, 59 years) with stage T1 NSCLC underwent integrated PET/CT and surgical staging. Two observers (one radiologist and one nuclear medicine physician) evaluated prospectively and in consensus the mediastinal nodes by analyzing both PET (functional) and CT (anatomic) images. Nodal stages were determined using the American Joint Committee on Cancer staging system and surgical and histologic findings as the reference standard. Statistical evaluation of malignant lymph nodes was performed on per-nodal-station and per-person bases. RESULTS: A total of 568 mediastinal nodal stations were evaluated. Nodes were positive for malignancy in 34 (23%) of 150 patients and 55 (10%) of 568 nodal stations. For depiction of malignant nodes, the respective sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of integrated PET/CT were 42% (23 of 55), 100% (513 of 513), 100% (23 of 23), 94% (513 of 545), and 94% (536 of 568) on per-nodal-station basis and 47% (16 of 34), 100% (116 of 116), 100% (16 of 16), 87% (116 of 134), and 88% (132 of 150) on a per-patient basis. CONCLUSION: Integrated FDG PET/CT provides high specificity and positive predictive value of mediastinal nodal staging in stage T1 NSCLC, although the sensitivity is low.
**Practical integration of [18F]-FDG-PET and PET-CT in the planning of radiotherapy for non-small cell lung cancer (NSCLC): the technical basis, ICRU-target volumes, problems, perspectives.**

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The value of positron emission tomography using [18F]-fluoro-deoxy-glucose (FDG-PET) for pretherapeutic evaluation of patients with non-small cell lung cancer (NSCLC) is beyond doubt. Due to the increasing availability of PET and PET-CT scanners the method is now widely available, and its technical integration has become possible for radiotherapy planning systems. Due to the depiction of malignant tissue with high diagnostic accuracy, the use of FDG-PET in radiotherapy planning of NSCLC is very promising. However, by uncritical application, PET could impair rather than improve the prognosis of patients. Therefore, in the present paper we give an overview of technical factors influencing PET and PET-CT data, and their consequences for radiotherapy planning. We further review the relevant literature concerning the diagnostic value of FDG-PET and on the integration of FDG-PET data in RT planning for NSCLC. We point out the possible impact in gross tumor volume (GTV) definition and describe methods of target volume contouring of the primary tumor, as well as concepts for the integration of diagnostic information on lymph node involvement into the clinical target volume (CTV), and the possible implications of PET data on the definition of the planning target volume (PTV). Finally, we give an idea of the possible future use of tracers other than [18F]-FDG in lung cancer.

**Giant cell arteritis mimicking multiple myeloma; diagnosed by PET scan.**

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This case report describes a patient who presented with severe anemia, monoclonal gammopathy, a high erythrocyte sedimentation rate and significant weight loss. These features were highly suggestive of multiple myeloma. Bone marrow aspiration was negative for myeloma on two occasions. A positron emission tomography (PET) scan showed extensive 2-flourodeoxy-glucose uptake in the vascular tree consistent with arteritis. A temporal artery biopsy established the diagnosis of giant cell arteritis (GCA). There were no typical symptoms of GCA, such as headache, visual disturbance, or polymyalgia rheumatica. The patient was treated with steroids, which resulted in the resolution of anemia, monoclonal gammopathy, and other symptoms.

**Use of positron emission tomography in spindle cell carcinoma of the penis.**

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A 60-year-old man presented with spindle cell carcinoma of the penis. He underwent surgery and additional positron emission tomography and computed tomography scans to evaluate for possible metastases. Positron emission tomography showed a left inguinal and paravesical hot spot on the right. Only the left inguinal lesion could be confirmed on computed tomography. The patient underwent additional surgery with curative intent. Three months later, the patient underwent repeat computed tomography, which revealed an osteolytic process in the right acetabulum. This lesion corresponded with the right paravesical hot spot on the positron emission tomography scan 3 months earlier.

**PET in face and neck tumours.**

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FDG-PET is a useful tool in the imaging of head and neck tumours. It can be used to stage the primary tumour, to assess response to therapy and most importantly for the detection of recurrent tumour. The advantages and limitations of this technique are discussed in this article. (c) International Cancer Imaging Society.

