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Literaturübersicht PET/CT 2011

Onkologie

FDG Fluordesoxyglukose

Allgemein

Eur Radiol. 2011 Jun;21(6):1277-85. Epub 2011 Jan 28.
PET/CT without capacity limitations: a Danish experience from a European perspective.
Høilund-Carlsen PF, Gerke O, Vilstrup MH, Nielsen AL, Thomassen A, Hess S, Høilund-Carlsen M, Vach W, Petersen H.
Department of Nuclear Medicine, PET & Cyclotron Unit, Odense University Hospital, Sdr. Boulevard 29, DK-5000, Odense C, Denmark.
pfhc@ouh.regionsyddanmark.dk
We report the 3-year clinical experience of a large new Danish PET/CT centre without capacity limitations in relation to national and European
developments.
The use of PET/CT in cancer was registered from early 2006 to early 2009 to judge the impact on patient management and to compare it with
national and European trends. 6056 PET/CT examinations were performed in 4327 patients. Activity increased by 86 examinations per month
compared with the same month the year before. Referrals came primarily from oncology (23.0%), haematology (21.6%), surgery (12.6%),
internal medicine (12.7%) and gynaecology (5.5%). Referral indications were diagnosis (31.3%), staging (22.3%), recurrence detection (21.2%),
response evaluation (17.0%) and other (8.2%). Response from nearly 60% of users showed that PET/CT caused a change in diagnosis and/or
staging and/or treatment plan in 36.0% of cases. During the study period, there was a steep increase in the national use of FDG and in the
European use of PET/CT. We recorded a constantly increasing use of PET/CT that caused a change in diagnosis and/or staging and/or treatment
plan in 36.0% of cases. In line with national and European trends this may suggest a shift in favour of functional rather than anatomical imaging.

Semin Oncol. 2011 Feb;38(1):70-86.
Positron emission tomography imaging of cancer biology: current status and future prospects.
Chen K, Chen X.
Molecular Imaging Center, Department of Radiology, Keck School of Medicine, University of Southern California, Los Angeles, CA 90033,
USA. chenkai@usc.edu
Positron emission tomography (PET) is one of the most rapidly growing areas of

medical imaging, with many applications in the clinical management of patients with cancer. The principal goal of PET imaging is to visualize, characterize, and measure biological processes at the cellular, subcellular, and molecular levels in living subjects using noninvasive procedures. PET imaging takes advantage of the traditional diagnostic imaging techniques and introduces positron-emitting probes to determine the expression of indicative molecular targets at different stages of cancer progression. Although [(18)F]fluorodeoxyglucose ([(18)F]FDG)-PET has been widely utilized for staging and restaging of cancer, evaluation of response to treatment, differentiation of post-therapy alterations from residual or recurrent tumor, and assessment of prognosis, [(18)F]FDG is not a target-specific PET tracer. Over the last decade, numerous target-specific PET tracers have been developed and evaluated in preclinical and clinical studies. This review provides an overview of the current status and trends in the development of non-[(18)F]FDG PET probes in oncology and their application in the investigation of cancer biology.

Expert Rev Anticancer Ther. 2011 Feb;11(2):195-204.
Clinical applications of positron emission tomography in sarcoma management.
Quak E, van de Luijtgaarden AC, de Geus-Oei LF, van der Graaf WT, Oyen WJ.
Source
Department of Nuclear Medicine, Internal Postal Code 444, Radboud University Nijmegen Medical Centre, PO Box 9101, 6500 HB Nijmegen, The Netherlands.
Positron emission tomography (PET) with the fluorine-18-labeled glucose analog FDG is a technique that noninvasively visualizes glucose metabolism in the human body. In oncology, the addition of FDG-PET to the conventional anatomical imaging techniques provides very useful clinical information in diagnosis, staging, treatment response monitoring and follow-up. In the heterogeneous group of patients with sarcoma, FDG-PET has been shown to be of great value in improving patient care. In this article we will discuss the current role of FDG-PET in the management of patients with sarcoma and its value in assessing tumor grade, guiding biopsy, staging, monitoring treatment response, restaging and prognostication. Our future expectation is that the value of PET will only augment owing to the implementation of FDG-PET in clinical guidelines, the increasing availability worldwide, and the development of new tracers and new hybrid imaging techniques.

J Surg Oncol. 2011 May 1;103(6):602-6. doi: 10.1002/jso.21695.
Single photon emission tomography/computed tomography (SPET/CT) and

positron emission tomography/computed tomography (PET/CT) to image cancer.
Alberini JL, Edeline V, Giraudet AL, Champion L, Paulmier B, Madar O, Poinsignon A, Bellet D, Pecking AP.
Service de Médecine nucléaire, Institut Curie, Hôpital René Huguenin, 35 rue Dailly, F 92210 Saint-Cloud,
France. alberini@crh1.orgHybrid systems associating the sharpness of anatomic images coming from computed tomography (CT) and
radionuclide functional imaging (SPET or PET) are opening a new era in oncology. This multimodal imaging method is nowroutinely used for
the diagnosis, extent, follow up, treatment response and detection of occult disease in different types of malignancies with a significant impact on
the treatment strategy leading for a change for more than **68% of all investigated** patients.

Hirnmetastasen

Lungenkrebstag 16.11.2011

- solitäre Hirnmetastasen OHNE extracranielle Tumormanifestation <65J Karnofsky > 70% profitieren von Therapie solitärer Hirnmetastasen. >3cm, Ödem werden operiert, <3cm eloquentes Areal eher Radiochirurgie
- zusätzliche Ganzhirnbestrahlung (WBRT) senkt Rate für Lokalrezidiv und neue Hirnmetastasen um >25%! (aber: kein Einfluß auf Gesamtüberleben)
- außer bei Leukencephalopathie nur minimale meßbare Einschränkung der Hinrleistungsfunktion, meist durch Rezidiv/Progress bedingt
- OP von Hirnmetastasen bei >3,5 cm, <3-4 Läsionen, Hirnödem, infratentoriell, symptomatisch, CUP
- KEINE OP bei moribunder Pat., Patientenwille, unkontrollierte extrakranielle Erkrankung, Meningeosis carcinomatosa
- Metastasen sind arterielle Embolisationen am Übergang von Arteriole zu Kapillare (grey white matter junction) und infiltrieren bis 1 cm die Umgebung. Müssen mit "Sicherheitsabstand" wie Glioblastom operiert werden. Cave eloquente Areale.

stereotaktische Verfahren: nichtinvasive Radiochirurgie (LINAC, Gamma knife, Cyberknife) <3cm, <4 Läsionen, Unterschiede in Komfort, ergebnisse gleich.
Invasive Radiochirurgie (Brachytherapie, interstitielle Therapie, I-125 seed

Implantation) max. 3-4cm, ermöglicht histologische Sicherung in gleicher Sitzung

NSCLC

Lung Cancer. 2011 Aug;73(2):121-6. Epub 2011 Apr 27. The role of positron emission tomography in management of small cell lung cancer. Thomson D, Hulse P, Lorigan P, Faivre-Finn C. Department of Clinical Oncology, The Christie NHS Foundation Trust, Wilmslow Road, Withington, Manchester M20 4BX, UK.
Accurate radiological staging of small-cell lung cancer (SCLC) is of paramount importance in selection of individual patients with limited stage disease for potentially curative treatment while avoiding toxic treatment in those with distant metastatic disease. [(18)F] flurodeoxy-D-glucose (FDG) positron emission tomography (PET) is an attractive tool for this purpose but there is limited evidence to support its use in the routine staging of SCLC. Whether therapeutic decisions based on FDG-PET imaging should be made remains uncertain. There is only preliminary evidence for use of FDG-PET as a prognostic biomarker, in the assessment of response to treatment and delineation of disease in conformal radiation planning.

Eur J Radiol. 2011 May 3. [Epub ahead of print]
Prognostic value of preoperative FDG-PET in stage IA lung adenocarcinoma.
Murakami S, Saito H, Sakuma Y, Kondo T, Oshita F, Ito H, Tsuboi M, Hasegawa C, Yokose T, Kameda Y, Nakayama H, Yamada K.
Department of Thoracic Oncology, Kanagawa Cancer Center Hospital, Yokohama, Kanagawa, Japan.
Maximum standardized uptake value (SUVmax) of 18F-fluorodeoxyglucose positron emission tomography (FDG-PET) has been found to have
prognostic value. We previously reported the correlation between SUVmax and pathological invasive area, and determined an SUVmax cut-off
value of 2.15 for predicting the recurrence potential of an invasive area of diameter 5mm. Here, we evaluate the validity of FDG-PET for
prediction of recurrence in pathological stage IA lung adenocarcinoma. From February 2006 to May 2008, 100 patients with pathological stage
IA lung adenocarcinoma underwent complete resection at our hospital. Tumors were classified as air-type or solid-type based on thin-section
computed tomography (TS-CT) findings and the influence of TS-CT classification, SUVmax, and clinicopathologic features were evaluated in
terms of the incidence of recurrence. Unlike air-type adenocarcinomas, recurrent disease was detected in 8 of 62 solid-type adenocarcinomas.
SUVmax and diameter of invasive area were significantly correlated with recurrence and a shorter time to recurrence. All 8 recurrent cases had

pathological invasive area >5mm. All except one case of recurrence were solid-type adenocarcinomas with SUVmax≥2.15. Three-year disease-
free survival rates were 100% in air-type adenocarcinomas, 97.1% in solid-type adenocarcinomas with SUVmax<2.15, and 74.1% in solid-type
adenocarcinoma with SUVmax≥2.15. Combined evaluation of TS-CT classification and SUVmax had significant value in predicting recurrence
in stage IA lung adenocarcinoma, reflecting the aggressiveness of primary lung adenocarcinoma. Prediction of tumor aggressiveness could
contribute to decision-making regarding the choice of surgical procedure and treatment after surgery.

J Clin Oncol. 2011 May 1;29(13):1701-8. Epub 2011 Mar 21.

Early prediction of nonprogression in advanced non-small-cell lung cancer treated with erlotinib by using [(18)F]fluorodeoxyglucose and [(18)F]fluorothymidine positron emission tomography.

Zander T, Scheffler M, Nogova L, Kobe C, Engel-Riedel W, Hellmich M, Papachristou I, Toepelt K, Draube A, Heukamp L, Buettner R, Ko YD,
Ullrich RT, Smit E, Boellaard R, Lammertsma AA, Hallek M, Jacobs AH, Schlesinger A, Schulte K, Querings S, Stoelben E, Neumaier B,
Thomas RK, Dietlein M, Wolf J.

Source

Department I of Internal Medicine, Center for Integrated Oncology Köln Bonn, University Hospital of Cologne, 50924 Cologne, Germany.

Positron emission tomography (PET) with both 2'-deoxy-2'-[(18)F]fluoro-D-glucose (FDG) and 3'-[(18)F]fluoro-3'-deoxy-L-thymidine (FLT)
was evaluated with respect to the accuracy of early prediction of nonprogression following erlotinib therapy, independent from epidermal growth
factor receptor (EGFR) mutational status, in patients with previously untreated advanced non-small-cell lung cancer (NSCLC). Thirty-four
patients with untreated stage IV NSCLC were evaluated in this phase II trial. Changes in FDG and FLT uptake after 1 (early) and 6 (late) weeks
of erlotinib treatment were compared with nonprogression measured by computed tomography after 6 weeks of treatment, progression-free
survival (PFS), and overall survival (OS). Changes in FDG uptake after 1 week of therapy predicted nonprogression after 6 weeks of therapy with
an area under the receiver operating characteristic curve of 0.75 (P = .02). Furthermore, patients with an early metabolic FDG response (cutoff
value: 30% reduction in the peak standardized uptake value) had significantly longer PFS (hazard ratio [HR], 0.23; 95% CI, 0.09 to 0.59; P =
.002) and OS (HR, 0.36; 95% CI, 0.13 to 0.96; P = .04). Early FLT response also

predicted significantly longer PFS (HR, 0.31; 95% CI, 0.10 to 0.95; P = .04) but not OS and was not predictive for nonprogression after 6 weeks of therapy. Early FDG-PET predicts PFS, OS, and nonprogression after 6 weeks of therapy with erlotinib in unselected, previously untreated patients with advanced NSCLC independent from EGFR mutational status.

Oncologist. 2011;16(3):319-26. Epub 2011 Feb 21.
Role of 18F-fluorodeoxyglucose positron emission tomography in predicting epidermal growth factor receptor mutations in non-small cell lung cancer.
Mak RH, Digumarthy SR, Muzikansky A, Engelman JA, Shepard JA, Choi NC, Sequist LV.
Harvard Radiation Oncology Program, Boston, MA, USA.
To compare (18)F-fluorodeoxyglucose positron emission tomography (FDG-PET) and computed tomography (CT) imaging characteristics in non-small cell lung cancer (NSCLC) with or without epidermal growth factor receptor (EGFR) mutations.
We retrospectively identified NSCLC patients who underwent EGFR mutation testing and pretreatment FDG-PET and CT scans. The maximum standard uptake value (SUV(max)) of the primary tumor and any metastases was measured and normalized to the SUV of blood in the pulmonary artery. We compared normalized SUV(max) values between EGFR-mutant and wild-type patients and modeled radiographic and clinical predictors of EGFR mutation status. Receiver operator characteristic (ROC) curves were used to identify potential SUV cutoffs predictive of genotype. We included 100 patients (24 EGFR-mutant and 76 wild-type). There was a trend for higher normalized SUV(max) in the primary tumors among patients with EGFR-wild-type versus mutant (median, 3.4; range, 0.6-12.8; versus median, 2.9; range, 0.4-5.0; p = .09).
Normalized SUV(max) of nodal and distant metastases, and CT characteristics were not associated with genotype. On multivariate analysis, low normalized SUV(max) of the primary tumor was predictive for EGFR mutation (odds ratio, 0.72; 95% confidence interval, 0.53-0.98; p = .034).
ROC curve analyses yielded an area under the curve of 0.62, and identified a potential cutoff of ≥ 5.0 to distinguish wild-type from mutant tumors.In this retrospective study, high FDG avidity (normalized SUV(max) ≥ 5) correlated with EGFR-wild-type genotype. Although genotyping remains the gold standard, further work to validate FDG-PET as a surrogate for tumor genotype may provide useful information in patients without available tumor tissue.

Int J Radiat Oncol Biol Phys. 2011 Apr 4. [Epub ahead of print] F-18-FDG-PET

Confined Radiotherapy of Locally Advanced NSCLC With Concomitant Chemotherapy: Results of the **PET-PLAN Pilot Trial**. Fleckenstein J, Hellwig D, Kremp S, Grgic A, Gröschel A, Kirsch CM, Nestle U, Rübe C. **Department of Radiotherapy and Radiation Oncology, Saarland University Medical School, Homburg, Germany.**
The integration of fluoro-deoxy-D-glucose positron emission tomography (FDG-PET) in the process of radiotherapy (RT) planning of locally advanced non-small-cell lung cancer (NSCLC) may improve diagnostic accuracy and minimize interobserver variability compared with target volume definition solely based on computed tomography. Furthermore, irradiating only FDG-PET-positive findings and omitting elective nodal regions may allow dose escalation by treating smaller volumes. The aim of this prospective pilot trial was to evaluate the therapeutic safety of FDG-PET-based RT treatment planning with an autocontour-derived delineation of the primary tumor. Eligible patients had Stages II-III inoperable NSCLC, and simultaneous, platinum-based radiochemotherapy was indicated. FDG-PET and computed tomography acquisitions in RT treatment planning position were coregistered. The clinical target volume (CTV) included the FDG-PET-defined primary tumor, which was autodelineated with a source-to-background algorithm, plus FDG-PET-positive lymph node stations. Limited by dose restrictions for normal tissues, prescribed total doses were in the range of 66.6 to 73.8 Gy. The primary endpoint was the rate of out-of-field isolated nodal recurrences (INR). As per intent to treat, 32 patients received radiochemotherapy. In 15 of these patients, dose escalation above 66.6 Gy was achieved. No Grade 4 toxicities occurred. After a median follow-up time of 27.2 months, the estimated median survival time was 19.3 months. During the observation period, one INR was observed in 23 evaluable patients. FDG-PET-confined target volume definition in radiochemotherapy of NSCLC, based on a contrast-oriented source-to-background algorithm, was associated with a low risk of INR. It might provide improved tumor control because of dose escalation.

Clin Nucl Med. 2011 Jun;36(6):429-33.
Value of dual-time-point FDG PET/CT for mediastinal nodal staging in non-small-cell lung cancer patients with lung comorbidity.
Hu M, Han A, Xing L, Yang W, Fu Z, Huang C, Zhang P, Kong L, Yu J.
Department of Radiation Oncology and Shandong Province Key Laboratory of Radiation Oncology, Shandong Cancer Hospital, Shandong
Academy of Medical Sciences, Jinan, People's Republic of China.
To evaluate the efficacy of dual-time-point F-18 fluorodeoxyglucose positron emission tomography (FDG PET)/ computed tomography (CT) for
mediastinal nodal staging in non-small-cell lung cancer patients with lung comorbidity. Fifty-three pathologically proven non-small-cell lung
cancer patients with pulmonary comorbidity and 49 patients as controlled group without comorbidity were enrolled. PET/CT was performed at 1-
hour (whole body) post-FDG injection and repeated 2 hours (thoracic) after injection.

All patients received radical surgery with system
mediastinal lymph node (LN) dissection. The results of LN detection by single-time-point and dual-time-point scan were compared with the
histopathologic findings. On a per-patient basis, in patients with pulmonary comorbidity, the sensitivity, specificity, accuracy, and positive
predictive values (PPV), and negative predictive values of single-time-point scan were 87.5%, 59.5%, 67.9%, 48.3%, and 91.7%, respectively.
Those values of dual-time-point scan were 93.8%, 67.6%, 75.5%, 55.6%, and 96.2%, respectively. In patients without comorbidity, dual-time-
point scan was similar in those values to single-time-point. On a per-nodal station basis, the specificity, accuracy, and PPV of dual-time-point
scan were better than those of single-time-point with statistically significant differences (P = 0.017, 0.002, and 0.027, respectively) in patients
with pulmonary comorbidity, but the difference was not statistically significant in patients with no pulmonary comorbidity. Dual-time-point FDG
PET/CT is more effective for mediastinal nodal staging than single-time-point in patients with pulmonary comorbidity. Dual-time-point scan was
useful for diagnosis of mediastinal LN metastases in reducing the false-positive results in all patients, but improved specificity, accuracy, and
PPV only in patients with pulmonary comorbidity.

Int J Radiat Oncol Biol Phys. 2011 Mar 25. [Epub ahead of print]
Noninvasive Evaluation of Microscopic Tumor Extensions Using Standardized Uptake Value and Metabolic Tumor Volume in Non- Small-Cell Lung Cancer.
Meng X, Sun X, Mu D, Xing L, Ma L, Zhang B, Zhao S, Yang G, Kong FM, Yu J.
Department of Radiation Oncology, Shandong Cancer Hospital & Institute, Jinan, China.
To prospectively evaluate whether maximal microscopic extensions (MEmax) correlate with maximal standardized uptake value (SUVmax) and
metabolic tumor volume (MTV) at 18F-fluorodeoxyglucose (FDG) positron emission tomography/computed tomography (PET/CT) images in
non-small-cell lung cancer (NSCLC). Thirty-nine patients with Stage I-IIIA NSCLC underwent surgery after FDG-PET/CT scanning. SUVmax
and MTV were calculated on the PET/CT images. The maximum linear distance from the tumor margin to the farthest extent of the tumor in
every dimension was measured at the tumor section. The correlations among MEmax, SUVmax, MTV and other clinical pathologic parameters
were analyzed. MEmax for all patients had a significant correlation with SUVmax (r = 0.777, p = 0.008) and MTV (r = 0.724, p < 0.001). When
expressed in terms of the probability of covering ME with respect to a given margin, we suggested that margins of 1.93 mm, 3.90 mm, and 9.60

mm for SUVmax ≤5, 5-10, and >10 added to the gross tumor volume would be adequate to cover 95% of ME. This study demonstrated that
tumors with high SUVmax and MTV have more MEmax and would therefore require more margin expansion from gross tumor volume to
clinical target volume. FDG-PET/CT, especially for SUVmax, is promising and effective and merits additional study in noninvasive delimiting of
the clinical target volume margin for NSCLC.

SCLC

Lungenkrebstag 16.11.2011

- SCLC: Staging wie NSCLC im TNM System, inkl. Lymphknotenstatus. OP-Indikation ähnlich wie NSCLC (Abgrenzung Karzinoid!), dann Chemo und bei Ansprechen Ganzhirnbestrahlung
- bei Chemotherapie hat sich in den letzten 10 Jahren nichts geändert. Erstlinie 4 Zyklen (LD) oder 6 Zyklen (ED) Cisplatin Etoposid, bei Frührezidiv <6Monate Topotecan, bei Spätrezidiv >6 Monate erneute Induktion Cisplatin Etoposid
- ASCO 2011: kein Beitrag zu genetisch stratifiziertem personalisiertem Ansatz
- SCLC: Rebiopsie bei Nichtansprechen! Cave Mischzelltumoren, Karzinoid
- SCLC:Chemo SOFORT nach Diagnosestellung beginnen nicht erst nach Symptomen

Staging nach 1. Zyklus 4 Zyklen LD 6 Zyklenn ED Cisplatin besser als Carboplatin Kein Anthrazyklin ED Carboplatin präferiert bessere Verträglichkeit Intensivierung HDCT/ASCT ohne gesicherten Wert Slotman JCO 2009 ZNS Bestrahlung nach Ansprechen auf Chemo bei ED /stable disease Steigerung des 1 Jahres Überlebens von 13 auf 27% PLOS One 2009: über 27 Jahre in randomisierten Phase II Studien keine Verbesserung

- Genomics: K-ras Mutation bei AdenoCa sagt Ansprechen auf Cetuximab (Erbitux) und panitumumab (vectibix) voraus. Wildtyp: gutes Ansprechen, aktivierende Mutation schlechtes Ansprechen auf EGFR InhibitorenEGFR Mutation sagt Ansprechen auf Erlotinib voraus. EGFR por: 60% Ansprechen auf Tarceva

SCLC: alle Tumoren einheitliche Mutationsmuster, sowohl die ansprechenden als auch die nicht ansprechenden. eventuell biologischer Ansatz möglich?

NHL Non-Hodgkin-Lymphom

J Clin Oncol. 2011 May 10;29(14):1844-54. Epub 2011 Apr 11.
Role of functional imaging in the management of lymphoma.
Cheson BD
Division of Hematology/Oncology , Georgetown University Hospital, 3800 Reservoir Rd, NW , W ashington, DC 20007, US A.
bdc4@georgetown.edu
18-F-fluorodeoxyglucose (FDG) -positron emission tomography (PET), and more recently PET/computed tomography (CT), is the most sensitive
and specific imaging technique currently available for patients with lymphoma. Nevertheless, despite being increasingly used in pretreatment
assessment, midtreatment evaluation of response, post-treatment restaging, and surveillance during follow-up of patients with lymphoma, its
impact on clinical outcome in most clinical situations remains to be confirmed. PET/CT provides its greatest clinical benefit in the post-treatment
evaluation of Hodgkin's lymphoma and diffuse large B-cell lymphoma; however, the role of metabolic imaging in other indications and in other
histologies remains to be demonstrated. Ongoing risk-adapted studies will hopefully provide evidence for clinical improvement on the basis of
altering treatment as a result of interim PET results. Efforts are ongoing to better standardize the conduct and interpretation of FDG-PET scans.
FDG-PET has the potential to improve lymphoma patient management; however, its usefulness will likely vary by histology, stage, therapy, and
clinical setting.

Neoplasma. 2011;58(4):291-7.
Determining the extent and stage of disease in patients with newly diagnosed non-Hodgkin's lymphoma using 18F-FDG-PET/CT.
Papajik T, Myslivecek M, Skopalova M, Malan A, Buriankova E, Koza V, Hnatkova M, Trneny M, Sedova Z, Kubova Z, Koranda P, Flodr P,
Jarkovsky J, Dusek L, Indrak K.
Department of Hemato-Oncology, University Hospital Olomouc and Faculty of Medicine and Dentistry, Palacky University I.P.Pavlova
Olomouc, Czech Republic. tomas.papajik@fnol.cz
Positron emission tomography (PET) using 2-[fluorine-18]-fluoro-2-deoxy-D-glucose (18F-FDG) combined with computed tomography (CT)
represents a three-dimensional imaging method suitable for staging in patients with non-Hodgkin's lymphomas (NHLs). The aim of our
prospective multicenter study was to assess the value of initial PET/CT as compared with CT and PET alone for determining the stage and extent
of the disease. A total of 122 patients with newly diagnosed NHL were examined

using PET/CT. Four patients with resected lymphoma lesion
and negative PET/CT were therefore excluded from the study. Of the remaining 118 cases, a total of 117 (99%) were described as 18F-FDG-avid.
When compared with PET/CT, CT and PET showed very good sensitivity of lymph node imaging (97% and 100%, respectively); the specificity,
however, was significantly lower (66.7% and 94.4%, respectively; p=0.0001). When detecting organ lesions, the sensitivity of CT and PET was
lower than that of PET/CT (92.5% and 96.3%, respectively; p=0.0001); specificity was significantly decreased in CT and a little lower in PET
(59.5% and 91.9%; p=0.0001). When compared with CT alone, PET/CT changed staging of the disease in 11 patients (9%) and was able to detect
a total of 82 discrepancies in 67 of the 117 patients (57%). In conclusion, PET/CT is a new standard in imaging the involvement of lymph nodes
and extranodal organs in NHL patients regardless of their histopathological types. Both sensitivity and specificity of the examination are higher
than those of CT as well as PET alone.

Eur J Cancer. 2011 Jun;47(9):1312-8. Epub 2011 Feb 18.
**Prognostic significance of interim 1␣F-FDG PET/CT after three or four cycles of R-CHOP chemotherapy in the treatment of diffuse
large B-cell lymphoma.**
Yang DH, Min JJ, Song HC, Jeong YY, Chung WK, Bae SY, Ahn JS, Kim YK, Bom HS, Chung IJ, Kim HJ, Lee JJ.
Department of Hematology-Oncology, Chonnam National University Hwasun Hospital, Hwasun, Jeollanam-do, Republic of Korea.
(18)F-fluoro-2-dexoy-D-glucose-positron emission tomography (FDG-PET)/computerised tomography (CT) has been used for staging and
monitoring responses to treatment in patients with diffuse large B cell lymphoma (DLBCL). The sequential interim PET/CT was prospectively
investigated to determine whether it provided additional prognostic information and could be a positive predictable value within patients with the
same international prognostic index (IPI) after the use of rituximab in DLBCL. One hundred and sixty-one patients with newly diagnosed
DLBCL were enroled; the assessment of the PET/CT was performed at the time of diagnosis and mid-treatment of rituxibmab,
cyclophosphamide, doxorubicin, vincristine and prednisolone (R-CHOP). Sixty-seven patients (41.6%) presented with advanced stage disease
and 27 (16.8%) had bulky lesions. Forty-three patients (26.7%) continued to have positive metabolic uptakes with a significantly high relapse rate
(62.8%) compared to the patients with a negative interim PET/CT (12.1%) (P<0.01). After a median follow-up of 30.8months, the positivity of
interim PET/CT was found to be a prognostic factor for both overall survival (OS) and

progression-free survival (PFS), with a hazard ratio of
4.07 (2.62-6.32) and 5.46 (3.49-8.52), respectively. In the low-risk IPI group, the 3-year OS and PFS rates were significantly different in the
patients with positive (53.3% and 52.5%) and negative (93.8% and 88.3%) interim PET/CT, respectively (P<0.01). These significant prognostic
differences of interim PET/CT responses were consistent with the results of the patients with high-risk IPI group (P<0.01). Interim PET/CT
scanning had a significant predictive value for disease progression and survival of DLBCL in post-rituximab treatment; it might be the single
most important determinant of clinical outcome in patients with the same IPI risk.

Eur J Haematol. 2011 Aug;87(2):123-9. doi: 10.1111/j.1600-0609.2011.01645.x.
The utility of positron emission tomography/computed tomography in the staging of extranodal natural killer/T-cell lymphoma.
Fujiwara H, Maeda Y, Nawa Y, Yamakura M, Ennishi D, Miyazaki Y, Shinagawa K, Hara M, Matsue K, Tanimoto M.
Division of Hematology/Oncology, Department of Medicine, Kameda General Hospital, Chiba, Japan.
Natural killer (NK)/T-cell lymphoma cases are rarely discovered using positron emission tomography/computed tomography (PET/CT). We
compared the utility of PET/CT and that of conventional methods (CMs; CT with IV contrast, biopsies from primary sites, and bone marrow
examinations) in the staging of extranodal NK/T-cell lymphoma. Nineteen untreated patients with extranodal NK/T-cell lymphoma at three
institutions were analyzed. PET/CT and CMs were applied for initial workups following diagnosis. PET/CT and CMs were compared and
evaluated for their ability to detect tumor lesions and their influence on the staging and treatment strategies. In total, 116 lesions were detected by
CM and PET/CT. Using PET/CT, 108 lesions (93%) were discovered. The number of nodal lesions was 28: all were positive by PET/CT and 26
(93%) by CMs. The number of extranodal lesions was 89: 84 (94%) and 54 (61%) lesions were positive by PET/CT and CMs, respectively.
PET/CT was superior to CMs in detecting cutaneous lesions [31/31 lesions (100%) vs. 20/31 lesions (65%), respectively; P=0.042]. Bone
marrow involvement was confirmed pathologically in only seven patients; four cases (57%) were positive by PET/CT. Using CMs, ten patients
(53%) were stages I-II and nine (47%) were stages III-IV. Using PET/CT, eight patients (42%) were in stages I-II and 11 (58%) were in stages
III-IV. PET/CT findings altered the stage and treatment strategy in two cases (11%). Our study demonstrated that PET/CT is a useful tool for
detecting extranodal lesions in NK/T-cell lymphoma, particularly cutaneous lesions. PET/CT may therefore influence future staging and
treatment strategies.

Joly F, Paciencia M, Bor C, Aide N.
Hell J Nucl Med. 2011 Jan-Apr;14(1):2-5.
Nuclear medicine in myeloma: the state of the science and emerging trends.
Sood A, Revannasiddaiah S, Kumar R.
We present the different imaging modalities in relation to myeloma, ranging from the time tested X-ray radiography to the newer promising methods of fluorine-18 fluorodesoxyglucose-positron emission tomography ((18)F-FDG-PET) and technetium-99m methoxy isobutyl isonitrite ((99m)Tc-MIBI) scintigraphy. A small discussion regarding newer methods such as fluoride-18 positron emission tomography ((18)F-PET), fluorine-18-fluoro-deoxy-L-thymidine positron emission tomography ((18)F-FLT PET), carbon-11 methionine positron emission tomography ((11)C-methionine PET) and the tritiated thymidine labeling index is also included. They have different mechanisms of tracer uptake enabling the visualization of the spectrum of the disease manifestations ranging from osteoblastic to osteolytic lesions, and also the study of the metabolic status, proliferative and protein activity, in skeletal and in extra-skeletal sites.

HD Morbus Hodgkin

Adv Hematol. 2011;2011:271595. Epub 2010 Dec 22.
Prognostication and Risk-Adapted Therapy of Hodgkin's Lymphoma Using Positron Emission Tomography.
Kasamon YL.
Department of Oncology and Medicine, Johns Hopkins University School of Medicine, 1650 Orleans Street, Baltimore, MD 21231, USA.
The use of (18)F-fluorodeoxyglucose positron emission tomography (FDG-PET) for response assessment in lymphoma is now widespread.
Prognostic information obtained from PET performed after two to three cycles of chemotherapy may guide more individualized, risk-adapted
therapeutic strategies. Progress in the risk stratification of Hodgkin's lymphoma through midtreatment PET is reviewed, with a focus on
management implications in newly diagnosed and relapsed disease. How to tailor treatment on the basis of the interim PET result is not yet
defined but is the subject of ongoing trials.

Eur J Nucl Med Mol Imaging. 2011 Sep 6. [Epub ahead of print]

Early interim (18)F-FDG PET in Hodgkin's lymphoma: evaluation on 304 patients.
Zinzani PL, Rigacci L, Stefoni V, Broccoli A, Puccini B, Castagnoli A, Vaggelli L, Zanoni L, Argnani L, Baccarani M, Fanti S.
Institute of Hematology and Medical Oncology "L. e A. Seràgnoli", Policlinico "Sant'Orsola-Malpighi", University of Bologna, Bologna, Italy.
The use of early (interim) PET restaging during first-line therapy of Hodgkin's lymphoma (HL) in clinical practice has considerably increased because of its ability to provide early recognition of treatment failure allowing patients to be transferred to more intensive treatment regimens.Between June 1997 and June 2009, 304 patients with newly diagnosed HL (147 early stage and 157 advanced stage) were treated with the ABVD regimen at two Italian institutions. Patients underwent PET staging and restaging at baseline, after two cycles of therapy and at the end of the treatment.Of the 304 patients, 53 showed a positive interim PET scan and of these only 13 (24.5%) achieved continuous complete remission (CCR), whereas 251 patients showed a negative PET scan and of these 231 (92%) achieved CCR. Comparison between interim PET- positive and interim PET-negative patients indicated a significant association between PET findings and 9-year progression-free survival and 9- year overall survival, with a median follow-up of 31 months. Among the early-stage patients, 19 had a positive interim PET scan and only 4 (21%) achieved CCR; among the 128 patients with a negative interim PET scan, 122 (97.6%) achieved CCR. Among the advanced-stage patients, 34 showed a persistently positive PET scan with only 9 (26.4%) achieving CCR, whereas 123 showed a negative interim PET scan with 109 (88.6%) achieving CCR.Our results demonstrate the role of an early PET scan as a significant step forward in the management of patients with early-stage or advanced-stage HL.

Kopf-Hals-Tumoren

Diagnostic performance of post-treatment FDG PET or FDG PET/CT imaging in head and neck cancer: a systematic review and meta-analysis.
Gupta T, Master Z, Kannan S, Agarwal JP, Ghsoh-Laskar S, Rangarajan V, Murthy V, Budrukkar A.
Department of Radiation Oncology, Tata Memorial Centre, Kharghar, Navi Mumbai, India, tejpalgupta@rediffmail.com.
Our objective was to conduct a systematic review and meta-analysis of studies assessing the diagnostic performance of (18)F-fluorodeoxyglucose
positron emission tomography (FDG PET) with or without computed tomography (CT) in post-treatment response assessment and/or surveillance

imaging of head and neck squamous cell carcinoma (HNSCC).
A systematic search of the indexed medical literature was done using appropriate keywords to identify relevant studies. Metrics of diagnostic test
accuracy, viz. sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were extracted from individual studies
and combined using a random effects model to yield weighted mean pooled estimates with 95% confidence intervals (95% CI). The impact of
timing of post-treatment scan, study quality and advancements in PET technology was explored through meta-regression. A total of 51 studies
involving 2,335 patients were included in the meta-analysis. The weighted mean (95% CI) pooled sensitivity, specificity, PPV and NPV of post-
treatment FDG PET(CT) for the primary site was 79.9% (73.7-85.2%), 87.5% (85.2-89.5%), 58.6% (52.6-64.5%) and 95.1% (93.5-96.5%),
respectively. Similar estimates for the neck were 72.7% (66.6-78.2%), 87.6% (85.7-89.3%), 52.1% (46.6-57.6%) and 94.5% (93.1-95.7%),
respectively. Scans done ≥12 weeks after completion of definitive therapy had moderately higher diagnostic accuracy on meta-regression analysis
using time as a covariate. The overall diagnostic performance of post-treatment FDG PET(CT) for response assessment and surveillance imaging
of HNSCC is good, but its PPV is somewhat suboptimal. Its NPV remains exceptionally high and a negative post-treatment scan is highly
suggestive of absence of viable disease that can guide therapeutic decision-making. Timing of post-treatment imaging has a significant, though
moderate impact on diagnostic accuracy.

Int J Radiat Oncol Biol Phys. 2011 Feb 5. [Epub ahead of print]
The Role of Pretreatment FDG-PET in Nasopharyngeal Carcinoma Treated with Intensity-Modulated Radiotherapy.
Liu WS, Wu MF, Tseng HC, Liu JT, Weng JH, Li YC, Lee JK.
School of Medicine, Chung Shan Medical University and Department of Radiation Oncology, Chung Shan Medical University Hospital, Taichung, Taiwan.
Pretreatment with 2- [(18)F] fluorodeoxyglucose positron emission tomography ((18)F-FDG-PET) was evaluated as a predictor of local failure- free survival (LFFS), disease-free survival (DFS), and overall survival (OS) in patients with nonkeratinizing nasopharyngeal carcinoma (NPC) treated with intensity-modulated radiation therapy (IMRT) alone or concurrently with chemotherapy (CCRT). Seventy-five M0 NPC patients who received FDG-PET before treatment were analyzed. The primary tumor FDG uptake was measured as the maximum standardized uptake value (SUVmax). The LFFS, DFS, and OS were calculated by the Kaplan-Meier method, and the differences were evaluated on log-rank test. The prognostic significance was assessed by univariate and multivariate analyses. Eighteen patients received IMRT

alone and 57 received CCRT. The mean SUVmax was significantly higher in 12 patients with locoregional or distant failure than in those without failure (p <0.001). On multivariate analysis, the SUVmax was the only significant variable for 5-year LFFS (p = 0.017) and DFS (p = 0.000) but not for OS (p = 0.065). SUVmax is a potential independent prognostic predictor of clinical outcomes in patients with nasopharyngeal carcinoma treated with IMRT alone or with CCRT. A high (18)F-FDG uptake (SUVmax >5) indicates poor outcome in patients with NPC.

J Nucl Med. 2011 Mar;52(3):331-4. Epub 2011 Feb 14.
Molecular imaging in radiotherapy planning for head and neck tumors.
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vincent.gregoire@uclouvain.be
Molecular imaging uses noninvasive techniques to visualize various biologic pathways and physiologic characteristics of tumors and normal
tissues. In relation to radiation therapy, PET with the tracer (18)F-FDG offers a unique opportunity to refine the target volume delineation in
patients with squamous cell carcinoma of the head and neck, in turn affecting dose distribution and, it is hoped, patient outcome. Even more so,
in the framework of adaptive treatment and theragnostics, whereby dose distribution is adapted in space and time over the typical course of
radiotherapy, molecular imaging with PET offers an elegant research avenue to further improve the therapeutic ratio. Such implementation could
be of particular interest with tracers other than (18)F-FDG, such as tracers of hypoxia and proliferation.

Int J Radiat Oncol Biol Phys. 2011 Jan 27. [Epub ahead of print]
Analysis of Pretreatment FDG-PET SUV Parameters in Head-and-Neck Cancer: Tumor SUV(mean) has Superior Prognostic Value.
Higgins KA, Hoang JK, Roach MC, Chino J, Yoo DS, Turkington TG, Brizel DM.
Department of Radiation Oncology, Duke University Medical Center, Durham, NC.
To evaluate the prognostic significance of different descriptive parameters in head-and-neck cancer patients undergoing pretreatment [F-18] fluoro-D-glucose-positron emission tomography (FDG-PET) imaging.Head-and-neck cancer patients who underwent FDG-PET before a course of curative intent radiotherapy were retrospectively analyzed. FDG-PET imaging parameters included maximum (SUV(max)), and mean (SUV(mean)) standard uptake values, and total lesion glycolysis (TLG). Tumors and lymph nodes were defined on co-registered axial computed tomography (CT) slices. SUV(max) and SUV(mean) were measured within these anatomic regions. The relationships between pretreatment SUV(max), SUV(mean), and TLG for the primary site and lymph nodes were assessed using a

univariate analysis for disease-free survival (DFS), locoregional control (LRC), and distant metastasis-free survival (DMFS). Kaplan-Meier survival curves were generated and compared via
the log rank method. SUV data were analyzed as continuous variables. A total of 88 patients was assessed. Two-year OS, LRC, DMFS, and
DFS for the entire cohort were 85%, 78%, 81%, and 70%, respectively. Median SUV(max) for the primary tumor and lymph nodes was 15.4 and
12.2, respectively. Median SUV(mean) for the primary tumor and lymph nodes was 7 and 5.2, respectively. Median TLG was 770. Increasing
pretreatment SUV(mean) of the primary tumor was associated with decreased disease-free survival ($p = 0.01$). Neither SUV(max) in the primary
tumor or lymph nodes nor TLG was prognostic for any of the clinical endpoints. Patients with pretreatment tumor SUV(mean) that exceeded the
median value (7) of the cohort demonstrated inferior 2-year DFS relative to patients with SUV(mean) ≤ the median value of the cohort, 58% vs.
82%, respectively, $p = 0.03$. Increasing SUV(mean) in the primary tumor was associated with inferior DFS. Although not routinely reported,
pretreatment SUV(mean) may be a useful prognostic FDG-PET parameter and should be further evaluated prospectively.

Eur J Nucl Med Mol Imaging. 2011 Aug;38(8):1449-58. Epub 2011 Apr 2.
Can FDG PET predict radiation treatment outcome in head and neck cancer? Results of a prospective study. Schinagl DA, Span PN, Oyen WJ, Kaanders JH.
Department of Radiation Oncology, Radboud University Nijmegen Medical Centre, Nijmegen 6500 HB, The Netherlands. d.schinagl@rther.umcn.nl
In head and neck cancer (HNC) various treatment strategies have been developed to improve outcome, but selecting patients for these intensified treatments remains difficult. Therefore, identification of novel pretreatment assays to predict outcome is of interest. In HNC there are indications that pretreatment tumour (18)F-fluorodeoxyglucose (FDG) uptake may be an independent prognostic factor. The aim of this study was to assess the prognostic value of FDG uptake and CT-based and FDG PET-based primary tumour volume measurements in patients with HNC treated with (chemo)radiotherapy. A total of 77 patients with stage II-IV HNC who were eligible for definitive (chemo)radiotherapy underwent coregistered pretreatment CT and FDG PET. The gross tumour volume of the primary tumour was determined on the CT (GTV(CT)) and FDG PET scans. Five PET segmentation methods were applied: interpreting FDG PET visually (PET(VIS)), applying an isocontour at a standardized uptake value (SUV) of 2.5 (PET(2.5)), using fixed thresholds of 40% and 50% (PET(40%), PET(50%)) of the maximum intratumoral FDG activity (SUV(MAX)) and applying an adaptive threshold based on the signal-to-background (PET(SBR)). Mean FDG uptake for each PET-based volume was recorded (SUV(mean)). Subsequently, to determine the metabolic volume, the integrated SUV was calculated as the product of PET- based volume and SUV(mean). All these variables were analysed as potential predictors of local control (LC), regional recurrence-free survival

(RRFS), distant metastasis-free survival (DMFS), disease-free survival (DFS) and overall survival (OS) In oral cavity/oropharynx tumours PET(VIS) was the only volume-based method able to predict LC. Both PET(VIS) and GTV(CT) were able to predict DMFS, DFS and OS in these subsites. Integrated SUVs were associated with LC, DMFS, DFS and OS, while SUV(mean) and SUV(MAX) were not. In hypopharyngeal/laryngeal tumours none of the variables was associated with outcome. There is no role yet for pretreatment FDG PET as a predictor of (chemo)radiotherapy outcome in HNC in daily routine. However, this potential application needs further exploration, focusing both on FDG PET-based primary tumour volume, integrated SUV and SUV(MAX) of the primary tumour.

Clin Oncol (R Coll Radiol). 2011 Oct;23(8):512-7. Epub 2011 Apr 17.
Neck Dissection can be avoided after Sequential Chemoradiotherapy and Negative Post-treatment Positron Emission Tomography-Computed Tomography in N2 Head and Neck Squamous Cell Carcinoma.
Loo SW, Geropantas K, Beadsmoore C, Montgomery PQ, Martin WM, Roques TW.
Department of Oncology, Norfolk and Norwich University Hospitals NHS Foundation Trust, Norwich, UK.
This study assessed neck control in patients with N2 head and neck squamous cell carcinoma (HNSCC) treated with sequential chemoradiotherapy (SCRT) and the incidence of neck recurrence when neck dissection was withheld in those with negative post-treatment fluorine-18 fluorodeoxyglucose positron emission tomography (FDG PET). Thirty-four consecutive patients with N2 HNSCC who were treated with radical intent using SCRT were included. Twenty-seven patients received concomitant platinum-based chemotherapy with their radiotherapy. Nineteen patients were treated with intensity-modulated radiotherapy. PET-computed tomography (PET-CT) was obtained 3 months after the completion of radical radiotherapy. Neck dissection was carried out only in those with increased FDG uptake in the neck. The median follow-up was 39.1 months. One patient had increased FDG uptake in the neck post-treatment, which was false positive for malignancy. The remaining 33 patients were observed without neck dissection. No regional recurrence occurred. The negative predictive value (NPV) of post-treatment PET-CT was 100%. Good disease control in the neck can be achieved in patients with N2 HNSCC with SCRT. Post-treatment PET-CT has a high NPV. Neck dissection can be avoided if post-treatment PET-CT is negative.