**PET: other thoracic malignancies.**

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The vast majority of esophageal cancers are fluorodeoxyglucose (FDG) avid; the primary use for positron emission tomography (PET) in patients with esophageal cancer is in the detection of distant metastases, because known distant metastatic disease precludes surgical resection. High standardized uptake values (SUVs) may be predictive of poor prognosis. PET findings may be used to assess therapy response and evaluate for esophageal tumour recurrence after treatment. PET findings may be non-specific in different types of thymic
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lesions, although thymic carcinomas tend to be extremely FDG avid. PET can be helpful in detecting distant spread from invasive thymomas and thymic carcinomas. Similarly, PET may be used to assess the extent of disease in patients with malignant pleural mesothelioma, thereby facilitating optimal therapy approaches. (c) International Cancer Imaging Society.

FDG-PET in colorectal cancer.

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[18F]Fluorodeoxyglucose (FDG) positron emission tomography (PET) is a useful imaging tool in the evolving management of patients with colorectal carcinoma. This technique is able to measure and visualize metabolic changes in cancer cells. This feature results in the ability to distinguish viable tumor from scar tissue, in the detection of tumor foci at an earlier stage than possible by conventional anatomic imaging and in the measurement of alterations in tumor metabolism, indicative of tumor response to therapy. Nowadays, FDG-PET plays a pivotal role in staging patients before surgical resection of recurrence and metastases, in the localization of recurrence in patients with an unexplained rise in serum carcinoembryonic antigen and in assessment of residual masses after treatment. In the presurgical evaluation, FDG-PET may be best used in conjunction with anatomic imaging in order to combine the benefits of both anatomical (CT) and functional (PET) information, which leads to significant improvements in preoperative liver staging and preoperative judgment on the feasibility of resection. Integration of FDG-PET into the management algorithm of these categories of patients alters and improves therapeutic management, reduces morbidity due to futile surgery, leads to substantial cost savings and probably also to a better patient outcome. FDG-PET also appears to have great potential in monitoring the success of local ablative therapies soon after intervention and in the prediction and evaluation of response to radiotherapy, systemic therapy, and combinations thereof. This review aims to outline the current and future role of FDG-PET in the field of colorectal cancer. (c) International Cancer Imaging Society.

PET in lymphoma.

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This review attempts to discuss the role of positron emission tomography (PET) imaging for staging, treatment response and follow-up of patients with lymphoma. The pitfalls and impact of PET imaging on the clinical management are also addressed. (c) International Cancer Imaging Society.

PET/CT: will it change the way that we use CT in cancer imaging?

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Accurate staging of cancer is of fundamental importance to treatment selection and planning. Current staging paradigms focus, first, on a detailed delineation of the primary tumour in order to determine its suitability for resection, and, thereafter, on assessment of the presence of metastatic spread that would alter the surgical approach, or mandate non-surgical therapies. This approach has, at its core, the assumption that the best, and sometimes the only, way to cure a patient of cancer is by surgical resection. Unfortunately, all non-invasive techniques in current use have imperfect ability to identify those primary tumours that are able to be completely excised, and even worse ability to define the extent of metastatic spread. Nevertheless, because of relatively low cost and widespread availability, computed tomography (CT) scanning is the preferred methodology for tumour, nodal and systemic metastasis (TNM) staging. This is often supplemented by other tests that have improved performance in particular staging domains. For example, magnetic resonance imaging (MRI), mammography, or endoscopic ultrasound may be used as complementary tests for T-staging; surgical nodal sampling for N-staging; and bone scanning, MRI or ultrasound for M-staging. Accordingly, many patients undergo a battery of investigations but, even then, are found to have been incorrectly staged based on subsequent outcomes. Even for those staged surgically, pathology can only identify metastases within the resection specimens and has no capability for detecting remote disease. As a result of this, many patients undergo futile operations for disease that could never have been cured by surgery. In the case of restaging, the situation is even worse. The sequelae of prior treatment can be difficult to differentiate from residual cancer and the likelihood of successful salvage therapy is even less than at presentation. More deleteriously, patients may be subjected to additional morbidity treatments when cure has already been achieved. Thus, in post-treatment follow-up, the presence and extent of disease is equally critical to treatment selection and patient outcome as it is in primary staging. One of the major strengths of positron emission tomography (PET)/CT as a cancer staging modality is its ability to identify systemic metastases. At any phase of cancer evaluation, demonstration of systemic metastasis has profound therapeutic and prognostic implications. Only in the absence of systemic metastasis does nodal status become important, and only when unresectable nodal metastasis has been excluded does T-stage become important. There are now accumulating data that PET/CT could be used as the first, rather than the last test to assess M- and N-stage for evaluating cancers with an intermediate to high pre-test likelihood of metastatic disease based on poor long-term survival. In this scenario, there is great opportunity for subsequently selecting and tailoring the performance of anatomically based imaging modalities to define the structural relations of abnormalities identified by PET, when this information would be of relevance to management planning. Primary staging of oesophageal cancer and restaging of colorectal cancer are illustrative examples of a new paradigm for cancer imaging. (c) International Cancer Imaging Society.
PET imaging of tumour hypoxia.