Radiother Oncol. 2011 Aug 30. [Epub ahead of print]
(18)F-FDG-PET imaging in radiotherapy tumor volume delineation in treatment of head and neck cancer.
Delouya G, Igidbashian L, Houle A, Bélair M, Boucher L, Cohade C, Beaulieu S,

Filion EJ, Coulombe G, Hinse M, Martel C, Després P, Nguyen-Tan PF.
Department of Radiation Oncology, Centre Hospitalier de l'Université de Montréal (CHUM), Montréal, Canada.
To determine the impact of (18)F-fluorodeoxyglucose positron emission tomography (PET) in radiotherapy target delineation and patient management for head and neck squamous cell carcinoma (HNSCC) compared to computed tomography (CT) alone.Twenty-nine patients with HNSCC were included. CT and PET/CT obtained for treatment planning purposes were reviewed respectively by a neuroradiologist and a nuclear medicine specialist who were blinded to the findings from each other. The attending radiation oncologist together with the neuroradiologist initially defined all gross tumor volume of the primary (GTVp) and the suspicious lymph nodes (GTVn) on CT. Subsequently, the same radiation oncologist and the nuclear medicine specialist defined the GTVp and GTVn on (18)F-FDG-PET/CT. Upon disagreement between CT and (18)F-FDG-PET on the status of a particular lymph node, an ultrasound-guided fine needle aspiration was performed. Volumes based on CT and (18)F-FDG-PET were compared with a paired Student's t-test. For the primary disease, four patients had previous diagnostic tonsillectomy and therefore, FDG uptake occurred in 25 patients. For these patients, GTVp contoured on (18)F-FDG-PET (GTVp-PET) were smaller than the GTVp contoured on CT (GTVp-CT) in 80% of the cases, leading to a statistically significant volume difference (p=0.001). Of the 60 lymph nodes suspicious on PET, 55 were also detected on CT. No volume change was observed (p=0.08). Ten biopsies were performed for lymph nodes that were discordant between modalities and all were of benign histology. Distant metastases were found in two patients and one had a newly diagnosed lung adenocarcinoma. GTVp-CT was significantly larger when compared to GTVp-PET. No such change was observed for the lymph nodes. (18)F-FDG-PET modified treatment management in three patients, including two for which no curative radiotherapy was attempted. Larger multicenter studies are needed to ascertain whether combined (18)F-FDG-PET/CT in target delineation can influence the main clinical outcomes.

Mol Imaging Biol. 2011 Feb;13(1):172-7.
Comparison of FLT-PET and FDG-PET for visualization of head and neck squamous cell cancers.
Hoshikawa H, Nishiyama Y, Kishino T, Yamamoto Y, Haba R, Mori N.
Department of Otolaryngology, Faculty of Medicine, Kagawa University, 1750-1 Ikenobe, Miki-cho, Kita-gun, Kagawa 761-0793, Japan. hiro@med.kagawa-u.ac.jp
We compared 3'[F-18]fluoro-3'-deoxythymidine (FLT) positron emission tomography (PET) and 2-deoxy-2-[F-18]fluoro-D-glucose (FDG) for PET visualization of head and neck squamous cell cancers (HNSCCs) and evaluated which might better reflect proliferative activity as indicated by the Ki-67 index. A total of 43 patients with HNSCCs were examined with FLT-PET and FDG-PET. The PET images were evaluated qualitatively for regions of focally increased metabolism and for semiquantitative analysis the maximum standardized uptake value (SUV) was

calculated. For depiction of primary tumours, the sensitivity of both approaches was 100%. The mean (± SD) SUV for FLT (5.65 ± 2.96) was significantly lower than that for FDG (10.9 ± 4.91; p < 0.0001). No significant differences were found for the T category. However, the mean (± SD) FLT SUV was significantly higher in poorly than in well-differentiated tumours (6.49 ± 3.13 vs. 4.2 ± 2.08; p < 0.04). Similarly, FDG SUVs in poorly and moderately differentiated tumours (12.72 ± 4.8 and 11.46 ± 4.64) were significantly higher than in well-differentiated tumours (7.45 ± 3.51; p < 0.004 and p < 0.02). No significant correlation was observed with the Ki-67 index for either. FLT-PET showed as high a sensitivity as FDG-PET for the detection of primary HNSCC lesions, although uptake of FLT was significantly lower than that of FDG.

OesophagusCa einschl. gastroösophagealer Übergang

J Gastrointest Surg. 2011 May;15(5):719-29.
Update on staging and surgical treatment options for esophageal cancer.
Low DE.
Thoracic Surgery and Thoracic Oncology, C6-GS, Virginia Mason Medical Center, 1100 Ninth Ave, Seattle, WA 98101, USA. donald.low@vmmc.org
Esophageal cancer remains a challenging clinical problem, with overall long-term survivorship consistently at a level of approximately 30%. The incidence of esophageal cancer is increasing worldwide, with the most dramatic increase being seen with respect to esophageal adenocarcinoma. Pretreatment staging accuracy has improved with the utilization of CT and PET scans, as well as endoscopic ultrasound and endoscopic mucosal resection. In an increasing percentage of patients, endoscopic techniques are being utilized in selected patients for the treatment of high-grade dysplasia in Barrett's and intramucosal cancer. Surgery remains the treatment of choice in all appropriate patients with invasive and locoregional esophageal cancer, although multimodality therapy is now used in most patients with stage II or stage III disease. Outcomes for esophagectomy have been dominated by concerns regarding high mortality and morbidity; however, mortality rates associated with esophageal resection have dramatically decreased, especially in high-volume specialty centers. This manuscript highlights some of the evolutionary issues associated with staging and endoscopic and surgical treatments of Barrett's and esophageal cancer.

Ann Surg Oncol. 2011 May 6. [Epub ahead of print]

Value of EUS in Determining Curative Resectability in Reference to CT and FDG-PET: The Optimal Sequence in Preoperative Staging of Esophageal Cancer?

Schreurs LM, Janssens AC, Groen H, Fockens P, van Dullemen HM, van Berge Henegouwen MI, Sloof GW, Pruim J, van Lanschot JJ, Steyerberg EW, Plukker JT.

Department of Surgery/Surgical Oncology, University Medical Center Groningen, Groningen, The Netherlands.

The separate value of endoscopic ultrasonography (EUS), multidetector computed tomography (CT), and (18)F-fluorodeoxyglucose positron emission tomography (FDG-PET) in the optimal sequence in staging esophageal cancer has not been investigated adequately. The staging records of 216 consecutive operable patients with esophageal cancer were reviewed blindly. Different staging strategies were analyzed, and the likelihood ratio (LR) of each module was calculated conditionally on individual patient characteristics. A logistic regression approach was used to determine the most favorable staging strategy. Initial EUS results were not significantly related to the LRs of initial CT and FDG-PET results. The positive LR (LR+) of EUS-fine-needle aspiration (FNA) was 4, irrespective of CT and FDG-PET outcomes. The LR+ of FDG-PET varied from 13 (negative CT) to 6 (positive CT). The LR+ of CT ranged from 3-4 (negative FDG-PET) to 2-3 (positive FDG-PET). Age, histology, and tumor length had no significant impact on the LRs of the three diagnostic tests. This study argues in favor of PET/CT rather than EUS as a predictor of curative resectability in esophageal cancer. EUS does not correspond with either CT or FDG-PET. LRs of FDG-PET were substantially different between subgroups of negative and positive CT results and vice versa.

Clin Nucl Med. 2011 Oct;36(10):854-9.

F-18 FDG PET/CT Contributes to More Accurate Detection of Lymph Nodal Metastasis From Actively Proliferating Esophageal Squamous Cell Carcinoma.

Tanabe S, Naomoto Y, Shirakawa Y, Fujiwara Y, Sakurama K, Noma K, Takaoka M, Yamatsuji T, Hiraki T, Okumura Y, Mitani M, Kaji M, Kanazawa S, Fujiwara T.

From the Departments of *Gastroenterological Surgery, Transplant and Surgical Oncology, and †Radiology, Graduate School of Medicine, Dentistry, and Pharmaceutical Sciences, Okayama University, Okayama, Japan; ‡Department of Radiology, Kawasaki Medical School Kawasaki Hospital, Okayama, Japan; and §Okayama Diagnostic Imaging Center, Okayama, Japan : Evaluating the status of disease progression is critical for planning a therapeutic strategy for esophageal cancer. In this regard, F-18 fluorodeoxyglucose-labeled positron emission tomography (PET) is one of the most useful diagnostic modalities. However, there is room to improve its diagnostic performance, such as distinguishing lymph nodal metastases from false positives. In this study, we examined the diagnostic accuracy of fluorodeoxyglucose PET accompanied by computed tomography imaging (PET/CT)

to detect regional lymph nodal metastasis from esophageal squamous cell carcinoma (ESCC). : A total of 102 patients diagnosed as ESCC were subjected to this study. These patients had a preoperative PET/CT examination to evaluate the existence of metastasis. The values of maximum standardized uptake value (SUVmax) in primary tumors and in metastasized lymph nodes were measured to analyze their relationship with various clinicopathologic characteristics including the status of tumor cell proliferation, which was assessed by immunohistochemistry for Ki-67.: The SUVmax of the primary tumor was positively correlated with tumor size and vessel invasion, and was positively related with the SUVmax of lymph nodal metastasis, especially in cases of poorly differentiated ESCC. The SUVmax of metastasized lymph nodes was higher in larger-sized metastasized lymph nodes, whereas the Ki-labeling index of lymph nodal metastasis was positively related with the SUVmax per unit area (SUVmax/mm). The diagnostic accuracy of PET/CT (87.3%) was higher than that of conventional CT scans (78.4%). : The improved diagnostic accuracy of PET/CT can be explained by its ability to detect actively progressive metastasis at an early phase regardless of size.

Eur J Radiol. 2011 Mar 31. [Epub ahead of print]

Clinical usefulness of dual-time FDG PET-CT in assessment of esophageal squamous cell carcinoma.

Shum WY, Hsieh TC, Yeh JJ, Chen JH, Su CC, Liang JA, Kao CH.

Graduate Institute of Clinical Medical Science, China Medical University, Taichung, Taiwan; Department of Oncology, Jen-Ai Hospital-Ta Li, Taichung, Taiwan.

We conducted this study to investigate the value of the dual-time 2-[(18)F]fluoro-2-deoxy-d-glucose (FDG) positron emission tomography- computed tomography (PET-CT) in assessment of the primary tumor, loco-regional lymph node and distant metastasis in patients with esophageal squamous cell carcinoma. Twenty-six patients with histologically proved esophageal squamous cell carcinoma underwent dual-time FDG PET-CT before radical surgery. The standardized uptake values (SUV(max)) were obtained including early SUV(max) and delayed SUV(max), respectively. The retention index (RI) was also calculated. The results were evaluated retrospectively according to the final pathologic findings. Four diagnostic criteria including (1) early SUV(max) 2.5 alone, (2) RI 10% alone, (3) a combination of early SUV(max) 2.5 and RI 10%, and (4) a combination of early SUV(max) 2.5 or RI 10% were used for differentiating malignancy from a benign lesion, respectively. The sensitivity of FDG PET-CT in detecting the primary tumor with combination of early SUV(max) 2.5 or RI 10% was 96.2%. It was statistically significantly higher than the results using the other three criteria ($p<0.0001$). For loco-regional lymph node detection, there was no significant difference among the 4 criteria. For distal metastases, the significantly

higher specificity (100%) was found when using combination of early SUV(max) 2.5 and RI 10% or using early SUV(max) 2.5 alone than using the other two criteria (p=0.0058). With regard to accuracy, no significant correlations were observed among primary tumor, loco-regional lymph nodes and distant metastasis (p>0.05). The preliminary result of this study demonstrated that dual-time point FDG PET-CT had limited value in detection of primary tumor and loco-regional lymph nodes metastasis. For the distant metastasis, the sensitivity and specificity would be improved if RI 10% is used as a supplemental criterion. Efforts should be made to improve the ability of the dual-time FDG PET-CT technique to assess primary tumor and loco-regional lymph nodes metastasis.

Cancer. 2011 Mar 31. doi: 10.1002/cncr.26122. [Epub ahead of print]
Prognostic significance of baseline positron emission tomography and importance of clinical complete response in patients with esophageal or gastroesophageal junction cancer treated with definitive chemoradiotherapy.
Suzuki A, Xiao L, Hayashi Y, Macapinlac HA, Welsh J, Lin SH, Lee JH, Bhutani MS, Maru DM, Hofstetter WL, Swisher SG, Ajani JA. Department of Gastrointestinal Medical Oncology, The University of Texas MD Anderson Cancer Center, Houston, Texas.
Metabolic imaging is of interest in esophageal cancer; however, the usefulness of initial standardized uptake value (SUV) in positron emission tomography (PET) is unknown in patients with esophageal or gastroesophageal carcinoma treated with definitive chemoradiotherapy. The authors hypothesized that initial SUV would correlate with patient outcome. The authors retrospectively analyzed esophageal or gastroesophageal carcinoma patients who had baseline PET and endoscopic ultrasonography in addition to other routine staging. All patients received definitive chemoradiotherapy. Multiple statistical methods were used. The authors analyzed 209 consecutive esophageal or gastroesophageal carcinoma patients treated with definitive chemoradiation for outcome; of these, 180 had baseline PET for additional analyses. The median overall survival (OS) for all patients was 20.7 months (95% confidence interval, 18.8-26.3). Patients with clinical complete response (CR) lived longer than those with less than clinical CR (P < .0001). The median initial SUV was 12.7 (range, 0-51). Higher initial SUV was associated with longer tumors (P = .0001), higher T-stage status (P < .0001), positive N-stage status (P = .0001), higher overall stage (P < .0001), lack of clinical CR (P = .0002), and squamous cell histology (P < .0001). In the univariate analysis, initial SUV was associated with OS (Cox model, P = .016; log-rank test, P = .002). In the multivariate analysis, initial SUV dichotomized by the median value (P = .024) and tumor grade (P = .016) proved to be independent OS prognosticators. Median initial SUV for clinical CR patients was 10.2, compared with 15.3 for less than clinical CR patients (P = .0058). The data indicate that a higher initial SUV is associated with poorer OS in patients with esophageal or gastroesophageal carcinoma receiving definitive chemoradiation. Upon validation,

baseline PET may become a useful stratification factor in randomized trials and for individualizing therapy.

BMC Cancer. 2011 Jun 24;11:266.

Sequential FDG-PET and induction chemotherapy in locally advanced adenocarcinoma of the Oesophago-gastric junction (AEG): the Heidelberg Imaging program in Cancer of the oesophago-gastric junction during Neoadjuvant treatment: HICON trial.

Lorenzen S, von Gall C, Stange A, Haag GM, Weitz J, Haberkorn U, Lordick F, Weichert W, Abel U, Debus J, Jäger D, Münter MW.

Source

National Center for Tumor Diseases (NCT), University of Heidelberg, Germany. sylvielorenzen@gmx.de

Abstract

BACKGROUND:

18-Fluorodeoxyglucose-PET (18F-FDG-PET) can be used for early response assessment in patients with locally advanced adenocarcinomas of the oesophagogastric junction (AEG) undergoing neoadjuvant chemotherapy. It has been recently shown in the MUNICON trials that response-guided treatment algorithms based on early changes of the FDG tumor uptake detected by PET are feasible and that they can be implemented into clinical practice. Only 40%-50% of the patients respond metabolically to therapy. As metabolic non-response is known to be associated with a dismal prognosis, metabolic non-responders are increasingly treated with alternative neoadjuvant chemotherapies or chemoradiation in order to improve their clinical outcome. We plan to investigate whether PET can be used as response assessment during radiochemotherapy given as salvage treatment in early metabolic non-responders to standard chemotherapy.

METHODS/DESIGN:

The HICON trial is a prospective, non-randomized, explorative imaging study evaluating the value of PET as a predictor of histopathological response in metabolic non-responders. Patients with resectable AEG type I and II according to Siewerts classification, staged cT3/4 and/or cN+ and cM0 by endoscopic ultrasound, spiral CT or MRI and FDG-PET are eligible. Tumors must be potentially R0 resectable and must have a sufficient FDG-baseline uptake. Only metabolic non-responders, showing a < 35% decrease of SUV two weeks after the start of neoadjuvant chemotherapy are eligible for the study and are taken to intensified taxane-based RCT (chemoradiotherapy (45

Gy) before surgery. 18FDG-PET scans will be performed before (= Baseline) and after 14 days of standard neoadjuvant therapy as well as after the first cycle of salvage docetaxel/cisplatin chemotherapy (PET 1) and at the end of radiochemotherapy (PET2). Tracer uptake will be assessed semiquantitatively using standardized uptake values (SUV). The percentage difference ΔSUV = 100 (SUV Baseline - SUV PET1)/SUV Baseline will be calculated and assessed as an early predictor of histopathological response. In a secondary analysis, the association between the difference SUV PET1 - SUV PET2 and histopathological response will be evaluated.

DISCUSSION:
The aim of this study is to investigate the potential of sequential 18FDG-PET in predicting histopathological response in AEG tumors to salvage neoadjuvant radiochemotherapy in patients who do not show metabolic response to standard neoadjuvant chemotherapy.

J Nucl Med. 2011 Aug;52(8):1189-96. Epub 2011 Jul 15.

(18)F-FDG PET-guided salvage neoadjuvant radiochemotherapy of adenocarcinoma of the esophagogastric junction: the MUNICON II trial.

zum Büschenfelde CM, Herrmann K, Schuster T, Geinitz H, Langer R, Becker K, Ott K, Ebert M, Zimmermann F, Friess H, Schwaiger M, Peschel C, Lordick F, Krause BJ.

Source

3rd Department of Medicine (Haematology and Medical Oncology), Klinikum rechts der Isar, Technische Universität München, Munich, Germany. christian.mzb@lrz.tum.de

Abstract

Previous studies demonstrated that chemotherapy-induced changes in tumor glucose metabolism measured with (18)F-FDG PET identify patients who benefit from preoperative chemotherapy and those who do not. The prognosis for chemotherapy metabolic nonresponders is poorer than for metabolic responders. Therefore, we initiated this prospective trial to improve the clinical outcome of metabolic nonresponders using a salvage neoadjuvant radiochemotherapy.

METHODS:
Fifty-six patients with locally advanced adenocarcinomas of the esophagogastric junction were included. Tumor glucose uptake was assessed

by (18)F-FDG PET before chemotherapy and 14 d after initiation of chemotherapy. PET nonresponders received salvage neoadjuvant radiochemotherapy, whereas metabolic responders received neoadjuvant chemotherapy for 3 mo before surgery.

RESULTS:
Thirty-three patients were metabolic responders, and 23 were nonresponders. Resection was performed on 54 patients. R0 resection rate was 82% (95% confidence interval [CI], 66%-91%) in metabolic responders and 70% (95% CI, 49%-84%) in metabolic nonresponders (P = 0.51). Major histologic remissions were observed in 12 metabolic responders (36%; 95% CI, 22%-53%) and 6 nonresponders (26%; 95% CI, 13%-46%). One-year progression-free rate was 74% ± 8% in PET responders and 57% ± 10% in metabolic nonresponders (log rank test, P = 0.035). One-year overall survival was comparable between the groups (~80%), and 2-y overall survival was estimated to be 71% ± 8% in metabolic responders and 42% ± 11% in PET nonresponders (hazard ratio, 1.9; 95% CI, 0.87-4.24; P = 0.10).

CONCLUSION:
This prospective study showed the feasibility of a PET-guided treatment algorithm. However, by comparing the groups of nonresponding patients in the current trial and the previous published MUNICON (Metabolic response evalUatioN for Individualisation of neoadjuvant Chemotherapy in Esophageal and esophagogastric adeNocarcinoma) I trial, increased histopathologic response was observed after salvage radiochemotherapy, but the primary endpoint of the study to increase the R0 resection rate was not met. The prognosis of the subgroup of PET nonresponders remains poor, indicating their different tumor biology.

Ann Surg. 2009 Dec;250(6):888-94.

[18F]-Fluorodeoxyglucose-positron emission tomography for the assessment of histopathologic response and prognosis after completion of neoadjuvant chemoradiation in esophageal cancer.

Vallböhmer D, Hölscher AH, Dietlein M, Bollschweiler E, Baldus SE, Mönig SP, Metzger R, Schicha H, Schmidt M.

Source

General, Visceral, and Cancer Surgery, University of Cologne, Germany.

Abstract

OBJECTIVE:
To evaluate the potential of [(18)F]-fluorodeoxyglucose-positron emission tomography (FDG-PET) after the completion of neoadjuvant chemoradiation for the assessment of histopathologic response and prognosis in the multimodality treatment of patients with esophageal cancer.

BACKGROUND:
Combined chemoradiation with and without surgery are widely accepted treatment options for patients with locally advanced esophageal cancer. Evidence suggests that patients with response to chemoradiation have no additional benefit from surgery compared with definitive chemoradiation. However, there is still a great lack in noninvasive markers for response assessment in patients with esophageal cancer undergoing multimodality treatment. Interestingly, recent studies imply that FDG-PET significantly correlates with histopathologic response and survival in patients with esophageal cancer undergoing neoadjuvant chemotherapy followed by surgical resection.

METHODS:
Study patients were recruited from a prospective clinical observation trial on neoadjuvant chemoradiation for esophageal cancer between 1997 and 2006. The study included 119 (98 men, 21 women; median age, 59.4 years; squamous cell cancer: 66; adenocarcinoma: 53) patients with locally advanced esophageal cancer (cT2- 4, N(x), M(0)). All patients received neoadjuvant chemoradiation (cisplatin, 5-FU, 36 Gy) and subsequently underwent transthoracic en bloc esophagectomy. Histomorphologic regression was defined as major histopathologic response when resected specimens contained less than 10% vital residual tumor cells (major response: 47 patients [39.5%]; minor response: 72 patients [60.5%]). FDG-PET was performed before and 2 to 3 weeks after the end of chemoradiation with assessment of the intratumoral FDG-uptake (pretreatment standardized uptake value; post-treatment standardized uptake value; percentage change). These variables were correlated with histopathologic response and survival.

RESULTS:
Major histomorphologic response was confirmed as an important prognostic factor (P = 0.005; log-rank test). Neoadjuvant chemoradiation led to a significant reduction of intratumoral FDG-uptake (P = 0.0001). A nonsignificant association was seen between major responders and FDG-PET results (P = 0.056). However, the receiver operating characteristic analysis could not identify a standardized uptake value threshold with a relevant predictive value

for histomorphologic response. No significant association between metabolic imaging and prognosis was found.

CONCLUSION:
FDG-PET seems not to be an imaging system that effectively characterizes the groups of major and minor response as well as survival in patients with esophageal cancer after multimodality treatment.

Radiology. 2010 Mar;254(3):707-17.

Prediction of tumor response to neoadjuvant therapy in patients with esophageal cancer with use of 18F FDG PET: a systematic review.

Kwee RM.

Source

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Abstract

Purpose: To systematically review the accuracy of fluorine 18 ((18)F) fluorodeoxyglucose (FDG) positron emission tomography (PET) in the prediction of tumor response to neoadjuvant therapy in patients with esophageal cancer. Materials and Methods: The MEDLINE and EMBASE databases were systematically searched for relevant studies. Methodologic quality of the included studies was assessed. Sensitivities and specificities of (18)F FDG PET in individual studies were calculated and underwent meta-analysis with a random effects model. A summary receiver operating characteristic curve (sROC) was constructed with the Moses-Shapiro-Littenberg method. A chi(2) test was performed to test for heterogeneity (defined as P < .10). Potential sources for heterogeneity were explored by assessing whether certain covariates significantly (P < .05) influenced the relative diagnostic odds ratio. Results: Twenty reports, comprising a total of 849 patients with esophageal cancer, were included. Overall, the studies were of moderate methodologic quality. Sensitivity and specificity of (18)F FDG PET ranged from 33% to 100% and from 30% to 100%, respectively, with pooled estimates of 67% (95% confidence interval: 62%, 72%) and 68% (95% confidence interval: 64%, 73%), respectively. The area under the sROC curve was 0.7815. There was significant heterogeneity in both the sensitivity and specificity of the included studies (P < .0001). Spearman rho between the logit of sensitivity and the logit of 1-specificity was 0.086 (P = .719), which

suggested that there was no threshold effect. Studies performed outside of the United States and studies of higher methodologic quality yielded significantly higher overall accuracy. Conclusion: On the basis of current evidence, (18)F FDG PET should not yet be used in routine clinical practice to guide neoadjuvant therapy decisions in patients with esophageal cancer. (c) RSNA, 2010 Supplemental material: http://radiology.rsna.org/lookup/suppl/doi:10.1148/radiol.09091324/-/DC1.