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Tumour hypoxia represents a significant challenge to the curability of human tumours leading to treatment resistance and enhanced tumour progression. Tumour hypoxia can be detected by non-invasive and invasive techniques but the inter-relationships between these remains largely undefined. [18F]Fluoromisonidazole-3-fluoro-1-(2’-nitro-1’-imidazolyl)-2-propanol ([18F]MISO) and Cu-diacetyl-bis(N4-methylthiosemicarbazone (Cu-ATSM)-positron emission tomography (PET), and blood oxygen level-dependent (BOLD)-magnetic resonance imaging (MRI) are the lead contenders for human application based on their non-invasive nature, ease of use and robustness, measurement of hypoxia status, validity, ability to demonstrate heterogeneity and general availability; PET techniques are the primary focus of this review. (c) International Cancer Imaging Society.

From anatomical to biological target volumes: the role of PET in radiation treatment planning.

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Progress in radiation oncology requires a re-evaluation of the methods of target volume delineation beyond anatomical localization. New molecular imaging techniques for tumour visualisation such as positron emission tomography (PET) provide insight into tumour characteristics and can be complementary to the anatomical data of computed tomography or magnetic resonance imaging. In this review, three issues are discussed: First, can PET identify a tumour more accurately? Second, can biological tumour characteristics be visualised? Third, can intratumoural heterogeneity of these characteristics be identified? (c) International Cancer Imaging Society.

Gallbladder tuberculosis: false-positive PET diagnosis of gallbladder cancer.

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Gallbladder tuberculosis (GT) is an extremely rare disease, and very few cases have been reported in the literature. The first case of GT was described in 1870 by Gaucher. A correct preoperative diagnosis of GT is unusual, and it is frequently confused with various gallbladder diseases. We present a new case of a patient who underwent surgery with the preoperative diagnosis of gallbladder cancer after a false positive positron emission tomography scan in the diagnostic work-up.

Unexpected finding of elevated glucose uptake in fibrous dysplasia mimicking malignancy: contradicting metabolism and morphology in combined PET/CT.

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Fibrous dysplasia is a common benign disorder of bone in which fibro-osseous tissue replaces bone spongosia. Lesions have a typical appearance on computed tomography (CT) images and regularly show a markedly increased uptake in bone scintigraphy using (99m)Tc-labelled methylene diphosphonate ((99m)Tc-MDP) as radiotracer. The glucose avidity of these lesions depicted by positron emission tomography (PET) using the radiolabelled glucose derivative (18)F-fluoro-2-deoxy-glucose (FDG) is less well known since FDG-PET does not have a role in the assessment of this disease. However, single cases have been reported in which fibrous dysplasia was present in patients undergoing FDG-PET scanning for oncological reasons, and no significant FDG uptake was observed for lesions identified as fibrous dysplasia. We report on a 24-year-old man with known fibrous dysplasia who underwent combined FDG-PET/CT scanning because of suspected recurrence of testicular cancer. In contrast to prior reports, a markedly elevated uptake of FDG was seen in numerous locations that were identified as fibrous dysplasia by CT. Based on this result, we conclude that fibrous dysplasia may mimic malignancy in FDG-PET and that coregistered CT may help to resolve these equivocal findings.