Schilddrüsencarcinom

Clin Endocrinol (Oxf). 2011 May;74(5):644-8. doi: 10.1111/j.1365-2265.2011.04005.x.
18FDG-positron emission tomography/computed tomography (PET/CT) scanning in thyroid nodules with nondiagnostic cytology.
Giovanella L, Suriano S, Maffioli M, Ceriani L.
Department of Nuclear Medicine and Thyroid Centre, Oncology Institute of Southern Switzerland, Bellinzona, Switzerland. luca.giovanella@eoc.ch
To assess the role of positron emission tomography/computed tomography (PET/CT) scans with (18) FDG ((18)FDG-PET/CT) in the evaluation of thyroid nodules with nondiagnostic cytology. Eighty-eight patients with a single euthyroid nodule and repeatedly nondiagnostic ultrasound- guided fine-needle cytology (US-FNC) were enrolled in the present study. Nodules concentrating (18)FDG were considered positive (i.e. suspicious for malignancy). Histological findings were obtained after surgery in all patients. None of 41 patients with negative (18)FDG-PET/CT scan had a final histological diagnosis of malignancy (i.e. no false-negative results). Twenty-nine patients with final histological diagnosis of thyroid cancer had positive (18)FDG-PET/CT scan. Eighteen patients with final histological diagnosis of benign lesions (including four with follicular adenomas) also had positive (18)FDG-PET/CT scans. The sensitivity, specificity, accuracy, positive predictive value (PPV) and
negative predictive value (NPV) were 100%, 69%, 79%, 62% and 100%, respectively. A negative (18)FDG-PET/CT scan accurately excludes
malignancy in thyroid nodules with non-diagnostic US-FNC procedures. Histology is still necessary to distinguish benign from malignant disease
in (18)FDG-PET/CT-positive nodules, but unnecessary surgery could have been reduced from 88 to 41 cases (46%) in our series.

Acta Radiol. 2011 Aug 26. [Epub ahead of print]
The clinical significance and management of incidental focal FDG uptake in the

thyroid gland on positron emission tomography/computed tomography (PET/CT) in patients with non-thyroidal malignancy.
Wong C, Lin M, Chicco A, Benson R.
University of New South Wales, Australia.
BackgroundIncidental focal fluorine-18-2-fluoro-2-deoxy-D-glucose (FDG) uptake in the thyroid is not uncommon. A significant proportion is due to intercurrent thyroid cancer on further evaluation.PurposeTo investigate and discuss the clinical significance and management of incidental focal FDG uptake in the thyroid gland on positron emission tomography/computed tomography (PET/CT) in patients with non-thyroidal malignancy.Material and MethodsWe investigated 188/7896 (2.4%) patients who had incidental focal thyroid uptake on FDG PET/CT in an oncology population over a 45-month period. Diagnosis was confirmed in 63 patients of whom 59 patients had histopathological verification.ResultsThirty-two percent of confirmed cases were malignant comprising intercurrent thyroid cancer in three-quarters of these patients. Maximum standardized uptake values of the thyroid lesions and SUV ratios compared with background thyroid and mediastinal uptake were not predictive of a benign or malignant etiology. In patients with incidental thyroid cancers, more than half had non-papillary and intermediate to high-risk pathology.ConclusionFocal FDG uptake in the thyroid gland on PET/CT showed a malignancy risk of 32%. The intensity of uptake does not predict histology and underpins the importance of further investigations to exclude intercurrent thyroid cancer in suitable patients.

CUP Carcinoma unknown primary

Oncologist. 2011;16(4):445-51. Epub 2011 Mar 22.
18F-FDG PET/CT as a diagnostic tool in patients with extracervical carcinoma of unknown primary site: a literature review.
Moller AK, Loft A, Berthelsen AK, Damgaard Pedersen K, Graff J, Christensen CB, Perell K, Petersen BL, Daugaard G.
Department of Oncology 5073, Copenhagen University Hospital Rigshospitalet, Blegdamsvej 9, DK-2100 Copenhagen Ø, Denmark. anne.kirstine.moeller@rh.regionh.dk
Carcinoma of unknown primary (CUP) represents a heterogeneous group of metastatic malignancies for which no primary tumor site can be identified after extensive diagnostic workup. Failure to identify the primary site may negatively influence patient management. The aim of this review was to evaluate (18)F-fluorodeoxyglucose positron emission tomography/computed tomography ((18)F-FDG PET/CT) as a diagnostic tool in patients with extracervical CUP. A comprehensive literature search was performed and four publications were identified (involving 152 patients) evaluating (18)F-FDG PET/CT in CUP patients with extracervical

metastases. All studies were retrospective and heterogeneous in inclusion criteria, study design, and diagnostic workup prior to (18)F-FDG PET/CT. (18)F-FDG PET/CT detected the primary tumor in 39.5% of patients with extracervical CUP. The lung was the most commonly detected primary tumor site (50%). The pooled estimates of sensitivity, specificity, and accuracy of (18)F-FDG PET/CT in the detection of the primary tumor site were 87%, 88%, and 87.5%, respectively. The present review of currently available data indicates that (18)F-FDG PET/CT might contribute to the identification of the primary tumor site in extracervical CUP. However, prospective studies with more uniform inclusion criteria are required to evaluate the exact value of this diagnostic tool.

Chin Med J (Engl). 2011 Apr;124(7):1010-4.
Clinical applications of 18F-fluorodeoxyglucose positron emission tomography/computed tomography in carcinoma of unknown primary.
Hu M, Zhao W, Zhang PL, Ju GF, Fu Z, Zhang GL, Kong L, Yang YQ, Ma YD, Yu JM.
Department of Radiation Oncology and Shandong Province Key Laboratory of Radiation Oncology, Shandong Cancer Hospital, Shandong
Academy of Medical Sciences, Jinan, Shandong 250117, China.
Carcinoma of unknown primary (CUP) encompasses a heterogeneous group of tumors with varying clinical features. The management of patients
of CUP remains a clinical challenge. The purpose of this study was to evaluate the clinical applications of integrated (18)F-fluorodeoxyglucose
positron emission tomography/computed tomography (FDG PET/CT) information in patients with CUP, including detecting the occult primary
tumor and effecting on disease therapy. One hundred and forty-nine patients with histologically-proven metastases of CUP were included. For all
patients, the conventional diagnostic work-up was unsuccessful in localizing the primary site. Whole-body PET/CT images were obtained
approximately 60 minutes after intravenous injection of 350 - 425 MBq of (18)F-FDG. In 24.8% of patients, FDG PET/CT 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/CT in detecting unknown primary tumors were 86.0%, 87.7%, and 87.2%, respectively. FDG PET/CT imaging also led to the detection of
previously unrecognized metastases in 29.5% of patients. Forty-seven (31.5%, 47 of 149) patients underwent a change in therapeutic
management. FDG PET/CT is a valuable tool in patients with CUP, because it assisted in detecting unknown primary tumors and previously
unrecognized distant metastases, and optimized the management of these patients.

PancreasCa

World J Gastroenterol. 2011 Jan 14;17(2):231-5.
18F-fluorodeoxyglucose positron emission tomography in the diagnosis of small pancreatic cancer.
Okano K, Kakinoki K, Akamoto S, Hagiike M, Usuki H, Yamamoto Y, Nishiyama Y, Suzuki Y.
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To investigate the role of (18)F-fluorodeoxyglucose positron emission tomography (FDG-PET) in the diagnosis of small pancreatic cancer. This
study involved 31 patients with proven invasive ductal cancer of the pancreas. The patients were divided into 3 groups according to the maximum
diameter of the tumor: TS1 (maximum tumor size ≤ 2.0 cm), TS2 (> 2.0 cm and ≤ 4.0 cm) or TS3-4 (> 4.0 cm). The relationships between the TS
and various diagnostic tools, including FDG-PET with dual time point evaluation, were analyzed. The tumors ranged from 1.3 to 11.0 cm in
diameter. Thirty of the 31 patients (97%) had a positive FDG-PET study. There were 5 patients classified as TS1, 15 as TS2 and 11 as TS3-4.
The sensitivity of FDG-PET, computed tomography (CT) and magnetic resonance imaging (MRI) were 100%, 40%, 0% in TS1, 93%, 93%, 89%
in TS2 and 100%, 100%, 100% in TS3-4. The sensitivity of FDG-PET was significantly higher in comparison to CT and MRI in patients with
TS1 (P < 0.032). The mean standardized uptake values (SUVs) did not show a significant difference in relation to the TS (TS1: 5.8 ± 4.5, TS2:
5.7 ± 2.2, TS3-4: 8.2 ± 3.9), respectively. All the TS1 tumors (from 13 to 20 mm) showed higher SUVs in FDG-PET with dual time point
evaluation in the delayed phase compared with the early phase, which suggested the lesions were malignant. These results indicate that FDG-PET
with **dual time point evaluation** is a useful modality for the detection of small pancreatic cancers with a diameter of less than 20 mm.

Colorektales Karzinom

Dis Colon Rectum. 2011 May;54(5):518-25.
Metabolic response of rectal cancer assessed by 18-FDG PET following chemoradiotherapy is prognostic for patient outcome.
Yeung JM, Kalff V, Hicks RJ, Drummond E, Link E, Taouk Y, Michael M, Ngan S, Lynch AC, Heriot AG.
Department of Surgical Oncology, Peter MacCallum Cancer Centre, St. Andrew's

Place, East Melbourne, Victoria, Australia.
Complete pathological response has proven prognostic benefits in patients with locally advanced rectal cancer treated with neoadjuvant chemoradiotherapy. Sequential 18-FDG PET may be an early surrogate for pathological response to chemoradiotherapy. The aim of this study was to identify whether metabolic response measured by FDG PET following chemoradiotherapy is prognostic for tumor recurrence and survival following neoadjuvant therapy and surgical treatment for primary rectal cancer. Patients with primary rectal cancer treated by long-course neoadjuvant chemoradiotherapy followed by surgery had FDG PET performed before and 4 weeks after treatment, before surgical resection was performed. Retrospective chart review was undertaken for patient demographics, tumor staging, recurrence rates, and survival. : Between 2000 and 2007, 78 patients were identified (53 male, 25 female; median age, 64 y). After chemoradiotherapy, 37 patients (47%) had a complete metabolic response, 26 (33%) had a partial metabolic response, and 14 (18%) had no metabolic response as assessed by FDG PET (1 patient had missing data). However, only 4 patients (5%) had a complete pathological response. The median postoperative follow-up period was 3.1 years during which 14 patients (19%) had a recurrence: 2 local, 9 distant, and 3 with both local and distant. The estimated percentage without recurrence was 77% at 5 years (95% CI 66%-89%). There was an inverse relationship between FDG PET metabolic response and the incidence of recurrence within 3 years (P = .04). Kaplan-Meier analysis of FDG PET metabolic response and overall survival demonstrated a significant difference in survival among patients in the 3 arms: complete, partial, and no metabolic response (P = .04); the patients with complete metabolic response had the best prognosis. Complete or partial metabolic response on PET following neoadjuvant chemoradiotherapy and surgery predicts a lower local recurrence rate and improved survival compared with patients with no metabolic response. Metabolic response may be used to stratify prognosis in patients with rectal cancer.

Colorectal Dis. 2011 Aug 11. doi: 10.1111/j.1463-1318.2011.02727.x. [Epub ahead of print]
The detection of incidental colorectal tumors with (18) F-FDG PET/CT scans: results of a prospective study.
Peng J, He Y, Xu J, Sheng J, Cai S, Zhang Z.
Department of Colorectal Surgery, Fudan University Shanghai Cancer Center, Shanghai, China Department of Oncology, Shanghai Medical College, Fudan University, Shanghai, China Department of Endoscopy, Fudan University Shanghai Cancer Center, Shanghai, China Department of Nuclear Medicine, Fudan University Shanghai Cancer Center, Shanghai, China. Purpose: This study assessed the clinical significance of incidental colorectal FDG uptake with (18) F-FDG PET/CT scans and evaluated the importance of colonoscopy when incidental colorectal FDG uptake was observed. Methods: A prospective study was designed conducted in a single institution in a two-year period. In patients undergoing PET/CT scan, all the cases of FDG uptake in colorectum were assigned to have colonoscopy and biopsy. The value

of PET/CT was studied by comparing with the colonoscopy and biopsy results. Results: Among 10,978 PET/CT scans, one or more focal FDG uptakes in colorectum was observed in 148 pts (1.35%). In 136 valid patients, malignant colorectal tumors and polyps were found in 23.5% and 20.5% of patients, while the other 56% of cases were found normal. A higher false positive rate was found in right colon compared with distal colorectum (66.2% vs 36.7%, P=0.004). A significant increase of the maximum standardized uptake value (SUVmax) was found among normal, polyps and cancer groups. Multivariate analysis revealed that SUVmax was the risk factor for predicting colorectal cancer or polyps and FDG uptake in right colon was a negative predicting factor for finding cancers or polyps. Conclusions: Our study proves the necessity of colonoscopy when incidental FDG uptake is found on PET/CT imaging. The false-positive FDG uptake is more commonly observed in right colon. Although SUVmax is higher in cancer patients, a high SUVmax value is not necessarily resulted in malignancies.

Radiother Oncol. 2011 Feb;98(2):270-6. Epub 2011 Feb 3.

FDG-PET provides the best correlation with the tumor specimen compared to MRI and CT in rectal cancer.

Buijsen J, van den Bogaard J, Janssen MH, Bakers FC, Engelsman S, Öllers M, Beets-Tan RG, Nap M, Beets GL, Lambin P, Lammering G.

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To compare CT-, MR- and PET-CT based tumor length measurements in rectal cancer with pathology. Twenty-six rectal cancer patients
underwent both MR and PET-CT imaging followed by short-course radiotherapy (RT 5×5 Gy) and surgery within 3 days after RT. Tumor length
was measured manually and independently by 2 observers on CT, MR and PET. PET-based tumor length measurements were also generated
automatically using the signal-to-background-ratio (SBR) method. All measurements were correlated with the tumor length on the pathological
specimen. CT-based measurements did not show a valuable correlation with pathology. MR-based measurements correlated only weakly, but still
significantly (Pearson correlation=0.55 resp. 0.57; p<0.001). Manual PET measurements reached a good correlation with pathology, but less
strong (Pearson correlation 0.72 and 0.76 for the two different observers) than automatic PET-CT based measurements, which provided the best
correlation with pathology (Pearson correlation of 0.91 (p<0.001)). Bland-Altman analysis demonstrated in general an overestimation of the
tumor diameter using manual measurements, while the agreement of automatic contours and pathology was within acceptable ranges. A direct
comparison of the different modalities revealed a significant better precision for PET-

based auto-contours as compared to all other measurements.
Automatically generated PET-CT based contours show the best correlation with the surgical specimen and thus provide a useful and powerful
tool to accurately determine the largest tumor dimension in rectal cancer. This could be used as a quick and reliable tool for target delineation in

PET-based Treatment Response Evaluation in Rectal Cancer: Prediction and Validation.
Janssen MH, Ollers MC, van Stiphout RG, Riedl RG, van den Bogaard J, Buijsen J, Lambin P, Lammering G.
Department of Radiation Oncology (MA ASTRO), GROW Research Institute, University Medical Centre Maastricht, Maastricht, the Netherlands.
To develop a positron emission tomography (PET)-based response prediction model to differentiate pathological responders from nonresponders. The predictive strength of the model was validated in a second patient group, treated and imaged identical to the patients on which the predictive model was based.
Fifty-one rectal cancer patients were prospectively included in this study. All patients underwent fluorodeoxyglucose (FDG) PET-computed tomography (CT) imaging both before the start of chemoradiotherapy (CRT) and after 2 weeks of treatment. Preoperative treatment with CRT was followed by a total mesorectal excision. From the resected specimen, the tumor regression grade (TRG) was scored according to the Mandard criteria. From one patient group (n = 30), the metabolic treatment response was correlated with the pathological treatment response, resulting in a receiver operating characteristic (ROC) curve based cutoff value for the reduction of maximum standardized uptake value (SUV(max)) within the tumor to differentiate pathological responders (TRG 1-2) from nonresponders (TRG 3-5). The applicability of the selected cutoff value for new patients was validated in a second patient group (n = 21). When correlating the metabolic and pathological treatment response for the first patient group using ROC curve analysis (area under the curve = 0.98), a cutoff value of 48% SUV(max) reduction was selected to differentiate pathological responders from nonresponders (specificity of 100%, sensitivity of 64%). Applying this cutoff value to the second patient group resulted in a specificity and sensitivity of, respectively, 93% and 83%, with only one of the pathological nonresponders being false positively predicted as pathological responding. For rectal cancer, an accurate PET-based prediction of the pathological treatment
response is feasible already after 2 weeks of CRT. The presented predictive model could be used to select patients to be considered for less
invasive surgical interventions or even a "wait and see" policy. Also, based on the predicted response, early modifications of the treatment
protocol are possible, which might result in an improved clinical outcome.

The value of FDG positron emission tomography/computerised tomography (PET/CT) in pre-operative staging of colorectal cancer: a systematic review and economic evaluation.

Brush J, Boyd K, Chappell F, Crawford F, Dozier M, Fenwick E, Glanville J, McIntosh H, Renehan A, Weller D, Dunlop M.

Source

Department of Radiology, Western General Hospital, Edinburgh, UK.

Abstract

OBJECTIVES:

In the UK, colorectal cancer (CRC) is the third most common malignancy (behind lung and breast cancer) with 37,514 cases registered in 2006: around two-thirds (23,384) in the colon and one-third (14,130) in the rectum. Treatment of cancers of the colon can vary considerably, but surgical resection is the mainstay of treatment for curative intent. Following surgical resection, there is a comprehensive assessment of the tumour, it's invasion characteristics and spread (tumour staging). A number of imaging modalities are used in the pre-operative staging of CRCs including; computerised tomography (CT), magnetic resonance imaging, ultrasound imaging and positron emission tomography (PET). This report examines the role of CT in combination with PET scanning (PET/CT 'hybrid' scan). The research objectives are: to evaluate the diagnostic accuracy and therapeutic impact of fluorine-18-deoxyglucose (FDG) PET/CT for the pre-operative staging of primary, recurrent and metastatic cancer using systematic review methods; undertake probabilistic decision-analytic modelling (using Monte Carlo simulation); and conduct a value of information analysis to help inform whether or not there is potential worth in undertaking further research.

DATA SOURCES:

For each aspect of the research - the systematic review, the handsearch study and the economic evaluation - a database was assembled from a comprehensive search for published and unpublished studies, which included database searches, reference lists search and contact with experts. In the systematic review prospective and retrospective patient series (diagnostic cohort) and randomised controlled trials (RCTs) were eligible for inclusion. Both consecutive series and series that are not explicitly reported as consecutive were included.

REVIEW METHODS:

Two reviewers extracted all data and applied the criteria independently and

resolved disagreements by discussion. Data to populate 2 × 2 contingency tables consisting of the number of true positives, true negatives, false positives and false negatives using the studies' own definitions were extracted, as were data relating to changes in management. Fourteen items from the Quality Assessment of Diagnostic Accuracy Studies checklist were used to assess the methodological quality of the included studies. Patient-level data were used to calculate sensitivity and specificity with confidence intervals (CIs). Data were plotted graphically in forest plots. For the economic evaluation, economic models were designed for each of the disease states: primary, recurrent and metastatic. These were developed and populated based on a variety of information sources (in particular from published data sources) and literature, and in consultation with clinical experts.

RESULTS:
The review found 30 studies that met the eligibility criteria. Only two small studies evaluated the use of FDG PET/CT in primary CRC, and there is insufficient evidence to support its routine use at this time. The use of FDG PET/CT for the detection of recurrent disease identified data from five retrospective studies from which a pooled sensitivity of 91% (95% CI 0.87% to 0.95%) and specificity of 91% (95% CI 0.85% to 0.95%) were observed. Pooled accuracy data from patients undergoing staging for suspected metastatic disease showed FDG PET/CT to have a pooled sensitivity of 91% (95% CI 87% to 94%) and a specificity of 76% (95% CI 58% to 88%), but the poor quality of the studies means the validity of the data may be compromised by several biases. The separate handsearch study did not yield any additional unique studies relevant to FDG PET/CT. Models for recurrent disease demonstrated an incremental cost-effectiveness ratio of £ 21,409 per quality-adjusted life-year (QALY) for rectal cancer, £ 6189 per QALY for colon cancer and £ 21,434 per QALY for metastatic disease. The value of handsearching to identify studies of less clearly defined or reported diagnostic tests is still to be investigated.

CONCLUSIONS:
The systematic review found insufficient evidence to support the routine use of FDG PET/CT in primary CRC and only a small amount of evidence supporting its use in the pre-operative staging of recurrent and metastatic CRC, and, although FDG PET/CT was shown to change patient management, the data are divergent and the quality of research is generally poor. The handsearch to identify studies of less clearly defined or reported diagnostic tests did not find additional studies. The primary limitations in the economic evaluations were

due to uncertainty and lack of available evidence from the systematic reviews for key parameters in each of the five models. In order to address this, a conservative approach was adopted in choosing DTA estimates for the model parameters. Probabilistic analyses were undertaken for each of the models, incorporating wide levels of uncertainty particularly for the DTA estimates. None of the economic models reported cost-savings, but the approach adopted was conservative in order to determine more reliable results given the lack of current information. The economic evaluations conclude that FDG PET/CT as an add-on imaging device is cost-effective in the pre-operative staging of recurrent colon, recurrent rectal and metastatic disease but not in primary colon or rectal cancers. There would be value in undertaking an RCT with a concurrent economic evaluation to evaluate the therapeutic impact and cost-effectiveness of FDG PET/CT compared with conventional imaging (without PET) for the pre-operative staging of recurrent and metastatic CRC.

MammaCa

J Med Imaging Radiat Oncol. 2011 Feb;55(1):58-64. doi: 10.1111/j.1754-9485.2010.02230.x.

Initial clinical test of a breast-PET scanner.

Raylman RR, Abraham J, Hazard H, Koren C, Filburn S, Schreiman JS, Kurian S, Majewski S, Marano GD.

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The goal of this initial clinical study was to test a new positron emission/tomography imager and biopsy system (PEM/PET) in a small group of selected subjects to assess its clinical imaging capabilities. Specifically, the main task of this study is to determine whether the new system can successfully be used to produce images of known breast cancer and compare them to those acquired by standard techniques. The PEM/PET system consists of two pairs of rotating radiation detectors located beneath a patient table. The scanner has a spatial resolution of 2 mm in all three dimensions. The subjects consisted of five patients diagnosed with locally advanced breast cancer ranging in age from 40 to 55 years old scheduled for pre-treatment, conventional whole body PET imaging with F-18 Fluorodeoxyglucose (FDG). The primary lesions were at least 2 cm in diameter. The images from the PEM/PET system demonstrated that this system is capable of identifying some lesions not visible in standard

mammograms. Furthermore, while the relatively large lesions imaged in this study where all visualised by a standard whole body PET/CT scanner, some of the morphology of the tumours (ductal infiltration, for example) was better defined with the PEM/PET system. Significantly, these images were obtained immediately following a standard whole body PET scan. The initial testing of the new PEM/PET system demonstrated that the new system is capable of producing good quality breast-PET images compared standard methods.

J Clin Oncol. 2011 Sep 1;29(25):3351-7. Epub 2011 Jul 25.

Pathologic complete response after neoadjuvant chemotherapy plus trastuzumab predicts favorable survival in human epidermal growth factor receptor 2-overexpressing breast cancer: results from the TECHNO trial of the AGO and GBG study groups.

Untch M, Fasching PA, Konecny GE, Hasmüller S, Lebeau A, Kreienberg R, Camara O, Müller V, du Bois A, Kühn T, Stickeler E, Harbeck N, Höss C, Kahlert S, Beck T, Fett W, Mehta KM, von Minckwitz G, Loibl S.

Source

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Abstract

PURPOSE:

To evaluate efficacy and safety of epirubicin and cyclophosphamide followed by paclitaxel and trastuzumab as neoadjuvant treatment in patients with human epidermal growth factor receptor 2 (HER2)-overexpressing breast cancer.

PATIENTS AND METHODS:

Patients with centrally confirmed HER2-overexpressing breast cancer (≥ 2 cm or inflammatory) received four 3-week cycles epirubicin and cyclophosphamide (90/600 mg/m(2)) followed by four 3-week cycles paclitaxel (175 mg/m(2)) and trastuzumab (6 mg/kg) before surgery. Trastuzumab was continued after surgery to complete 1 year of treatment. Primary end point was pathologic complete response (pCR) defined as no residual invasive tumor in breast and lymphatic tissue.

RESULTS:

Thirty-nine percent of 217 enrolled patients achieved a pCR. Breast conservation was possible in 64% of patients. Three-year disease-free survival (DFS) was 88% in patients with pCR compared to 73% in patients without pCR (P = .01). Three-year overall survival (OS) was 96% in patients with pCR compared to 86% in patients without pCR (P = .025). pCR was the only significant prognostic factor for DFS (hazard ratio [HR] 2.5; 95% CI, 1.2 to 5.1; P = .013) and OS (HR, 4.9; 95% CI, 1.4 to 17.4; P = .012) in multivariable

analysis. Cardiac toxicity was reported in eight patients (3.7%) of whom six presented with an asymptomatic left ventricular ejection fraction decrease and two with symptomatic chronic heart failure.
CONCLUSION:
Neoadjuvant combination of trastuzumab and chemotherapy resulted in a high pCR rate in HER2-overexpressing primary breast cancer. Patients with a pCR after neoadjuvant anti-HER2 therapy in combination with chemotherapy followed by maintenance trastuzumab have an improved long-term outcome. Patients without a pCR had an increased risk for relapse and death.

Br J Cancer. 2010 Jan 5;102(1):35-41. Epub 2009 Nov 17.

Assessment of residual tumour by FDG-PET: conventional imaging and clinical examination following primary chemotherapy of large and locally advanced breast cancer.

Dose-Schwarz J, Tiling R, Avril-Sassen S, Mahner S, Lebeau A, Weber C, Schwaiger M, Jänicke F, Untch M, Avril N.
Source

Department of Gynecology, Universitätsklinikum Hamburg-Eppendorf, Hamburg, Germany.

Abstract
BACKGROUND:
The aim of this was to evaluate FDG-PET (2-(fluorine-18)-fluoro-2-deoxy-D-glucose positron emission tomography) for assessment of residual tumour after primary chemotherapy of large and locally advanced breast cancer in comparison with conventional imaging modalities.

METHODS:
In a prospective multicentre trial, 99 patients underwent one or more breast imaging modalities before surgery in addition to clinical examination, namely, FDG-PET (n=89), mammography (n=47), ultrasound (n=46), and magnetic resonance imaging (MRI) (n=46). The presence of residual tumour by conventional imaging, dichotomised as positive or negative, and the level of FDG uptake (standardised uptake values, SUV) were compared with histopathology, which served as the reference standard. Patients with no residual tumour or only small microscopic foci of residual tumour were classified as having minimal residual disease and those with extensive microscopic and macroscopic residual tumour tissue were classified as having

gross residual disease.

RESULTS:
By applying a threshold SUV of 2.0, the sensitivity of FDG-PET for residual tumour was 32.9% (specificity, 87.5%) and increased to 57.5% (specificity, 62.5%) at a threshold SUV of 1.5. Conventional imaging modalities were more sensitive in identifying residual tumour, but had a low corresponding specificity; sensitivity and specificity were as follows: MRI 97.6 and 40.0%, mammography 92.5 and 57.1%, ultrasound 92.0 and 37.5%, respectively. Breast MRI provided the highest accuracy (91.3%), whereas FDG-PET had the lowest accuracy (42.7%).

CONCLUSIONS:
FDG-PET does not provide an accurate assessment of residual tumour after primary chemotherapy of breast cancer. Magnetic resonance imaging offers the highest sensitivity, but all imaging modalities have distinct limitations in the assessment of residual tumour tissue when compared with histopathology.

J Nucl Med. 2011 Oct;52(10):1526-34. Epub 2011 Aug 30.

The yield of 18F-FDG PET/CT in patients with clinical stage IIA, IIB, or IIIA breast cancer: a prospective study.

Groheux D, Giacchetti S, Espié M, Vercellino L, Hamy AS, Delord M, Berenger N, Toubert ME, Misset JL, Hindié E.
Source

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Abstract
The purpose of this study was to prospectively evaluate the role of (18)F-FDG PET/CT in patients with stage IIA, IIB, or IIIA breast cancer.

METHODS:
During 56 mo, 131 consecutive patients with large (>2 cm) breast cancer and clinical stage IIA, IIB, or IIIA (based on clinical examination, mammography, breast MRI, and ultrasonography) underwent (18)F-FDG PET/CT. The nuclear physician was unaware of the results of any other procedure (bone scan, chest radiography, liver ultrasound, or thoracoabdominal CT scan).

RESULTS:
Of the 131 examined patients, 36 had clinical stage IIA (34 T2N0 and 2 T1N1), 48 stage IIB (20 T3N0 and 28 T2N1), and 47 stage IIIA (29 T3N1, 9 T2N2, and

9 T3N2). (18)F-FDG PET/CT modified staging for 5.6% of stage IIA patients, for 14.6% of stage IIB patients, and for 27.6% of stage IIIA patients. However, within stage IIIA, the yield was specifically high among the 18 patients with N2 disease (56% stage modification). When considering stage IIB and primary operable IIIA (T3N1) together, the yield of (18)F-FDG PET/CT was 13% (10/77); extraaxillary regional lymph nodes were detected in 5 and distant metastases in 7 patients. In this series, (18)F-FDG PET/CT outperformed bone scanning, with only 1 misclassification versus 8 for bone scanning (P = 0.036).

CONCLUSION:
(18)F-FDG PET/CT provided useful information in 13% of patients with clinical T3N0, T2N1, or T3N1 disease. The yield was more modest in patients with stage IIA. The high yield in the case of N2 disease demonstrates that stage IIIA comprises 2 quite distinct groups of patients.

Hell J Nucl Med. 2011 May-Aug;14(2):135-9.

The role of (18)F-FDG PET/CT in initial staging of patients with locally advanced breast carcinoma with an emphasis on M staging.

Mittal BR, Manohar K, Kashyap R, Bhattacharya A, Singh B, Singh G.

Source

Department of Nuclear Medicine and General Surgery, Postgraduate Institute of Medical Education and Research, 160 012 Chandigarh, India.
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Abstract
Locally advanced breast cancer (LABC) is a distinct entity in breast carcinoma with high incidence of distant metastases (M). However, there is scarce data in the literature addressing the role of fluorine-18-fluorodeoxyglucose-positron emission tomography/computed tomography ((18)F-FDG PET/CT) in LABC. This study was performed to assess the sensitivity of (18)F-FDG PET/CT in confirming known lymph nodal and M and in identifying new ones in LABC. We performed a retrospective analysis of data of 16 patients with LABC who underwent histopathology, for the diagnosis of LABC and clinical examination, chest X-rays, ultrasound of the abdomen and whole body bone scans. Findings for M obtained by all the above examinations were compared to the (18)F-FDG PET/CT findings that followed. Lymph nodal and distant metastases detected by all other examinations were detected by (18)F-FDG PET/CT in all patients, except subcentimetric metastases in 2 patients in the axilla that were detected in another examination later. Additionally, (18)F-FDG PET/CT identified

unknown ipsilateral, supraclavicular, internal mammary metastases and upstaged disease in 3 patients and additional distant metastases were noted in 3/16 patients. In conclusion, our study suggests that more extra axillary lymph nodal and distant metastases can be identified by (18)F-FDG PET/CT as compared to a group of clinical, X-rays, ultrasound and bone scan examinations together.

Cancer. 2009 Nov 1;115(21):5038-47.

18F-fluorodeoxyglucose positron emission tomography/computed tomography (FDG-PET/CT) imaging in the staging and prognosis of inflammatory breast cancer.

Alberini JL, Lerebours F, Wartski M, Fourme E, Le Stanc E, Gontier E, Madar O, Cherel P, Pecking AP.

Source

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Abstract

BACKGROUND:

: To prospectively assess fluorodeoxyglucose positron emission tomography/computed tomography (FDG-PET/CT) staging and prognosis value in patients with suspected inflammatory breast cancer (IBC).

METHODS:

: Sixty-two women (mean age 50.7 +/- 11.4 years) presenting with unilateral inflammatory breast tumors (59 invasive carcinomas; 3 mastitis) underwent a PET/CT scan before biopsy.

RESULTS:

: PET/CT scan was positive for the primary malignant tumor in 100% and false positive in 2 of 3 benign mastitis. In 59 IBC patients, FDG nodal foci were detected in axillary (90%; n = 53) and extra-axillary areas (56%; n = 33) ipsilateral to the cancer. Compared with clinical examination, the axillary lymph node status by PET/CT was upstaged and downstaged in 35 and 5 patients, respectively. In 7 of 9 N0 patients, the axillary lymph node positivity on PET/CT was correct, as revealed by pathological postsurgery assessment (not available in the 2 remaining patients). The nodal foci were compared with preoperative fine needle aspiration and/or pathological postchemotherapy findings available in 44 patients and corresponded to 38 true positive, 4 false-

negative, and 2 false-positive cases. In 18 of 59 IBC patients (31%), distant lesions were found. On the basis of a univariate analysis of the first enrolled patients (n = 42), among 28 patients who showed intense tumoral uptake (standard uptake value(max)>5), the 11 patients with distant lesions had a worse prognosis than the 17 patients without distant lesions (P = .04).

CONCLUSIONS:
: FDG-PET/CT imaging provides additional invaluable information regarding nodal status or distant metastases in IBC patients and should be considered in the initial staging. It seems also that some prognostic information can be derived from FDG uptake characteristics. Cancer 2009. (c) 2009 American Cancer Society.

J Nucl Med. 2010 Aug;51(8):1213-8. Epub 2010 Jul 21.

18F-FDG PET/CT findings and circulating tumor cell counts in the monitoring of systemic therapies for bone metastases from breast cancer.

De Giorgi U, Mego M, Rohren EM, Liu P, Handy BC, Reuben JM, Macapinlac HA, Hortobagyi GN, Cristofanilli M, Ueno NT.
Source

Department of Breast Medical Oncology, The University of Texas MD Anderson Cancer Center, Houston, Texas 77030, USA.

Abstract
Our objective was to compare the predictive significance of (18)F-FDG PET/CT findings and circulating tumor cell (CTC) count in patients with bone metastases from breast cancer treated with standard systemic therapy.

METHODS:
Breast cancer patients with progressive bone-only metastatic disease without visceral metastases starting a new line of systemic therapy underwent (18)F-FDG PET/CT and had CTC counts determined before and during treatment. Disease status was reassessed by CTC count (> or = 5 vs. < 5 CTC/7.5 mL of blood) and (18)F-FDG PET/CT approximately 2-4 mo after initiation of the new systemic therapy.

RESULTS:
CTC counts at follow-up agreed with the (18)F-FDG PET/CT assessment in 43 (78%) of the 55 evaluable patients. Of the 12 patients with discordant CTC and (18)F-FDG PET/CT results, 8 (66%) had > or = 5 CTCs, with no evidence of

progressive disease at the time of the (18)F-FDG PET/CT study, whereas 4 (33%) had < 5 CTCs, with evidence of progressive disease by (18)F-FDG PET/CT. (18)F-FDG PET/CT findings and follow-up CTC counts were found to be significantly associated with both progression-free survival (P = 0.02 and P < 0.0001, respectively) and overall survival (P = 0.02 and P = 0.01, respectively). In multivariate analysis, the (18)F-FDG PET/CT assessment remained as the only predictive factor for progression-free survival (P < 0.0001), whereas estrogen receptor status was the only predictive factor for overall survival (P = 0.01).

CONCLUSION:
(18)F-FDG PET/CT is a useful tool for therapeutic monitoring in patients with bone metastases from breast cancer. Prospective studies are needed to define the role of (18)F-FDG PET/CT and CTC in the setting of response discordance to establish bone-dominant disease as a tumor-response measurable disease.

J Clin Oncol. 2009 Jul 10;27(20):3303-11. Epub 2009 May 18.

Circulating tumor cells and [18F]fluorodeoxyglucose positron emission tomography/computed tomography for outcome prediction in metastatic breast cancer.

De Giorgi U, Valero V, Rohren E, Dawood S, Ueno NT, Miller MC, Doyle GV, Jackson S, Andreopoulou E, Handy BC, Reuben JM, Fritsche HA, Macapinlac HA, Hortobagyi GN, Cristofanilli M.
Source

The University of Texas M. D. Anderson Cancer Center, Houston, 77030, USA.

Abstract
PURPOSE:
Circulating tumor cells (CTCs) and [(18)F]fluorodeoxyglucose (FDG) positron emission tomography (PET)/computed tomography (CT) are two new promising tools for therapeutic monitoring. In this study, we compared the prognostic value of CTC and FDG-PET/CT monitoring during systemic therapy for metastatic breast cancer (MBC).

PATIENTS AND METHODS:
A retrospective analyses of 115 MBC patients who started a new line of therapy and who had CTC counts and FDG-PET/CT scans performed at baseline and at 9 to 12 weeks during therapy (midtherapy) was performed. Patients were categorized according to midtherapy CTC counts as favorable

(ie, < five CTCs/7.5 mL blood) or unfavorable (> or = five CTCs/7.5 mL blood) outcomes. CTC counts and FDG-PET/CT response at midtherapy were compared, and univariate and multivariate analyses were performed to identify factors associated with survival.

RESULTS:
In 102 evaluable patients, the median overall survival time was 14 months (range, 1 to > 41 months). Midtherapy CTC levels correlated with FDG-PET/CT response in 68 (67%) of 102 evaluable patients. In univariate analysis, midtherapy CTC counts and FDG-PET/CT response predicted overall survival (P < .001 and P = .001, respectively). FDG-PET/CT predicted overall survival (P = .0086) in 31 (91%) of 34 discordant patients who had fewer than five CTCs at midtherapy. Only midtherapy CTC levels remained significant in a multivariate analysis (P = .004).

CONCLUSION:
Detection of five or more CTCs during therapeutic monitoring can accurately predict prognosis in MBC beyond metabolic response. FDG-PET/CT deserves a role in patients who have fewer than five CTCs at midtherapy. Prospective trials should evaluate the most sensitive and cost-effective modality for therapeutic monitoring in MBC.

Eur J Nucl Med Mol Imaging. 2011 Feb;38(2):293-301. Epub 2010 Sep 30.

Tumour markers and FDG PET/CT for prediction of disease relapse in patients with breast cancer.

Evangelista L, Baretta Z, Vinante L, Cervino AR, Gregianin M, Ghiotto C, Saladini G, Sotti G.

Source

Radiotherapy and Nuclear Medicine Unit, Istituto Oncologico Veneto IOV-IRCCS, Padova, Italy. laura.evangelista@ioveneto.it

Abstract

PURPOSE:
The aim of the study was to assess the role of CA 15.3, CT and positron emission tomography (PET)/CT in patients with breast cancer and suspected disease relapse after primary treatment.

METHODS:
We studied 111 consecutive patients (mean age 61 ± 12 years) with previous

breast cancer, already treated and with clinical or biochemical suspicion of disease relapse. All patients underwent CT and (18)F-fluorodeoxyglucose (FDG) PET/CT. In all patients, the value of CA 15.3 was compared to PET/CT and CT. The final diagnosis of relapse was established by invasive and noninvasive follow-up and was compared with CA 15.3, CT and PET/CT results. Univariate and multivariate analyses were used to identify the independent predictors of disease relapse and receiver-operating characteristic (ROC) curve for the identification of optimal CA 15.3 cutoff.

RESULTS:
Of all patients, 40 (36%) showed an increased CA 15.3 value, CT was positive in 73 (66%), whereas at PET/CT imaging 64 (58%) showed positive findings for disease relapse. Of 40 patients with increased marker levels, 22 patients had positive CT and 30 positive PET/CT (55 vs 75%, $p<0.001$). At the end of follow-up, recurrence occurred in 32 (29%) patients, 16 (50%) of whom showed high levels of CA 15.3. PET/CT predicted relapse in 26 (81%) patients, whereas CT correctly identified 23 (72%). At univariate analysis, recurrence was significantly associated with high CA 15.3 values ($p<0.05$) and positive PET/CT ($p<0.005$). At multivariable analysis only positive PET/CT remained an independent predictor of disease relapse ($p<0.05$). ROC analysis showed an optimal cutoff point for CA 15.3 of 19.1 U/ml (AUC 0.65, $p<0.01$) to individuate positive PET/CT.

CONCLUSION:
FDG PET/CT is more sensitive than CT and CA 15.3 in the evaluation of disease relapse. PET/CT might be considered a complementary imaging technique during follow-up in patients with breast cancer.

Breast. 2009 Oct;18 Suppl 3:S66-73.
Molecular imaging of breast cancer.

Oude Munnink TH, Nagengast WB, Brouwers AH, Schröder CP, Hospers GA, Lub-de Hooge MN, van der Wall E, van Diest PJ, de Vries EG.
Source

Department of Medical Oncology, University Medical Center, Groningen, The Netherlands.

Abstract
Molecular imaging of breast cancer can potentially be used for breast cancer

screening, staging, restaging, response evaluation and guiding therapies. Techniques for molecular breast cancer imaging include magnetic resonance imaging (MRI), optical imaging, and radionuclide imaging with positron emission tomography (PET) or single photon emission computed tomography (SPECT). This review focuses on PET and SPECT imaging which can provide sensitive serial non invasive information of tumor characteristics. Most clinical data are gathered on the visualization of general processes such as glucose metabolism with the PET-tracer [(18)F]fluorodeoxyglucose (FDG) and DNA synthesis with [18F]fluoro-L-thymidine (FLT). Increasingly more breast cancer specific targets are imaged such as the estrogen receptor (ER), growth factors and growth factor receptors. Imaging of the ER with the PET tracer 16-alpha-[(18)F]fluoro-17-beta-estradiol (FES) has shown a good correlation between FES tumor uptake and ER density. (111)In-trastuzumab SPECT to image the human epidermal growth factor receptor 2 (HER2) showed that in most patients with metastatic HER2 overexpressing disease more lesions were detected than with conventional staging procedures. The PET tracer (89)Zr-trastuzumab showed excellent, quantifiable, and specific tumor uptake. (111)In-bevacizumab for SPECT and (89)Zr-bevacizumab for PET-imaging have been developed for vascular endothelial growth factor (VEGF) imaging as an angiogenic marker. Lastly, tracers for the receptors EGFR, IGF-1R, PDGF-betaR and the ligand TGFbeta are under development. Although molecular imaging of breast cancer is still not commonly used in daily clinical practice, its application portfolio is expanding rapidly.

J Nucl Med. 2010 Apr;51(4):543-50. Epub 2010 Mar 17.

18F-FDG PET of locally invasive breast cancer and association of estrogen receptor status with standardized uptake value: microarray and immunohistochemical analysis.

Osborne JR, Port E, Gonen M, Doane A, Yeung H, Gerald W, Cook JB, Larson S.

Source

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Abstract

PET imaging is useful for evaluating locally advanced primary breast cancer. Expression of specific molecular markers in these cancers, such as estrogen receptor (ER), progesterone receptor (PR), and HER2 status, has direct

prognostic and therapeutic implications in patient management. This study aimed to determine whether a relationship exists between tumor glucose use and important molecular markers in invasive breast cancer. For our purposes, tumor glucose use is quantified by the PET-derived parameter maximum standardized uptake value (SUV).

METHODS:
Breast tumors from 36 patients were excised and examined histologically after PET. ER, PR, and HER2 status were determined for all lesions histopathologically. In addition, genomewide expression for a subset of 20 tumors was analyzed using the human genome U133A oligonucleotide microarray.

RESULTS:
A significant association was found between estrogen ER status and lesion SUV. ER-negative tumors (n = 17; median SUV, 8.5) demonstrated a significantly higher maximum SUV than did ER-positive tumors (n = 19; median SUV, 4.0) ($P < 0.001$). No significant association existed between SUV and PR status, HER2/neu status, lymph node involvement, or tumor size. Unsupervised hierarchic clustering of the 20 genetically profiled cancers segregated tumor samples into 2 primary groups of 10 patients each, largely corresponding to ER status.

CONCLUSION:
In locally invasive primary breast cancer, ER-negative tumors display higher (18)F-FDG uptake than ER-positive tumors. Microarray analysis confirms these data and identifies genes associated with increased glucose use as measured by PET. These genes significantly overlap those of a previously validated ER-status molecular phenotype. These preliminary data support a growing body of evidence that ER-positive and ER-negative breast cancers have distinct disease-specific patterns. Further validation prospectively and with larger numbers will be required to establish a robust molecular signature for metabolic uptake and patterns of aggressive behavior in advanced breast cancer.

Radiology. 2008 Apr;247(1):189-96.

Bone metastases in patients with metastatic breast cancer: morphologic and metabolic monitoring of response to systemic therapy with integrated PET/CT.

Tateishi U, Gamez C, Dawood S, Yeung HW, Cristofanilli M, Macapinlac HA.
Source

Department of Nuclear Medicine, University of Texas M.D. Anderson Cancer Center, Unit 1263, 1515 Holcombe Blvd, Houston, TX 77030, USA. utateish@ncc.go.jp

Abstract

PURPOSE:

To retrospectively compare morphologic and metabolic changes in bone metastases in response to systemic therapy in patients with metastatic breast cancer (MBC) with integrated positron emission tomography (PET)/computed tomography (CT).