Should FDG-PET scanning be routinely used for patients with an unknown head and neck squamous primary?


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Background: Between 1 and 2 per cent of head and neck squamous cell carcinoma patients will reveal no evidence of a primary malignancy. The management of this group poses many problems, including the morbidity associated with wide field irradiation as well
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as the difficulty in treatment when a primary does emerge. The aim of this study was to assess the use of fluoro-deoxy-glucose positron emission tomography (FDG-PET) imaging in patients presenting with an unknown head and neck primary and to consider its routine use in such patients.

Methods: We enrolled 25 patients into our study over a four year period. They all presented with a histologically proven, metastatic, squamous cell carcinoma of the neck for which no primary could be found despite full clinical, endoscopic and radiological evaluation with computed tomography (CT) and/or magnetic resonance imaging (MRI). Additionally, all the patients underwent imaging using FDG-PET. The images were interpreted by two radiologists experienced in PET imaging.

Results: A primary was identified in nine of the 25 patients (42 per cent); however, of these patients, six had false positive results and only three patients were true positives with supportive histology. In the remaining 16 patients, no abnormality was identified on CT, MRI or PET. Of these 16 patients, two eventually displayed a primary carcinoma, the other 14 patients remaining without evidence of any primary.

Conclusion: Despite the high number of positive PET scans, the actual true positive rate was 3/9 (33 per cent); conversely, the true negative rate was 14/16 (88 per cent). We conclude from this study that there is a role for FDG-PET in the patient with an unknown head and neck primary, particularly in the context of a negative PET scan.

Ann Oncol. 2006 Oct 23

A prospective study of PET/CT in initial staging of small-cell lung cancer: comparison with CT, bone scintigraphy and bone marrow analysis.

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BACKGROUND: Small-cell lung cancer (SCLC) accounts for 15%-20% of all lung cancer cases. Accurate and fast staging is mandatory when choosing treatment, but current staging procedures are time consuming and lack sensitivity.

PATIENTS AND METHODS: A prospective study was designed to examine the role of combined positron emission tomography/computed tomography (PET/CT) compared with standard staging (CT, bone scintigraphy and immunocytochemical assessment of bone marrow biopsy) of patients with SCLC. Thirty-four consecutive patients were included. Twenty-nine patients received initial PET/CT.

RESULTS: PET/CT caused change of stage in 5/29 (17%). Excluding patients with unconfirmed findings or pleural effusion, the sensitivity for accurate staging of patients with extensive disease was the following: for standard staging 79%, PET 93% and PET/CT 93%. Specificity was 100%, 83% and 100%, respectively.

CONCLUSION: The results from this first study on PET/CT in SCLC indicates that PET/CT can simplify and perhaps even improve the accuracy of the current staging procedure in SCLC. A larger clinical trial, preferably with consequent histological confirmation in case of discordance, however, is warranted.

Jpn J Clin Oncol. 2006 Oct 23

Prospective Study of Positron Emission Tomography for Evaluation of the Activity of Lapatinib, a Dual Inhibitor of the ErbB1 and ErbB2 Tyrosine Kinasen, in Patients with Advanced Tumors.


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BACKGROUND: To evaluate the role of FDG-PET in assessing anti-tumor efficacy of molecular targeted drugs, we prospectively performed FDG-PET and CT for response evaluation in patients treated with lapatinib, a dual inhibitor of ErbB1 and ErbB2 tyrosine kinases.

METHODS: Lapatinib was given orally once a day at doses ranging from 1200 to 1800 mg in a phase I study. CT and FDG-PET were performed before treatment, and at 1, 2 and 3 months after the initiation of the treatment and every 2 months thereafter.