MATERIALS AND METHODS:

The institutional review board waived the requirement for informed consent and approved this HIPAA-compliant study. A retrospective analysis was performed with 102 women (mean age, 55 years) with MBC who received systemic treatment. All patients underwent integrated PET/CT before and after treatment. Two reviewers analyzed the images in consensus. Morphologic changes, including morphologic patterns, and lesion attenuation were evaluated. Standardized uptake value (SUV) and total lesion glycolysis (TLG) were analyzed to evaluate metabolic changes. Uni- and multivariate analyses were performed to identify factors that enabled response duration (RD) to be predicted.

RESULTS:

At baseline, the morphologic patterns of the target lesions were lytic (n = 33), sclerotic (n = 22), mixed (n = 42), and unclassified (n = 5). Progression of sclerotic change after treatment was identified in 49 patients (48%). After treatment, the mean attenuation of the lesion increased, whereas the mean SUV and TLG decreased. Increases in attenuation correlated significantly with decreases in SUV (r = -0.510, P < .001) and TLG (r = -0.491, P < . 001). Univariate analysis revealed that the increase in attenuation and the decrease in SUV were potential predictors of RD. Multivariate analysis revealed that an increase in the change in SUV was a significant predictor of RD (relative risk, 2.4; P = .003).

CONCLUSION:

A decrease in SUV after treatment was an independent predictor of RD in patients with MBC who had bone metastases.

Ann Nucl Med. 2005 Oct;19(7):573-9.

Comparison of 18FDG-PET with 99mTc-HMDP scintigraphy for the

detection of bone metastases in patients with breast cancer.

Abe K, Sasaki M, Kuwabara Y, Koga H, Baba S, Hayashi K, Takahashi N, Honda H.

Source

Department of Clinical Radiology, Kyushu University, 3-1-1 Maidashi, Higashi-ku, Fukuoka 812-8582, Japan. k-abe@radiol.med.kyushu-u.ac.jp

Abstract

OBJECTIVE:

Bone is one of the most common sites of metastasis in breast cancer patients. Although bone scintigraphy is widely used to detect metastatic breast cancer, the usefulness of 18FDG-PET for detecting bone metastasis has not been clearly evaluated. The purpose of this study was to compare the diagnostic accuracy of 18FDG-PET with bone scintigraphy in detecting bone metastasis in breast cancer patients.

METHODS:

Forty-four women aged 35 to 81 years (mean, 56 years) with breast cancer were examined in this study. Both 18FDG-PET and bone scintigraphy were performed for each patient with 0-69 day intervals (mean, 11.5 days). The results of each image interpretation were compared retrospectively. Whole-body bones were classified into 9 anatomical regions. Metastases were confirmed at 45/187 regions in 14 patients by bone biopsy or clinical follow-up including other imaging techniques for a period of at least 6 months afterwards.

RESULTS:

On a region basis, the sensitivity, specificity, and accuracy of 18FDG-PET were 84%, 99% and 95%, respectively. Although these results were comparable to those of bone scintigraphy, the combination of 18FDG-PET and bone scintigraphy improved the sensitivity (98%) and accuracy (97%) of detection. False negative lesions of bone scintigraphy were mostly bone marrow metastases and those of 18FDG-PET were mostly osteoblastic metastases. 18FDG-PET was superior to bone scintigraphy in the detection of osteolytic lesions (92% vs. 73%), but inferior in the detection of osteoblastic lesions (74% vs. 95%).

CONCLUSIONS:

This study shows that 18FDG-PET tends to be superior to bone scintigraphy in the detection of osteolytic lesions, but inferior in the detection of osteoblastic lesions. 18FDG-PET should play a complementary role in detecting bone metastasis with bone scintigraphy.

PET/CT Symposium MammCa Berlin 25. Mai 2011:
Prof. Untch Berlin-Buch
Mammazone-Befragung: MammaCa-Patientinnen wünschen fast immer intensivierte Nachsorge auch wenn ÜL-Vorteil nicht gesichert.
Luminal A is a common early stage of breast cancer in which the tumors look more like normal tissue compared to other tumor types and have receptors that are progesterone and estrogen positive and HER2-negative. HHP indicates that Luminal A has a low risk of recurrence, whereas HER-positive tumors are considered high risk.

Luminal B is similar to Luminal A in that the tumors also have progesterone and/or estrogen receptors except in smaller quantities. This type is also considered low risk.

HER2-positive tumors are higher-risk tumors than Luminal A and B and have had a number of gene mutations related to the epidermal growth factor.

Finally, basal-like breast cancers are sometimes referred to as "triple negative" in that they have negative readings of progesterone, estrogen, and HER2 but are considered high-risk because they have a tendency to grow rapidly.

Molekulare Marker beim Staging des MammaCa kosten 3000$ pro Pat., also mehr als ein PET/CT.
Für Aromatasehemmer werden weltweit 40 Mrd EUR ausgegeben. Nach 10 Jahren Unterschied im Gesamtüberleben bis auf Nachkommastelle identisch.
PET/CT kann Ansprechen voraussagen JCO Schwartz
Komplette Remission zum OP Zeitpunkt pCR korreliert mit besserem Gesamtüberleben
Frühansprechen nach 2 Zyklen mit PET/CT:

- Wer anspricht lebt länger
- Wer nicht anspricht und umsteigt lebt länger als wenn man weitermacht wie bisher.

Prof. Elling, Sana Klinikum
Ab 4 und mehr LK schlechte Prognose
ER+ und PR + bessere Prognose (seit Tam und AI)
Bei rezeptorneg Pat keine Verbesserung des ÜL in den letzten 20 Jahren
Verbessertes ÜL mit metastasiertem MammaCa 24-45 Monate
Seit 1975 von 15 auf 51 Monate (M D Anderson)

PET/CT Indikation:

- Hochrisikopat.
- Triple neg
- Hochgr. LK Befall
- Solitäre Metastase vor gezielter (kurativ intendierter) Therapie

Prof. Oberender:
TAMAR Studie
Versorgungsforschungsstudie
Neoadjuvante Chemo bei Hochrisikopatienten
Mit welcher diagnostischen Genauigkeit ist Frühes Therapieansprechen zu diagnostizieren.
Teilnehmende Krankenkassen:
DAK Siemens BKK, TK, AOK Bayern, BP

Prof. Kalinyak: PET Mammography PEM
HR breast PET
PEM mobiles Gerät 4-10 min per view CC und MLO annalog Mammographie mit Kompression
Berg Radiology 2011 PEM Pet Mammography
Narayanan AJR 2011 PEM standardisierte Interpretationskriterien
Hohe Spezifität und PPV
Bei Vorliegen eines Index Tumors von 1,5 cm, konnte bei 21% der Pat. ein ipsilat. Tumor von <0,7 cm nachgewiesen werden.
Muß noch durch Biopsie bestätigt werden.
Response des multifocalen oder contralateralen Befalls nicht identisch!
FDA approved, wird von amerikanischen Kostenträgern übernommen.

26. Nuklearmedizinertreffen 12.10.2011
Prof. Schmidt: Sentinel Lymphknotenszintigraphie
Ashikaga J Surg Oncol 2010
Axilläre LND vs SLN lymph node dissektion: Hochsignifikant kleinere Komplikationsraten p<0,001
Axilläre Rezidivrate nach neg. SLN EUR J Surg Oncol 0,8-2,3%
Micrometastasen < 2mm machen keinen signifikanten Unterschied.

Keine Lymphknotenbehandlung bei:

- SLN –

- SLN isolatetd tumor cells
- SLN micrometa < 2mm

Axilladissektion nur bei Hochrisikopat. mit Makrometastasen

Prof. Malter Chirurgie
Radikalität der Axilla-OP kann reduziert werden ohne das Ergebnis für die Pat. zu ändern.
Komplikationen bei 40% der klassischen Axilladissektion!!!!
Axilläre Lymphknotendissektion ändert nicht das Überleben, nur die Lokale Tumorkontrolle und das axilläre Rezidivrisiko
Level I unter M. pect minor
Level II hinter M. pect minor
Level III darüber!!!

OP Gebiet: Level I (schließt Sentinel ein) und max. Level II
Anforderung Qualitätssicherung: Level I und II mind. 10 LK (15-20)

Veränderung des Therapiefokus weg von der lokalen (axillären) Tumorkontrolle zur systemischen Therapie:

N1a : Verzicht auf Axilla-OP nach Aufklärung und Erfüllen der Voraussetzung
N2a: axilläre LN Dissektion

Harbeck ASCO 2009
Proteasenbestimmung erforderlich
SLN zur Dokumentation N0
Bei mehr als drei LK: Anpassung der Dosisdichte der Chemotherapie

Overgaard RT nach Mastektomie R+O 2007
BET und mehr als drei bef. LK: Rx auch der Lymphabflußwege (Axilla und supraklav)

Prof. Dietlein:
PET bzw. PET/CT Indikationen beim MammaCa:

1. Baseline Staging:

Groheux EUR J nucl med Mol Imaging 2011

Bei großen Tumoren: JCO 2008 Fuster

- 3 cm Sens 100% Spez 98% Änderung des konv. Stagings bei 42%!

Inflammatorisches MammaCa: Alberini EUR J Nucl Med Mol Imaging 2009: 31% M1!
FDG PET/CT sollte beim inflammatorischen MammaCa zum Primär- und Rezidivstaging eingesetzt werden.

2. Therapiemonitoring:
Intensiv stoffwechselaktive Tumoren: triple neg. G3
Für Therapiemonitoring geeignet: hoher SUV max-Ausgangswert
Straver EUR J Nucl Med Mol Imaging 2011: Tumor-Untergrund-Verhältnis > 5 oder SUV max >2,5 als Voraussetzung für Therapiemonitoring

ER neg Tumoren haben hohe SUV max-Werte
Osborne JNM 2010

Rousseau EUR J Nucl Med Mol Imaging 2011 early axillary lymph node response in response to neoadjuvant chemotherapy

Responder und non-responder
Harbeck JCO 2009 responder und non-responder nach 1. Zyklus 45% SUV max, nach 2. Zyklus 55% SUV max

Duch EUR J Nucl Mol Im 2009 cutoff 40%
Nach 2 Zyklen wurden 30% der Pat. identifiziert die keine response zeigten

Reduktion des SUVmax ist ein unabhängiger Prädiktor für die Dauer des Therapieansprechens bei Skelettmetastasen von MammaCa Patientinnen.
Tateishi Radiology 2008

3. OP-Planung
World J Surg 2009 Kim et al
Hohe Spezifität der FDG-PET: PET pos LK nicht falsch pos!
Reduktion unnötiger SNB
Gilardi EUR J Nucl Med Mol Imaging 2010
Wenn nach neoadj. Chemo noch FDG-+ LK nachweisbar dann Makrometastasen vorhanden. Indikation zur Axillären Lymphknotendissektion.

4. Rezidivdiagnostik
FDG PET/CT spielt eine Rolle bei <5 zirkulierende Tumorzellen in 7,5 ml Blut
De Giorgi JCO 2009, Ann Oncol 2010, JNM 2010

Champion Cancer 2008
FDG-PET/CT bei Tumormarkeranstieg (Ca 15-3 oder CEA erhöht): 54%
Modifikation der Behandlung
181/228 PET/CT pos

Evangelista EUR J Nucl Med Mol Im 2011 Univariate Regressionsanalyse für Vorhersage eines Rezidivs:
FDG-PET/CT ist sensitiver als Tumormarkeranstieg und CT

5. Zufallsbefund FGD-PET pos. Mammaherd bei PET/CT aus anderer Indikation:
Litmanovich EUR J Nucl Med Mol Imaging 2009
57% Malignom
andere Studie 29%

Zusammenfassung Indikationen FDG-PET/CT bei MammaCa:
Initialstaging

- bei großen Tumoren > 3cm
- inflammatorisches MammaCa
- ER Rezeptorstat

OP Planung: bei FDG pos Axilla-Befund gleich Axilla dissektion

RT Planung

Therapiemonitoring

- bei initial PET pos. Tumoren
- Herceptin abhängig von Zellinie
-

Rezidivverdacht

- Tumormarkeranstieg (Ca 15-3 oder CEA)
- Persitierende zirkulierende Tumorzellen

Neue PET Tracer!

Ovarialcarcinom

Nucl Med Biol. 2011 May;38(4):485-91. Epub 2011 Mar 3.
Noninvasive assessment of cell proliferation in ovarian cancer using [18F] 3'deoxy-3-fluorothymidine positron emission tomography/computed tomography imaging.
Richard SD, Bencherif B, Edwards RP, Elishaev E, Krivak TC, Mountz JM, DeLoia JA.
Department of Obstetrics, Gynecology and Reproductive Services, Division of Gynecologic Oncology, University of Pittsburgh, Pittsburgh, PA 15213, USA.
Positron emission tomography (PET)/computed tomography (CT) imaging of suspected new and recurrent ovarian carcinoma was performed to assess the relationship between [(18)F] 3'deoxy-3'fluorothymidine ((18)FLT) uptake and histopathological tissue markers of cellular proliferation (Ki67) and thymidine kinase-1 (TK-1) expression. Six subjects were included in this pilot study. Subjects were injected with 5 mCi of (18)FLT prior to a planned surgery and then scanned on a GE Discovery-ST PET/CT scanner within an hour of injection. Regions of interest in tumor and control tissue were identified on the diagnostic CT scans and marked for later surgical biopsy. Surgery was performed within 2 days after the scan. At the time of surgery, the regions of interest identified on PET/CT were available to guide the surgeon to the tumor biopsy sites. Tissue from normal ovarian tissue control regions was also sampled. (18)FLT uptake in tumor and control tissue regions was calculated by measuring the maximum standardized uptake values (SUV(max)). The excised tumor and normal ovarian tissue control tissues were analyzed by immunohistochemical staining for Ki67 and CD34. TK-1 messenger RNA expression was measured by real-time polymerase chain reaction. (18)FLT uptake (SUV(max)) was higher in malignant (mean 4.85/range 1.7-8.8) compared to benign (1.65/range 1.4-1.9) and normal ovarian control tissue (1.12/range 0.6-1.5). Mitotic index, as determined by Ki67 staining, was higher in malignant (18.89/range 11.97-27.19) compared to benign (0.59/range 0.23-0.95) and control tissue (0.45/range 0.06-1.20). TK-1 expression was also higher in malignant (35.52/range 5.21- 106.62) compared to benign (8.71/range 4.74-12.67) and control tissue (9.79/range 0.85-39.46). An increasing trend between (18)FLT uptake and Ki67 mitotic index is seen in malignant tissue CD 34 staining between malignant, benign and control tissues was not qualitatively different. An increasing trend between (18)FLT uptake and Ki67 mitotic

index is seen in malignant tissue. Additional studies will determine whether (18)FLT PET/CT is specific enough to distinguish between cancerous and noncancerous cells and to assess its role in ovarian carcinoma patient management.

Clin Nucl Med. 2011 Oct;36(10):889-93.
Noninvasive and invasive staging of ovarian cancer: review of the literature.
Fuccio C, Castellucci P, Marzola MC, Al-Nahhas A, Fanti S, Rubello D.
From the *Service of Nuclear Medicine, Hematology-Oncology and Laboratory Medicine Department, Azienda Ospedaliero-Universitaria di Bologna Policlinico Sant'Orsola-Malpighi, University of Bologna, Bologna, Italy; †Department of Nuclear Medicine, Medical Physics and Radiology, Santa Maria della Misericordia Hospital, Rovigo, Italy; and ‡Department of Nuclear Medicine, Hammersmith Hospital, London, United Kingdom.
The use of F-18 FDG PET/CT in the characterization of doubtful adnexal findings and in the staging of ovarian cancer is being extensively evaluated. The purpose of our article is to review the literature and to add our experience to the published works. We concluded that F-18 FDG PET/CT could represent an important method in addition to other imaging modalities (transvaginal ultrasound-, and contrast-enhanced computed tomography) in the characterization of adnexal masses and in the staging of ovarian cancer patients, particularly in assessing the presence of extra-abdominal metastatic spread.

Onkologische Herbsttagung Holweide 12.11.2011

- Strahlentherapie gynäkologischer Tumoren (Prof. Niehoff): initiales MRT zur Therapieplanung, extern vs. Brachytherapie. Leistenrezidiv = palliativ
- Eine HRT nach gynäkologischen Tumoren ist im Regelfall unbedenklich. Ausnahmen: endometriales Stromasarkom und Granulosazelltumor.

OvarialCa (Prof. Lichtenegger): Erst-OP im Zentrum verbessert das Gesamtüberleben. Optimale Debulking-OP (Peritonektomie, Leberinspektion, Omentektomie, ggf. Zwerchfellfreilegung oder Interponat) OHNE Tumorrest oder max. 1 cm Rest ist wichtigster unabhängiger Prognosefaktor. Optimal 60% @ 48 Mon. neoadj. Th. mit Carboplatin und Paclitaxel, ggf. Erhaltungstherapie mit Avastin

Clin Nucl Med. 2012 Jan;37(1):54-6.
FDG PET/CT in Ovarian Cancer: What About Treatment Response and Prognosis?

Grassetto G, Groheux D, Marzola MC, Hindié E, Al-Nahhas A, Rubello D.
Source

From the *Department of Nuclear Medicine, PET/CT Centre, Santa Maria della Misericordia Hospital, Rovigo, Italy; †Nuclear Medicine Service, Saint Louis Hospital, University of Paris, Paris, France; and ‡Department of Nuclear Medicine, Imperial College NHS Trust, Hammersmith Hospital, London, United Kingdom.

Ga68 DOTATOC/DOTATATE SSR-Bildgebung

Methods Mol Biol. 2011;727:105-22.
Functional imaging of neuroendocrine tumors.
Van Binnebeek S, Karges W, Mottaghy FM.
Department of Nuclear Medicine, University Hospital Leuven, Leuven, Belgium.
Neuroendocrine tumors (NET) have several distinct pathophysiological features that can be addressed by specific radiolabeled probes. An
overview on the different radiopharmaceuticals that have been developed for positron emission tomography (PET) of NET are presented. The
focus is on fluordeoxyglucose (F-18 FDG), biogenic amine precursors, somatostatin analogs, and hormone syntheses markers. Due to the highly
specific tracers lacking any clear anatomical landmarking, the advantages of integrated functional and morphological imaging systems such as
PET-CT are obvious. Based on the up to now published literature and one's own experience, it is concluded that amine precursors (e.g. fluor-
dihydroxyphenylalanin and hydroxytryptophane) should be employed in most gastroenteropancreatic NET, whereas F-18 FDG should be
preserved for more aggressive less-differentiated NETs. Hormone syntheses markers have up to now only been used in few centers and their
broad clinical value remains uncertain. The different available somatostatin analogs are the most promising tracers, since they can improve
dosimetry in cases where peptide receptor radiotherapies are planned. Of specific interest are the somatostatin analogs addressing several
subtypes of the somatostatin receptor (e.g. DOTANOC) that allow detecting also subtypes not expressing the "classically" addressed subtype 2
and 5. Since NET have a high variety of different features, the individual diagnostic approach using PET or integrated PET-CT should be
tailored, depending on the histological classification and the differentiation of the tumor.

Semin Nucl Med. 2011 Jul;41(4):314-21.

(68)Ga-labeled DOTA-peptides and (68)Ga-labeled radiopharmaceuticals for positron emission tomography: current status of research, clinical applications, and future perspectives.

Breeman WA, de Blois E, Sze Chan H, Konijnenberg M, Kwekkeboom DJ, Krenning EP.

Department of Nuclear Medicine, Erasmus MC Rotterdam, The Netherlands. w.a.p.breeman@erasmusmc.nl

In this review we give an overview of current knowledge of (68)Ga-labeled pharmaceuticals, with focus on imaging receptor-mediated processes.

A major advantage of a (68)Ge/(68)Ga generator is its continuous source of (68)Ga, independently from an on-site cyclotron. The increase in knowledge of purification and concentration of the eluate and the complex ligand chemistry has led to (68)Ga-labeled pharmaceuticals with major clinical impact. (68)Ga-labeled pharmaceuticals have the potential to cover all today's clinical options with (99m)Tc, with the concordant higher resolution of positron emission tomography (PET) in comparison with single photon emission computed tomography. (68)Ga-labeled analogs of octreotide, such as DOTATOC, DOTANOC, and DOTA-TATE, are in clinical application in nuclear medicine, and these analogs are now the most frequently applied of all (68)Ga-labeled pharmaceuticals. All the above-mentioned items in favor of successful application of (68)Ga-labeled radiopharmaceuticals for imaging in patients are strong arguments for the development of a (68)Ge/(68)Ga generator with Marketing Authorization and thus to provide pharmaceutical grade eluate. Moreover, now not one United States Food and Drug Administration-approved or European Medicines Agency-approved (68)Ga-radiopharmaceutical is available. As soon as these are achieved, a whole new radiopharmacy providing PET radiopharmaceuticals might develop.

Clin Nucl Med. 2011 Feb;36(2):124-6.

I-123 MIBG scintigraphy and 68Ga-DOTANOC PET/CT negative but F-18 DOPA PET/CT positive pheochromocytoma: a case report.

Grassi I, Nanni C, Vicennati V, Castellucci P, Allegri V, Montini GC, Pagotto U, di Dalmazi G, Pasquali R, Fanti S.

Unità Operativa di Medicina Nucleare, Policlinico S. Orsola-Malpighi, Bologna, Italy. ilary.grassi@libero.it

We observed a 34-year-old man who was incidentally found to have an adrenal mass during surgical follow-up for perforated ulcer. The patient was subjected to I-123 MIBG scintigraphy, 68Ga-DOTANOC PET/CT, and F-18 DOPA PET/CT. Only F-18 DOPA PET/CT showed evidence

of an avid adrenal mass. A CT-guided biopsy was performed and it was suggestive for pheochromocytoma. He underwent surgery and a
pheochromocytoma, about 40 mm in diameter, was detected. Traditionally, I-123 MIBG scintigraphy has been used in detecting chromaffin cell
tumors, but more recently it had been demonstrated that a certain part of pheochromocytoma could be false-negative on scintigraphy.
Pa

Semin Oncol. 2010 Dec;37(6):594-618.
Pancreatic endocrine tumors.
Oberg K. Department of Medical Sciences, Uppsala University Hospital, Uppsala, Sweden. kjell.oberg@medsci.uu.se
Pancreatic endocrine tumors have been steadily growing in incidence and prevalence during the last two decades, showing an incidence of 4- 5/1,000,000 population. They represent a heterogeneous group with very varying tumor biology and prognosis. About half of the patients present clinical symptoms and syndromes related to substances released from the tumors (Zollinger-Ellison syndrome, insulinoma, glucagonoma, etc) and the other half are so-called nonfunctioning tumors mainly presenting with symptoms such as obstruction, jaundice, bleeding, and abdominal mass. Ten percent to 15% of the pancreatic endocrine tumors are part of an inherited syndrome such as multiple endocrine neoplasia type 1 (MEN-1), von Hippel-Lindau (VHL), neurofibromatosis, or tuberousclerosis. The diagnosis is based on histopathology demonstrating neuroendocrine features such as positive staining for chromogranin A and specific hormones such as gastrin, proinsulin, and glucagon. Moreover, the biochemical diagnosis includes measurement of chromogranins A and B or specific hormones such as gastrin, insulin, glucagon, and vasoactive intestinal polypeptide (VIP) in the circulation. In addition to standard localization procedures, radiology (computed tomography [CT] scan, magnetic resonance imaging [MRI], ultrasound [US]), somatostatin receptor scintigraphy, and most recently positron emission tomography with specific isotopes such as (11)C-5 hydroxytryptamin ((11)C-5-HTP), fluorodopa and (68)Ga-1,4,7,10-tetra-azacyclododecane-N,N',N″,N‴- tetra-acetic acid (DOTA)-octreotate are performed. Surgery is still one of the cornerstones in the management of pancreatic endocrine tumors, but curative surgery is rarely obtained in most cases because of metastatic disease. Debulking and other cytoreductive procedures might facilitate systemic treatment. Cytotoxic drugs, biological agents, such as somatostatin analogs, alpha interferons, mammalian target of rapamycin (mTOR) inhibitors and tyrosine kinase inhibitors are routinely used. Tumor-targeted radioactive treatment is available in many centres in Europe and is effective in patients with tumors that express high content of somatostatin receptors type 2 and 5. In the future, treatment will be based on tumor biology and molecular genetics with the aim of so-called personalized medicine.