RESULTS: A total of 29 FDG-PET examinations were performed in eight patients with various solid tumors and the metabolic activity in the tumor was evaluated as SUVmax. The best responses, as assessed by CT, were as follows; one partial response, four stable disease and three disease progression. The partial response was observed in a patient with trastuzumab-resistant breast cancer, whose SUVmax was decreased by 60% from baseline. In all of the four patients whose best response was stable disease, the SUVmax was decreased by 6-42% one month after the start of treatment. Prolonged stable disease (10 months) was observed in a patient with colon cancer, whose SUVmax was decreased by 42%. In the patient group with disease progression, SUVmax was increased in two out of three patients.

CONCLUSIONS: FDG-PET detected decreases in the metabolic activity of the tumors in patients who experienced clinical benefits on treatment with lapatinib. Thus, FDG-PET may be useful for the evaluation of molecular targeted drugs, such as lapatinib.


Target volume definition for (18)F-FDG PET-positive lymph nodes in radiotherapy of patients with non-small cell lung cancer.


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PURPOSE: FDG PET is increasingly used in radiotherapy planning. Recently, we demonstrated substantial differences in target volumes when applying different methods of FDG-based contouring in primary lung tumours (Nestle et al., J Nucl Med 2005;46:1342-8). This paper focusses on FDG-positive mediastinal lymph nodes (LN(PET)).

METHODS: In our institution, 51 NSCLC patients who were candidates for radiotherapy prospectively underwent staging FDG PET followed by a thoracic PET scan in the treatment position and a planning CT. Eleven of them had 32 distinguishable non-confluent mediastinal or hilar nodal FDG accumulations (LN(PET)). For these, sets of gross tumour volumes (GTVs) were generated at both acquisition times by four different PET-based contouring methods (visual: GTV(vis); 40% SUV(max); GTV(40); SUV=2.5: GTV(2.5); target/background (T/B) algorithm: GTV(bg)).

RESULTS: All differences concerning GTV sizes were within the range of the resolution of the PET system. The detectability and technical delineability of the
Imatinib treatment of the GIST882 cells. Among these genes there was up-regulation of insulin-like growth factor binding protein-3
samples from patients with low residual FDG uptake, whereas there was an up to 12-fold reduction (-102% mean decrease; P = .03) in IGFBP-3, a protein that modulates proliferation and apoptosis. Western blot analysis confirmed the increase of IGFBP-3 only in imatinib-sensitive GIST882 cells. Up to a 7-fold induction (49% mean increase; P = .08) of IGFBP-3 mRNA was found in tumor to regulate numerous genes and specifically induces IGFBP-3 in GIST cells and tumor samples. IGFBP-3 levels also were found to be higher in patients with high residual FDG uptake after imatinib therapy.

CONCLUSIONS: In the current study, imatinib appears to regulate numerous genes and specifically induces IGFBP-3 in GIST cells and tumor samples. IGFBP-3 levels also were found to be higher in patients with high residual FDG uptake after imatinib therapy.

References:
2. The incremental value of (18)F-FDG PET/CT in paediatric malignancies. Bar-Sever Z, Keidar Z, Ben-Barak A, Bar-Shalom R, Postovsky S, Guralnik L, Ben Arush MW, Israel O. Division of Nuclear Medicine, Schneider Children's Medical Center of Israel, 14 Kaplan Street, Petach-Tikva, 49202, Israel.

PURPOSE: (18)F-fluorodeoxyglucose ((18)F-FDG) positron emission tomography (PET) imaging has been used in the assessment of paediatric malignancies. PET/CT increases the diagnostic accuracy in adult cancer patients. The present study assesses the incremental value of FDG PET/CT in paediatric malignancies. METHODS: A total of 118 (18)FDG PET/CT studies of 46 paediatric patients were reviewed retrospectively. PET and PET/CT results were classified as malignant, equivocal or benign, compared on a site- and study-based analysis, and also compared with the clinical outcome. RESULTS: Three hundred and twenty-four sites of increased FDG uptake were detected. Discordant PET and PET/CT interpretations were found in 97 sites (30%) in 27 studies (22%). PET yielded a statistically significant higher proportion of equivocal and a lower proportion of benign lesion and study results (p < 0.001) than PET/CT. With PET there were 153 benign (47%), 84 (26%) equivocal and 87 (27%) malignant sites, while PET/CT detected 226 benign (70%), 10 (3%) equivocal and 88 (27%) malignant lesions. PET/CT mainly improved the characterisation of uptake in brown fat (39%), bowel (17%), muscle (5%) and thymus (7%). The study-based analysis showed that 17 equivocal and seven positive PET studies (20%) were interpreted as benign on PET/CT, while three equivocal studies were interpreted as malignant. The study-based sensitivity and specificity of PET/CT were 92% and 78% respectively. CONCLUSION: PET/CT significantly improved the characterisation of abnormal (18)FDG foci in children with cancer, mainly by excluding the presence of active malignancy in sites of increased tracer activity.

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1. The incremental value of (18)F-FDG PET/CT in paediatric malignancies. Bar-Sever Z, Keidar Z, Ben-Barak A, Bar-Shalom R, Postovsky S, Guralnik L, Ben Arush MW, Israel O. Division of Nuclear Medicine, Schneider Children's Medical Center of Israel, 14 Kaplan Street, Petach-Tikva, 49202, Israel.

Early effects of imatinib mesylate on the expression of insulin-like growth factor binding protein-3 and positron emission tomography in patients with gastrointestinal stromal tumor.

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BACKGROUND: Imatinib has demonstrated marked clinical efficacy against gastrointestinal stromal tumor (GIST). Microarray technology, real-time polymerase chain reaction (PCR) validation, and fluorodeoxyglucose-positron emission tomography (FDG-PET) imaging were used to study the early molecular effects of imatinib antitumor activity in GIST. METHODS: After exposure of sensitive and resistant sarcoma cell lines to imatinib for 24 to 48 hours, the changes in gene expression were evaluated using a 1146 unique pathway array with Western blot validation. Real-time PCR was used to confirm changes in gene expression in human GIST samples (pretreatment biopsy and posttreatment surgical specimen after 3-7 days of therapy). FDG-PET was performed to correlate radiographic findings with the effects of imatinib on gene expression in GIST. RESULTS: In all, 55 genes demonstrated a > or = 2-fold change after imatinib treatment of the GIST882 cells. Among these genes there was up-regulation of insulin-like growth factor binding protein-3 (IGFBP-3), a protein that modulates proliferation and apoptosis. Western blot analysis confirmed the increase of IGFBP-3 only in imatinib-sensitive GIST882 cells. Up to a 7-fold induction (49% mean increase; P = .08) of IGFBP-3 mRNA was found in tumor samples from patients with low residual FDG uptake, whereas there was an up to 12-fold reduction (-102% mean decrease; P = .03) in IGFBP-3 in those patients with high residual FDG uptake after imatinib therapy. CONCLUSIONS: In the current study, imatinib appears to regulates numerous genes and specifically induces IGFBP-3 in GIST cells and tumor samples. IGFBP-3 levels also were found to be higher in patients with high residual FDG uptake after imatinib therapy.

References:
1. Early effects of imatinib mesylate on the expression of insulin-like growth factor binding protein-3 and positron emission tomography in patients with gastrointestinal stromal tumor. Trent JC, Ramdas L, Dupart J, Hunt K, Macapinlac H, Taylor E, Hu L, Salvado A, Abbruzzese JL, Pollock R, Benjamin RS, Zhang W. Department of Sarcoma Medical Oncology, the University of Texas M. D. Anderson Cancer Center, Houston, Texas 77030, USA. jtrent@mdanderson.org
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inversely correlated with residual FDG uptake in GIST patients early in imatinib therapy. These initial observations suggest that IGFBP-3 is an important early marker of antitumor activity of imatinib in GIST. 2006 American Cancer Society


Impact of whole-body MRI and FDG-PET on staging and assessment of therapy response in a patient with Ewing sarcoma.

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In patients with Ewing sarcoma, precise staging is not only crucial for the therapeutic regimen but also for a reliable evaluation of response to therapy. We report on a 15-year-old girl with metastatic spread of an Ewing sarcoma who, apart from conventional staging by bone scan, chest X-ray and CT, was subsidiary examined by FDG-PET and whole-body MRI before and after chemotherapy. Both modalities detected more bone lesions than the bone scan, which led to an altered strategy for radiotherapy. Both examinations might be a great asset to stage-adjusted therapy regimens, ultimately influencing patient outcome. Copyright (c) 2005 Wiley-Liss, Inc.