J Nucl Med. 2011 Jan;52(1):123-31. Epub 2010 Dec 13.
Imaging expression of the human somatostatin receptor subtype-2 reporter

gene with 68Ga-DOTATOC.
Zhang H, Moroz MA, Serganova I, Ku T, Huang R, Vider J, Maecke HR, Larson SM, Blasberg R, Smith-Jones PM.
Department of Neurology, Memorial Sloan-Kettering Cancer Center, New York, New York 10065, USA.
The human somatostatin receptor subtype 2 (hSSTr2)-68Ga-DOTATOC reporter system has several attractive features for potential translation to
human studies. These include a low expression of hSSTr2 in most organs, a rapid internalized accumulation of 68Ga-DOTATOC in the SSTr2-
expressing cells, and a rapid excretion of unbound radioligand by the renal system. We performed a series of in vitro and in vivo validation
studies of this reporter system.A retroviral vector containing a dual reporter, pQCXhSSTr2-IRES-GFP (IRES: internal ribosome entry site; GFP:
green fluorescent protein), was constructed and transduced into Jurkat, C6, and U87 cells. Stably transduced reporter cells were characterized in
vitro using optical and radiometric methods. Multiple tumor-bearing mice were evaluated with 68Ga-DOTATOC PET studies. The dual-reporter
genes were incorporated into all tumor cell lines, and their expression levels were confirmed by fluorescence-activated cell sorting (FACS), GFP
visualization, and reverse-transcriptase polymerase chain reaction (RT-PCR) analysis for hSSTr2. In vitro, hSSTr2 cell membrane expression was
36,000, 280,000, and 1,250,000 copies per cell for the SSTR2-transfected Jurkat, U87, and C6 cell lines. Small-animal PET of 68Ga-DOTATOC
in tumor-bearing mice demonstrated that the in vivo uptake of this radioligand was directly proportional to the in vitro expression of hSSTr2. The
in vivo uptake of 68Ga-DOTATOC, at 2 h after injection, was low in all organs except the kidneys (7.8 percentage of injected dose per gram
[%ID/g]) and as high as 15.2 %ID/g in transduced C6 tumors. The corresponding transduced-to-nontransduced tumor uptake ratio was 64, and
the tumor-to-muscle uptake ratio was around 500. 68Ga-DOTATOC is an excellent specific ligand for this hSSTr2 reporter system and for
hSSTr2 reporter gene PET. Because DOTATOC has undergone extensive clinical testing, this human reporter system has the potential for
translation to human studies.

J Nucl Med. 2011 Jun;52(6):886-90. Epub 2011 May 13.
Incidence of increased 68Ga-DOTANOC uptake in the pancreatic head in a large series of extrapancreatic NET patients studied with
sequential PET/CT.
Castellucci P, Pou Ucha J, Fuccio C, Rubello D, Ambrosini V, Montini GC, Pettinato V, Malizia C, Lodi F, Fanti S.
Nuclear Medicine Unit, Hematology-Oncology and Laboratory Medicine Department, Azienda Ospedaliero-Universitaria di Bologna Policlinico
S Orsola-Malpighi, University of Bologna, Bologna, Italy. paolo.castellucci@aosp.bo.it

The aim of our retrospective study was to assess the incidence of increased uptake of (68)Ga-DOTANOC in the head of the pancreas among a
large population of patients with extrapancreatic neuroendocrine tumors studied with serial (68)Ga-DOTANOC PET/CT. Patients who had
undergone at least two (68)Ga-DOTANOC PET/CT studies over time were included. Uptake in the head of the pancreas was measured and
compared with uptake in normal liver parenchyma (target-to-liver ratio). Patients were followed up for 6-24 mo. We reviewed 245 studies
performed on 100 patients and classified the pancreatic uptake as either diffuse or focal. Twenty-three patients (66 scans) showed diffuse uptake;
8 patients (16 scans) showed focal uptake. None of these 31 patients had negative findings on their subsequent scans, and vice versa. During
follow-up, localization of neuroendocrine tumors in the pancreas was not suspected in any patient. Focal and diffuse uptake of (68)Ga-
DOTANOC in the head of the pancreas occurred, respectively, in 23% and 8% of the patients. The main finding of our study was that increased
pancreatic uptake was stable over time.

Ann Nucl Med. 2008 May;22(4):237-43. Epub 2008 Jun 6.

Correlation of chromogranin A levels and somatostatin receptor scintigraphy findings in the evaluation of metastases in carcinoid tumors.

Namwongprom S, Wong FC, Tateishi U, Kim EE, Boonyaprapa S.

Source

Department of Nuclear Medicine, The University of Texas M.D. Anderson Cancer Center, 1515 Holcombe Blvd., Houston, TX 77030, USA. snamwong@mail.med.cmu.ac.th

Abstract

OBJECTIVE:
Chromogranin A (CgA) has been gaining acceptance as a helpful tumor marker in patients with neuroendocrine tumors, with respect to both diagnosis and prognosis. The objective of this study was to correlate serum CgA levels and somatostatin receptor scintigraphy (SRS) findings in the evaluation of metastases in carcinoid tumors.

MATERIALS AND METHODS:
A total of 125 patients(61 men and 64 women, aged from 23 to 84 years) with histologically diagnosed carcinoid tumor underwent serum CgA assay and SRS for detecting metastasis or disease recurrence. The quantitative determination of CgA was performed in serum using an enzyme immunoassay with a cut-off

value fixed at 39 U/l. Scintigraphies were performed with 200-220 MBq of In-111-DTPA-Phel-octreotide including whole-body images as well as single-photon emission computed tomography and computed tomography scans of the chest and abdomen.

RESULTS:
The primary tumors originated from the gastrointestinal tract in 115 of 125 patients (92.0%), the lung in 7 of 125 patients (5.6%), the kidney in 2 of 125 patients (1.6%), and the breast in 1 of 125 patients (0.8%). The primary tumors originated from the foregut, midgut, and hindgut in 13.6%, 71.2%, and 12.8%, respectively. Correlation of SRS with other imaging modalities and clinical follow-up findings revealed a sensitivity, a specificity, and an accuracy of 82.9%, 97.7%, and 88.0%, respectively, and for CgA 62.2%, 83.7%, and 69.6%, respectively. There was 1 false-positive and 14 false-negative SRS results and 7 false-positive and 31 false-negative CgA analyses. SRS demonstrated higher sensitivity, specificity, and accuracy than CgA for the evaluation of metastatic carcinoid tumors. The concordance between SRS and CgA results was 67.2%. Discrepancies, such as positive SRS with normal CgA levels, were noted in 26 (20.8%) cases, whereas negative SRS with high CgA levels was seen in 15 (12.0%) cases. Combining the results of CgA and SRS increased the sensitivity (92.7%) but decreased the specificity (81.4%) of tumor detection.

CONCLUSIONS:
In our study, SRS proved to be more sensitive, more specific, and more accurate than CgA for metastatic evaluation of carcinoid tumors. Positive SRS correlated with elevation of serum CgA levels. Serum CgA might have some diagnostic utility in patients with negative SRS studies. Nevertheless, both SRS and CgA should be considered useful tools in the evaluation of metastases in carcinoid patients.

Int J Radiat Oncol Biol Phys. 2011 Sep 1;81(1):277-83. Epub 2011 Feb 6.
Simultaneous (68)Ga-DOTATOC-PET/MRI for IMRT Treatment Planning for Meningioma: First Experience.
Thorwarth D, Henke G, Müller AC, Reimold M, Beyer T, Boss A, Kolb A, Pichler B, Pfannenberg C.
Section of Biomedical Physics, University Hospital for Radiation Oncology, Eberhard-Karls-Universität Tübingen, Tübingen, Germany.
To evaluate intensity-modulated radiotherapy (IMRT) treatment planning based on simultaneous positron-emission tomography and magnetic resonance imaging (PET/MRI) of meningioma. A meningioma patient was examined prior to radiotherapy

with dedicated planning computed tomography (CT), MRI, PET/CT with gallium-68-labeled DOTATOC ((68)Ga-DOTATOC), and simultaneous (68)Ga-DOTATOC-PET/MRI. The first gross target volume (GTV) was defined based on a combination of separate MR and (68)Ga-DOTATOC-PET/CT imaging (GTV(PET/CT+MR)). Then, the simultaneous PET/MR images were used to delineate a second GTV (GTV(PET/MR)) by following exactly the same delineation strategy. After an isotropic expansion of those volumes by a 4-mm safety margin, the resulting planning target volumes (PTVs) were compared by calculating the intersection volume and the relative complements. A cross-evaluation of IMRT plans was performed, where the treatment plan created for the PTV(PET/CT+MR) was applied to the PET/MR-based PTV(PET/MR). Generally, target volumes for IMRT treatment planning did not differ between MRI plus (68)Ga-DOTATOC-PET/CT and simultaneous PET/MR imaging. Only in certain regions of the GTV were differences observed. The overall volume of the PET/MR-based PTV was approximately the same as that obtained from PET/CT data. A small region of infiltrative tumor growth next to the main tumor mass was better visualized with combined PET/MR due to smaller PET voxel sizes and improved recovery. An IMRT treatment plan was optimized for the PTV(PET/CT+MR). The evaluation of this plan with respect to the PTV(PET/MR) showed parts of the target volume that would not have received the full radiation dose after delineation of the tumor, based on simultaneous PET/MR. This case showed that differences in target volumes delineated on the basis of separate MR and PET/CT and simultaneous PET/MR may be observed that can have significant consequences for an effectively applied radiotherapy treatment plan.

FEC Cholin PET/CT: ProstataCa und hepatozelluläres Ca

Nucl Med Commun. 2011 Jun;32(6):475-8.
Prostate-specific antigen kinetics and choline PET/CT in patients with biochemical relapse after primary treatment for prostate cancer.
Castellucci P, Fuccio C, Marzola MC, Al-Nahhas A, Rubello D, Fanti S.
PET-Oncology
Department of Nuclear Medicine, Hematology-Oncology and Laboratory Medicine, Azienda Ospedaliero-Universitaria di Bologna Policlinico Sant' Orsola-Malpighi, University of Bologna, Italy.
Over the past few years, several studies have proved the potential role of diagnostic procedures in patients with treated prostate cancer who develop biochemical relapse. Notably, no precise indications exist regarding the use of emerging modalities such as positron emission tomography/computerized tomography (PET/CT) scanning with radiolabeled choline. However, the literature suggests that the main and most important application of choline PET/CT at present is in disease restaging in cases of biochemical relapse for the detection of local, lymph node- related or distant recurrence. In this setting, it is well known that prostate-specific antigen (PSA) values play a significant role in the follow-up of these patients. This short review aims at summarizing the results of the most relevant published studies with particular interest directed towards a better understanding of the relationship between PSA kinetics and choline PET/CT detection rate and the potential use of PSA kinetics for an optimal selection of patients who may benefit most from this diagnostic procedure particularly at an early stage of biochemical recurrence.

Prostate Cancer Prostatic Dis. 2011 Aug 16. doi: 10.1038/pcan.2011.35. [Epub ahead of print]
(18)F-fluorocholine for prostate cancer imaging: a systematic review of the literature.
Bauman G, Belhocine T, Kovacs M, Ward A, Beheshti M, Rachinsky I.
Department of Oncology, The University of Western Ontario, London Health Sciences Centre-St Joseph's Healthcare Centre, London, Ontario,
Canada.
Positron emission tomography (PET or combined PET-computed tomography (PET/CT)) allows the non-invasive interrogation of metabolic
processes using radiolabeled probes. Altered choline metabolism has been noted as a characteristic of prostate cancer (PCa), and radiolabeled
choline and choline analogs have been investigated as PET/CT imaging agents for

prostate cancer; [(18)F]fluoromethyl-dimethyl-2-
hydroxyethyl-ammonium ((18)F-FCH) shows particular promise as a PCa imaging agent given its favorable physical and pharmacokinetic
properties. We conducted a systematic review of results to date with (18)F-FCH. As the tracer was first described by DeGrado in 2001, we
limited our search from January 2001 to August 2011.In all, 37 studies including 1244 patients met the inclusion criteria. Studies included those
detailing the radiosynthesis of (18)F-FCH, preclinical and early clinical dosimetry, and biodistribution (n=7); evaluation of local disease (n=6),
nodal disease (n=5), bone metastases and castrate-resistant disease (n=7), biochemical recurrence (n=11), radiotherapy planning (n=7) and
sources of false-positive studies (n=2); and some studies reported on multiple indications. Potential sources of variations in the studies affecting
reported performance included case series size, variation in extent of disease at imaging (including Gleason grade, and PSA), selection of gold
standards for comparison and variations in scan technique. On the basis of the review, we suggest potential scenarios where this metabolic
imaging might be considered for further evaluation in clinical trials for guiding PCa management.Prostate Cancer and Prostatic Diseases

Fluorocholine (18F) and sodium fluoride (18F) PET/CT in the detection of prostate cancer: prospective comparison of diagnostic performance determined by masked reading.

Langsteger W, Balogova S, Huchet V, Beheshti M, Paycha F, Egrot C, Janetschek G, Loidl W, Nataf V, Kerrou K, Pascal O, Cussenot O, Talbot
J.
PET-CT Center Linz, St Vincent's Hospital, Linz, Austria - jean-noel.talbot@tnn.aphp.fr.

AIM.The aim of this paper was to compare the diagnostic performance of positron emission tomography/computed tomography (PET/CT) with
fluorocholine (18F) (FCH) or fluoride(18F) (FNa) for the detection of bone metastasis in patients with prostate cancer complaining from
osteoarticular pain, taking into account whether they were referred for initial staging or recurrence localization. The initial hypothesis was that
FCH site-based specificity would be superior to that of F Na, with no loss in sensitivity. METHODS_ Forty-two patients were enrolled in this
prospective study, underwent both PET/CTs and were then followed-up for at least 6 months. The standard of truth (SOT) about the
presence/absence and location of bone metastasis could be determined in 40 patients, by 2 independent medical assessors, blinded to the results of
both PET/CTs. The comparison was performed according to the guideline of the European Medicines Agency, i.e. based on the results of blind

reading with SOT as reference. RESULTS:Bone extension was present in 22 patients and absent in 18. Patient-based performance for FCH vs.
FNa was 91% vs. 91% for sensitivity, 89% vs. 83% for specificity and 90% vs. 88% for accuracy (no significant difference). Of 360 skeletal
sites, 68 were malignant and 292 non-invaded. There was no significant difference in site-based performance in the group of patients referred at
initial staging, but in the group of patients referred for suspicion of recurrence, FCH was significantly more specific than FNa (96% vs. 91%,
P=0.033 with Obuchowski's correction) while sensitivity was the same, 89%. CONCLUSION: Both radiopharmaceuticals, based on a very
different metabolic approach, showed good diagnostic performance. If FCH is available, it should be preferred in patients after initial treatment.

Hepatol Res. 2011 Jul;41(7):611-7. doi: 10.1111/j.1872-034X.2011.00819.x.
Clinical applications of positron emission tomography in hepatic tumors.
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Department of Nuclear Medicine, Osaka City University Graduate School of Medicine, Osaka, Japan.
Fluorodeoxyglucose (FDG), which allows the evaluation of glucose metabolism, is widely used for tumor diagnosis using positron emission tomography (PET). FDG-PET, which is used for the diagnosis of intrahepatic tumor lesions, shows high FDG accumulation in cholangiocellular carcinoma (CCC) and metastatic liver cancer. FDG-PET shows high FDG accumulation in moderately or poorly differentiated hepatocellular carcinoma (HCC) and is useful for the diagnosis of extrahepatic HCC metastases and recurrences. However, because the imaging method frequently shows low FDG accumulation in well-differentiated HCC, it is not very useful for that diagnosis. For the diagnosis of well- differentiated HCC, F-18 fluorocholine for evaluation of phospholipid metabolism and C-11 acetate for evaluation of free fatty acid metabolism are useful in the diagnosis of that HCC. It is expected that the combination of these PET agents will enhance the diagnostic performance of FDG-PET for HCC in the future. The problem of a lack of anatomical information is being resolved with the development of the use of PET in combination with computed tomography or magnetic resonance imaging. For the problem of low resolution, PET devices using semiconductors have been developed.

J Nucl Med. 2011 Jan;52(1):81-9. Epub 2010 Dec 13.
Prostate cancer: PET with 18F-FDG, 18F- or 11C-acetate, and 18F- or 11C-choline.
Jadvar H.
Department of Radiology, Keck School of Medicine, University of Southern California, Los Angeles, California 90033, USA. jadvar@usc.eduProstate cancer is biologically and clinically a heterogeneous disease that makes imaging evaluation challenging.

The role of imaging in prostate cancer should include diagnosis, localization, and characterization (indolent vs. lethal) of the primary tumor, determination of extracapsular spread, guidance and evaluation of local therapy in organ-confined disease, staging of locoregional lymph nodes, detection of locally recurrent and metastatic disease in biochemical relapse, planning of radiation treatment, prediction and assessment of tumor response to salvage and systemic therapy, monitoring of active surveillance and definition of a trigger for definitive therapy, and prognostication of time to hormone refractoriness in castrate disease and overall survival. To address these tasks effectively, imaging needs to be tailored to the specific phases of the disease in a patient-specific, risk-adjusted manner. In this article, I review the preclinical and clinical evidence on the potential and emerging role of PET with the 3 most commonly studied radiotracers in prostate cancer, namely 18F-FDG, 18F- or 11C-acetate, and 18F- or 11C-choline.

Detection of hepatocellular carcinoma with PET/CT: a prospective comparison of 18F-fluorocholine and 18F-FDG in patients with cirrhosis or chronic liver disease.

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This prospective study aimed to compare the diagnostic performance of (18)F-fluorocholine and (18)F-FDG for detecting and staging hepatocellular carcinoma (HCC) in patients with chronic liver disease and suspected liver nodules. Whole-body PET/CT was performed in a random order at 10 min after injection of 4 MBq of (18)F-fluorocholine per kilogram and at 1 h after injection of 5 MBq of (18)F-FDG per kilogram. PET/CT results were read in a masked manner by 2 specialists, and diagnostic performance was assessed from the results of consensus masked reading. Those focal lesions appearing with increased or decreased activity, compared with background, on (18)F-fluorocholine PET/CT were considered positive for malignancy. The standard of truth was determined on a per-site basis using data from a histologic examination and a follow-up period of more than 6 mo; on a per-patient basis, the Barcelona criteria were also accepted as a proof of HCC in 5 patients. Eighty-one patients were recruited; standard of truth was determined in 59 cases. HCC was diagnosed in 34 patients. Therefore, sensitivity was 88% for (18)F-fluorocholine and 68% for (18)F-FDG (P = 0.07), and in 70 sites, sensitivity was 84% for (18)F-fluorocholine, significantly better than the 67% for (18)F-FDG (P = 0.01). Of the 11 patients with well-differentiated HCC, 6 had a positive result with (18)F-fluorocholine alone, whereas (18)F-FDG was never positive alone; corresponding site-based sensitivity was 94% for (18)F-fluorocholine and 59% for (18)F-FDG (P = 0.001).

The detection rate of 18 sites corresponding to other malignancies was 78% for

(18)F-fluorocholine and 89% for (18)F-FDG. In nonmalignant sites, (18)F-fluorocholine appeared less specific than (18)F-FDG (62% vs. 91% P < 0.01) because of uptake by focal nodular hyperplasia. (18)F-fluorocholine was significantly more sensitive than (18)F-FDG at detecting HCC, in particular in well-differentiated forms. In contrast, (18)F-FDG appeared somewhat more sensitive at detecting other malignancies and was negative in focal nodular hyperplasia. Thus (18)F-fluorocholine appears to be a useful PET/CT tracer for the detection and surveillance of HCC; however, performing PET/CT with both radiopharmaceuticals seems to be the best option.

18F-Fluoromethylcholine (FCH) PET imaging in patients with castration-resistant prostate cancer: prospective comparison with standard imaging.

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The aim of the study was to assess the utility of (18)F-fluorocholine (FCH), compared to standard imaging of bone scan (BS) and contrast-enhanced abdominopelvic computed tomography (CT), in patients with castration-resistant prostate carcinoma. FCH has shown promise as a metabolic imaging agent for prostate carcinoma. Twenty-six patients with castration-resistant prostate carcinoma had FCH, BS and CT imaging within a 2-month period. Individual FCH-positive lesions in bone were compared to the BS and soft tissue lesions were compared to CT. The lesions were then classified as concordant or discordant for the presence or absence of prostate cancer metastases. Discordant bone or soft tissue lesions were followed up with BS or CT, respectively, at 6-month intervals for up to 2 years or until a definitive diagnosis of the discordant lesion could be made. In 13 (50%) of the patients, all lesions identified were concordant; this included 5 patients in whom no lesions could be identified with any imaging modality. In 21 patients, 183 lesions were observed with 149 being concordant and 34 (19%) being discordant (13 patients). Based on follow-up, FCH correctly identified the presence or absence of disease in 27 of 34 lesions, and in 14 cases FCH-positive lesions, not identified on initial imaging, were confirmed as disease on follow-up. The sensitivity, specificity, accuracy, positive predictive and negative predictive values for lesion detection by FCH are 96% (92-98%), 96% (81-99%), 96% (93-97%), 99% (96-100%) and 81% (64-88%), respectively, with 95% confidence intervals shown in parentheses. In this patient cohort, FCH shows good initial concordance (81%) with BS and CT in the detection of metastatic prostate carcinoma. Follow-up of the cases where FCH was initially discordant with subsequent BS or CT shows that FCH was accurate in determining the presence or absence of prostate

metastasis in 79% of lesions. While FCH imaging as compared to BS and CT in this patient group has a good sensitivity and specificity for the detection of lesions representing prostate metastasis, further prospective studies are needed to determine its role.