Gynecol Oncol. 2006 Oct 13

Clinical impact of integrated PET/CT on the management of suspected cervical cancer recurrence.

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OBJECTIVES.: To assess the value and clinical impact of integrated PET/CT using (18)F-FDG in the diagnosis and management of women with suspected cervical cancer recurrence. METHODS.: Fifty-two patients with cervical cancer with suspected recurrence because of clinical, cytological, biochemical and radiological findings were retrospectively evaluated. A final diagnosis of recurrence was confirmed by histologic tissue biopsy or by further clinical or radiological evidence. The clinical impact of information provided by PET/CT on patient management was assessed on the basis of clinical follow-up data concerning further diagnostic or therapeutic approach. RESULTS.: Twenty-eight of 32 positive PET/CT scans (87.5%) were proven to have recurrent disease. Seventeen of 20 negative PET/CT scans (85.0%) had no evidence of disease. The sensitivity, specificity, and accuracy of PET/CT for detecting recurrence were 90.3%, 81.0%, and 86.5% respectively. PET/CT changed the management of 12 patients (23.1%) by changing treatment plan (5 patients), by initiating unplanned treatment strategy (4 patients), or by obviating the need for planned diagnostic procedures (3 patients). Median duration after performing PET/CT and last follow-up was 12 (range: 6-27) months, and the 2-year disease-free survival rate of patients with negative PET/CT scan for recurrence was significantly better than that of patients with positive PET/CT (85.0% vs. 10.9%, P=0.002). CONCLUSIONS.: In patients with a suspected recurrence of cervical cancer, integrated PET/CT using (18)F-FDG provides good anatomic and functional localization of suspicious lesions, and the better diagnostic interpretation has an impact not only on clinical management and treatment planning of patients, but also on disease-free survival.

Lung Cancer. 2006 Oct 12

Biological correlates of FDG uptake in non-small cell lung cancer.

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PURPOSE: Each pathological stage of non-small cell lung cancer (NSCLC) consists of a heterogeneous population containing patients at much higher risk than others. Noninvasive functional imaging modalities, such as (18)F-fluoro-deoxyglucose positron emission tomography (FDG-PET), could play a role in further characterization of NSCLCs. As many factors can influence the extent of FDG uptake, the underlying mechanisms for FDG accumulation in tumors, are still a matter of debate. The aim of the present study was to investigate these possible mechanisms in the primary site of early stage preoperatively untreated NSCLC. METHODS: 19 patients with early stage NSCLC, who had undergone both preoperative FDG-PET imaging and curative surgery, were enrolled in this study. Standardized uptake values (SUVs) were used for evaluation of primary tumor FDG uptake. Final diagnosis, tumor type, tumor cell differentiation and size of the primary tumors were confirmed histopathologically in resected specimens. Histologic sections were analyzed for amount of inflammation and necrosis. Expression of the glucose membrane transporters (GLUT-1 and GLUT-3); the isoforms of the glycolytic enzyme hexokinase (HK-I, HK-II and HK-III); and the cysteine protease caspase-3, was evaluated immunohistochemically. RESULTS: FDG uptake was significantly higher in squamous cell carcinomas (mean SUV 13.4+/−4.9, n=8) compared to adenocarcinomas (7.1+/−3.3, n=8, p=0.007), or large cell carcinomas (5.9+/−1.9, n=3, p=0.02). The degree of FDG accumulation seemed to depend especially on GLUT-1, GLUT-3 and tumor cell differentiation. The summed standardized values of these three parameters correlated significantly with the SUV (r=0.47, p=0.05). CONCLUSION: The present study supports the hypothesis that tumor cell differentiation in combination with overexpression of GLUT-1 and GLUT-3 determine the extent of FDG accumulation and that squamous cell carcinomas accumulate more FDG than adenocarcinomas or large cell carcinomas.

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