FET Fluorethyltyrosin Hirntumoren

O-(2-[18F]Fluoroethyl)-L-tyrosine (F-18 FET)
Clin Nucl Med. 2011 Oct;36(10):841-7.
Dynamic O-(2-[18F]fluoroethyl)-L-tyrosine (F-18 FET) PET for Glioma Grading: Assessment of Individual Probability of Malignancy.
Calcagni ML, Galli G, Giordano A, Taralli S, Anile C, Niesen A, Baum RP.
From the *Institute of Nuclear Medicine, Università Cattolica del Sacro Cuore, Rome, Italy; †Institute of Neurosurgery, Università Cattolica del Sacro Cuore, Rome, Italy; and ‡Department of Nuclear Medicine, Center for PET, Zentralklinik, Bad Berka, Germany.
To investigate the diagnostic value of some O-(2-[F]fluoroethyl)-L-tyrosine (F-18 FET) indices derived from the dynamic acquisition to differentiate low-grade gliomas from high-grade; (2) to analyze the course of tumor time-activity curves (TACs); and (3) to calculate the individual probability of a high-grade glioma using the logistic regression. : Seventeen low-grade (WHO I-II) and 15 high-grade (WHO III-IV) gliomas were studied with dynamic F-18 FET PET. Regions of interests were drawn over the tumor and contralateral brain, and TACs were analyzed. We considered early standardized uptake value (SUV), middle SUV, late SUV, early-to-middle SUV tumor ratio, early-to-late SUV tumor ratio; time to peak (Tpeak), in minutes, from the beginning of the dynamic acquisition up to the maximum SUV of the tumor; and SoD (sum of the frame-to-frame differences). To assess the individual probability of high-grade, logistic regression was also used. : High-grade gliomas showed significantly ($P < 0.0001$) higher values when compared with low-grade gliomas in early SUV, early-to-middle ratio, early-to- late ratio, Tpeak, and SoD. For the grading of gliomas, the best indices were early-to-middle ratio and Tpeak providing a diagnostic accuracy of 94%. TACs analysis provided an 87% diagnostic accuracy. For individual high-grade diagnosis, the logistic regression provided 93% sensitivity, 100% specificity, and 97% accuracy.: Early-to-middle SUV tumor ratio and Tpeak were the best indices for assessing the grading of gliomas. Since early-to-middle ratio derives from the first 35 minutes of the dynamic acquisition, the PET study could last half an hour instead of 1 hour. By logistic regression, it is possible to assess the individual probability of high-grade, useful for prognosis and treatment.

J Nucl Med. 2011 Jun;52(6):856-64.
O-(2-18F-fluoroethyl)-L-tyrosine PET predicts failure of antiangiogenic treatment in patients with recurrent high-grade glioma.
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The objective of this study was to compare MRI response assessment with metabolic O-(2-(18)F-fluoroethyl)-L-tyrosine ((18)F-FET) PET response evaluation during antiangiogenic treatment in patients with recurrent high-grade glioma (rHGG).
METHODS:
Eleven patients with rHGG were treated biweekly with bevacizumab-irinotecan. MR images and (18)F-FET PET scans were obtained at baseline and at follow-up 8-12 wk after treatment onset. MRI treatment response was evaluated by T1/T2 volumetry according to response assessment in neurooncology (RANO) criteria. For (18)F-FET PET evaluation, an uptake reduction of more than 45% calculated with a standardized uptake value of more than 1.6 was defined as a metabolic response (receiver-operating-characteristic curve analysis). MRI and (18)F-FET PET
Page 5**O-(2-[18F]Fluoroethyl)-L-tyrosine (F-18 FET)**
volumetry results and response assessment were compared with each other and in relation to progression-free survival (PFS) and overall survival (OS). At follow-up, MR images showed partial response in 7 of 11 patients (64%), stable disease in 2 of 11 patients (18%), and tumor progression in 2 of 11 patients (18%). In contrast, (18)F-FET PET revealed 5 of 11 metabolic responders (46%) and 6 of 11 nonresponders (54%). MRI and (18)F-FET PET showed that responders survived significantly longer than did nonresponders (10.24 vs. 4.1 mo, P = 0.025, and 7.9 vs. 2.3 mo, P = 0.015, respectively). In 4 patients (36.4%), diagnosis according to RANO criteria and (18)F-FET PET was discordant. In these cases, PET was able to detect tumor progression earlier than was MRI. In rHGG patients undergoing antiangiogenic treatment, (18)F-FET PET seems to be predictive for treatment failure in that it contributes important information to response assessment based solely on MRI and RANO criteria.

Int J Mol Imaging. 2011;2011:372509. Epub 2011 Apr 28.
The Clinical Value of PET with Amino Acid Tracers for Gliomas WHO Grade II.
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The clinical management of adults with low-grade gliomas (LGGs) remains a challenge. There is no curative treatment, and management of individual patients is a matter of deciding optimal timing as well as right treatment modality. In addition to conventional imaging techniques, positron emission tomography (PET) with amino acid tracers can facilitate diagnostic and therapeutic procedures. In this paper, the clinical applications of PET with amino acid tracers (11)C-methyl-L-methionine (MET) and (18)F-fluoro-ethyl-L-tyrosine (FET) for patients with LGG are summarized. We also discuss the value of PET for the long-term followup of this patient group. Monitoring metabolic activity by PET in individual patients during course of disease will provide insight in the biological behavior and evolution of these tumors. As such,

spatial changes in tumor activity over time, including shifts of hot-spot regions within the tumor, may reflect intratumoral heterogeneity and correlate to clinical parameters.

Int J Radiat Oncol Biol Phys. 2011 May 11. [Epub ahead of print]
An Interindividual Comparison of O-(2- [(18)F]Fluoroethyl)-L-Tyrosine (FET)- and L-[Methyl-(11)C]Methionine (MET)-PET in Patients With Brain Gliomas and Metastases.
Grosu AL, Astner ST, Riedel E, Nieder C, Wiedenmann N, Heinemann F, Schwaiger M, Molls M, Wester HJ, Weber WA.
Department of Radiation Oncology, Albert Ludwigs Universität Freiburg, Freiburg, Germany; Department of Radiation Oncology, Klinikum Rechts der Isar, Technische Universität München, Munich, Germany.L-[methyl-(11)C]methionine (MET)-positron emission tomography (PET) has a high sensitivity and specificity for imaging of gliomas and metastatic brain tumors. The short half-life of (11)C (20 minutes) limits the use of MET-PET to institutions with onsite cyclotron. O-(2- [(18)F]fluoroethyl)-L-tyrosine (FET) is labeled with (18)F (half-life, 120 minutes) and could be used much more broadly. This study compares the uptake of FET and MET in gliomas and metastases, as well as treatment-induced changes. Furthermore, it evaluates the gross tumor volume (GTV) of gliomas defined on PET and magnetic resonance imaging (MRI). We examined 42 patients with pretreated gliomas (29 patients) or brain metastases (13 patients) prospectively by FET- and MET-PET on the same day. Uptake of FET and MET was quantified by standardized uptake values. Imaging contrast was assessed by calculating lesion-to-gray matter ratios. Tumor extension was quantified by contouring GTV in 17 patients with brain gliomas. Gross tumor volume on PET was compared with GTV on MRI. Sensitivity and specificity of MET- and FET-PET for differentiation of viable tumor from benign changes were evaluated by comparing the PET result with histology or clinical follow-up. There was a strong linear correlation between standardized uptake values calculated for both tracers in cortex and lesions: $r = 0.78$ ($p = 0.001$) and $r = 0.84$ ($p < 0.001$), respectively. Image contrast was similar for MET- and FET-PET (lesion-to-gray matter ratios of 2.36 ± 1.01 and 2.33 ± 0.77, respectively). Mean GTV in 17 glioma patients was not significantly different on MET- and FET-PET. Both MET- and FET-PET delineated tumor tissue outside of MRI changes. Both tracers provided differentiated tumor tissue and treatment-related changes with a sensitivity of 91% at a specificity of 100%. O-(2- [(18)F]fluoroethyl)-L-tyrosine-PET and MET-PET provide comparable diagnostic information on gliomas and brain metastases. Like MET-PET, FET-PET can be used for differentiation of residual or recurrent tumor from treatment-related changes/pseudoprogression, as well as for delineation of gliomas.

Clin Neurol Neurosurg. 2011 Sep;113(7):541-7. Epub 2011 Apr 20.
Finding the anaplastic focus in diffuse gliomas: the value of Gd-DTPA enhanced MRI, FET-PET, and intraoperative, ALA-derived tissue fluorescence.
Ewelt C, Floeth FW, Felsberg J, Steiger HJ, Sabel M, Langen KJ, Stoffels G,

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Diffuse gliomas may harbor anaplastic foci which affect prognosis and determine adjuvant therapies. Such foci are not always detected by contrast-enhancement on MRI. Recently, other modalities have been introduced, such as FET-PET for pre-diagnostic imaging and 5- aminolevulinic derived tumor fluorescence for intraoperative identification of malignant glioma tissue. The relationship between these modalities
Page 6**O-(2-[18F]Fluoroethyl)-L-tyrosine (F-18 FET)**
and their value for guiding biopsies during resection has not yet been elucidated in the group of diffuse gliomas. FET-PET was performed in 30 consecutive patients with intracerebral lesions suggestive of diffuse gliomas on MRI with or without areas of contrast-enhancement. Prior to surgery patients were given 5-ALA at a dose of 20mg/kg body weight. Areas of FET uptake with a lesion/brain ratio of 1.6 or more were considered indicators of tumor. FET-PET data were corregistered with MRI data before surgery in order to obtain neuronavigated biopsies during resection, which were collected from FET positive and negative areas, analyzed for tumor fluorescence and correlated to contrast-enhancement on MRI. 13 of 30 tumors were diagnosed as gliomas WHO Grade II, 15 as gliomas WHO Grade III and 2 as gliomas WHO Grade IV. The mean lesion/brain tissue ratio of FET uptake was significantly greater for high-grade than for low-grade gliomas (averages SD 2.323±0.754 vs. 1.453±0.538 p=0.0014). A match of FET-pos/ALA-pos biopsies was found in 70.6% (12/17) of high-grade gliomas (WHO Grade III/IV) but only in 7.7% (1/13) of low grade gliomas. Gd-neg/FET-neg/ALA-neg biopsies yielded a low-grade tumor in 46.2% (6/13). A mismatch between FET uptake and 5-ALA (FET-pos/ALA-neg) was found in 46.2% (6/13) of the low-grade and in 17.6% (3/17) of the high-grade tumors. The combination of FET-PET- and 5-ALA-positivity yielded a sensitivity for identifying high-grade glioma foci of 70.5% and a specificity of 92.3%. In low grade gliomas 5-ALA fluorescence is the exception and FET PET is more sensitive. High grade areas in diffuse gliomas with anaplastic foci usually fluoresce, if they are FET PET positive. As a result, FET PET appears valuable for pre-operative identification of anaplastic foci and hot spots are strongly predictive for ALA-derived fluorescence, which highlight anaplastic foci during resection.

Radiother Oncol. 2011 Apr;99(1):44-8. Epub 2011 Mar 30.
FET-PET for malignant glioma treatment planning.
Niyazi M, Geisler J, Siefert A, Schwarz SB, Ganswindt U, Garny S, Schnell O, Suchorska B, Kreth FW, Tonn JC, Bartenstein P, la Fougère C, Belka C.
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The aim of this study was to compare MRI-based morphological gross tumour

volumes (GTVs) to biological tumour volumes (BTVs), defined by the pathological radiotracer uptake in positron emission tomography (PET) imaging with (18)F-fluoroethyltyrosine (FET), subsequently clinical target volumes (CTVs) and finally planning target volumes (PTVs) for radiotherapy planning of glioblastoma. Seventeen patients with glioblastoma were included into a retrospective protocol. Treatment-planning was performed using clinical target volume (CTV=BTV+20mm or CTV=GTV+20mm+inclusion of the edema) and planning target volume (PTV=CTV+5mm). Image fusion and target volume delineation were performed with OTP-Masterplan®. Initial gross tumour volume (GTV) definition was based on MRI data only or FET-PET data only (BTV), secondarily both data sets were used to define a common CTV. FET based BTVs (median 43.9 cm(3)) were larger than corresponding GTVs (median 34.1cm(3), p=0.028), in 11 of 17 cases there were major differences between GTV/BTV. To evaluate the conformity of both planning methods, the index (CTV(MRT)∩CTV(FET))/(CTV(MRT)∪CTV(FET)) was quantified which was significantly different from 1 (0.73 ± 0.03, p<0.001). With FET-PET-CT planning, the size and geometrical location of GTVs/BTVs differed in a majority of patients. It remains open whether FET-PET-based target definition has a relevant clinical impact for treatment planning.

Comparison of (18)F-FET PET and 5-ALA fluorescence in cerebral gliomas.

Floeth FW, Sabel M, Ewelt C, Stummer W, Felsberg J, Reifenberger G, Steiger HJ, Stoffels G, Coenen HH, Langen KJ.
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The aim of the study was to compare presurgical (18)F-fluoroethyl-L: -tyrosine ((18)F-FET) uptake and Gd-diethylenetriaminepentaacetic acid (DTPA) enhancement on MRI (Gd) with intraoperative 5-aminolevulinic acid (5-ALA) fluorescence in cerebral gliomas. (18)F-FET positron emission tomography (PET) was performed in 30 patients with brain lesions suggestive of diffuse WHO grade II or III gliomas on MRI. PET and MRI data were coregistered to guide neuronavigated biopsies before resection. After oral application of 5-ALA, 38 neuronavigated biopsies were taken from predefined tumour areas that were positive or negative for (18)F-FET or Gd and checked for 5-ALA fluorescence. (18)F-FET uptake with a mean tumour to brain ratio ≥1.6 was rated as positive.Of 38 biopsies, 21 corresponded to high-grade glioma tissue (HGG) of WHO grade III (n = 19) or IV (n = 2) and 17 biopsies to low-grade glioma tissue (LGG) of WHO grade II. In biopsies corresponding to HGG, (18)F-FET PET was positive in 86% (18/21), but 5-ALA and Gd in only 57% (12/21). A mismatch between Gd and 5-ALA was observed in 6 of 21 cases of HGG biopsy samples (3 Gd-positive/5-ALA-negative and 3 Gd-negative/5-ALA-positive). In biopsies corresponding to LGG, (18)F-FET was positive in 41% (7/17), while 5-ALA and Gd were negative in all but one instance. All tumour areas with 5-ALA fluorescence were positive on

(18)F-FET PET.
There are differences between (18)F-FET and 5-ALA uptake in cerebral gliomas owing to a limited sensitivity of 5-ALA to detect tumour tissue
especially in LGG. (18)F-FET PET is more sensitive to detect glioma tissue than 5-ALA fluorescence and should be considered as an additional
tool in resection planning.

Int J Radiat Oncol Biol Phys. 2011 May 1;80(1):176-84. Epub 2010 Jun 18.
Prognostic value of early [18F]fluoroethyltyrosine positron emission tomography after radiochemotherapy in glioblastoma multiforme.
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Early detection of treatment response in glioma patients after radiochemotherapy (RCX) is uncertain because treatment-related contrast
enhancement in magnetic resonance imaging can mimic tumor progression. Positron emission tomography (PET) using the amino acid tracer
[(18)F]fluoroethyltyrosine (FET) seems to be a promising tool for treatment monitoring. The aim of this prospective study was to evaluate the
prognostic value of early changes of FET uptake after postoperative RCX in glioblastomas. Twenty-two patients with glioblastoma were treated
by surgery and subsequent RCX (whole dose 60-72 Gy). The FET-PET studies were performed before RCX, 7-10 days and 6-8 weeks after
completion of RCX. Early treatment response in PET was defined as a decrease of the maximal tumor-to-brain ratio (TBR(max)) of FET uptake
after RCX of more than 10%. The prognostic value of early changes of FET uptake after RCX was evaluated using Kaplan-Maier estimates for
median disease-free survival and overall survival. The median overall and disease-free survival of the patients was 14.8 and 7.8 months. There
were 16 early responders in FET-PET (72.7%) and 6 nonresponders (27.3%). Early PET responders had a significantly longer median disease-
free survival (10.3 vs. 5.8 months; $p < 0.01$) and overall survival ("not reached" vs. 9.3 months; $p < 0.001$). No statistically significant differences
between the patient subgroups were found concerning the defined prognostic parameters. FET-PET is a sensitive tool to predict treatment
response in patients with glioblastomas at an early stage after RCX.

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NaF Fluorid-Skelett-PET/CT

Mol Imaging Biol. 2011 Apr 9. [Epub ahead of print]
Prospective Evaluation of (99m)Tc MDP Scintigraphy, (18)F NaF PET/CT, and (18)F FDG PET/CT for Detection of Skeletal Metastases.
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Technetium (Tc) methylene diphosphonate (MDP) has been the standard method for bone scintigraphy for three decades. (18)F sodium fluoride
((18)F NaF) positron emission tomography (PET)/computed tomography (CT) has better resolution and is considered superior. The role of 2-
deoxy-2-[(18)F]fluoro-D-glucose ((18)F FDG) PET/CT is proven in a variety of cancers, for which it has changed the practice of oncology.
There are few prospective studies comparing these three methods of detection of skeletal metastases. Thus, we were prompted to initiate this
prospective pilot trial. This is a prospective study (Sep 2007-Dec 2010) of 52 patients with proven malignancy referred for evaluation of skeletal metastases. There were 37 men and 15 women, 19-84 years old (average, 55.6 ± 15.9). Technetium-99m ((99m)Tc) MDP bone scintigraphy, (18)F NaF PET/CT, and (18)F FDG PET/CT were subsequently performed within 1 month. Skeletal lesions were detected by (99m)Tc MDP bone scintigraphy in 22 of 52 patients, by (18)F NaF PET/CT in 24 of 52 patients, and by (18)F FDG PET/CT in 16 of 52 patients. The image quality and evaluation of extent of disease were superior by (18)F NaF PET/CT over (99m)Tc MDP scintigraphy in all 22 patients with skeletal lesions on both scans and over (18)F FDG PET/CT in 11 of 16 patients with skeletal metastases on (18)F FDG PET/CT. In two patients, (18)F NaF PET/CT showed skeletal metastases not seen on either of the other two scans. Extraskeletal lesions were identified by (18)F FDG PET/CT in 28 of 52 subjects. Our prospective pilot-phase trial demonstrates superior image quality and evaluation of skeletal disease extent with (18)F NaF PET/CT over (99m)Tc MDP scintigraphy and (18)F FDG PET/CT. At the same time, (18)F FDG PET detects extraskeletal disease that can significantly change disease management. As such, a combination of (18)F FDG PET/CT and (18)F NaF PET/CT may be necessary for cancer detection. Additional evaluation with larger cohorts is required to confirm these preliminary findings.

Fluorocholine (18F) and sodium fluoride (18F) PET/CT in the detection of prostate cancer: prospective comparison of diagnostic performance determined by masked reading.
Langsteger W, Balogova S, Huchet V, Beheshti M, Paycha F, Egrot C, Janetschek G, Loidl W, Nataf V, Kerrou K, Pascal O, Cussenot O, Talbot
J.

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AIM.The aim of this paper was to compare the diagnostic performance of positron emission tomography/computed tomography (PET/CT) with
fluorocholine (18F) (FCH) or fluoride(18F) (FNa) for the detection of bone metastasis in patients with prostate cancer complaining from
osteoarticular pain, taking into account whether they were referred for initial staging or recurrence localization. The initial hypothesis was that
FCH site-based specificity would be superior to that of F Na, with no loss in sensitivity. METHODS_ Forty-two patients were enrolled in this
prospective study, underwent both PET/CTs and were then followed-up for at least 6 months. The standard of truth (SOT) about the
presence/absence and location of bone metastasis could be determined in 40 patients, by 2 independent medical assessors, blinded to the results of
both PET/CTs. The comparison was performed according to the guideline of the European Medicines Agency, i.e. based on the results of blind
reading with SOT as reference. RESULTS:Bone extension was present in 22 patients and absent in 18. Patient-based performance for FCH vs.
FNa was 91% vs. 91% for sensitivity, 89% vs. 83% for specificity and 90% vs. 88% for accuracy (no significant difference). Of 360 skeletal
sites, 68 were malignant and 292 non-invaded. There was no significant difference in site-based performance in the group of patients referred at
initial staging, but in the group of patients referred for suspicion of recurrence, FCH was significantly more specific than FNa (96% vs. 91%,
P=0.033 with Obuchowski's correction) while sensitivity was the same, 89%. CONCLUSION: Both radiopharmaceuticals, based on a very
different metabolic approach, showed good diagnostic performance. If FCH is available, it should be preferred in patients after initial treatment.

AJR Am J Roentgenol. 2011 Sep;197(3):713-9.
Skeletal Scintigraphy With 18F-NaF PET for the Evaluation of Bone Pain in Children.
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OBJECTIVE: Although not commonly used in current clinical practice, the PET agent (18)F-NaF provides an excellent alternative to the
standard tracers used for radionuclide bone scintigraphy. This article illustrates the use and appearance of (18)F-NaF PET and shows examples of
its utility in the assessment of bone pain in children. CONCLUSION: Skeletal imaging with (18)F-NaF harnesses both the superior imaging
characteristics of PET and the improved biodistribution of the fluoride tracer in comparison with standard nuclear techniques, resulting in

excellent-quality images that can effectively be used to investigate the cause of bone pain in children.

J Nucl Med. 2010 Dec;51(12):1826-9. Epub 2010 Nov 15.
Molecular mechanisms of bone 18F-NaF deposition.
Czernin J, Satyamurthy N, Schiepers C.
Ahmanson Biological Imaging Division, Department of Molecular and Medical Pharmacology, David Geffen School of Medicine, University of
California, Los Angeles, CA 90095-1782, USA. jczernin@mednet.ucla.edu
There is renewed interest in (18)F-NaF bone imaging with PET or PET/CT. The current brief discussion focuses on the molecular mechanisms of
(18)F-NaF deposition in bone and presents model-based approaches to quantifying bone perfusion and metabolism in the context of preclinical
and clinical applications of bone imaging with PET.

J Nucl Med. 2008 Jan;49(1):68-78. Epub 2007 Dec 12.
Skeletal PET with 18F-fluoride: applying new technology to an old tracer.

Grant FD, Fahey FH, Packard AB, Davis RT, Alavi A, Treves ST.
Source

Division of Nuclear Medicine/PET, Children's Hospital Boston, Boston, Massachusetts 02115, USA.

Abstract
Although (18)F-labeled NaF was the first widely used agent for skeletal scintigraphy, it quickly fell into disuse after the introduction of (99m)Tc-labeled bone-imaging agents. Recent comparative studies have demonstrated that (18)F-fluoride PET is more accurate than (99m)Tc-diphosphonate SPECT for identifying both malignant and benign lesions of the skeleton. Combining (18)F-fluoride PET with other imaging, such as CT, can improve the specificity and overall accuracy of skeletal (18)F-fluoride PET and probably will become the routine clinical practice for (18)F-fluoride PET. Although (18)F-labeled NaF and (99m)Tc-diphosphonate have a similar patient dosimetry, (18)F-fluoride PET offers shorter study times (typically less than 1 h), resulting in a more efficient workflow, improved patient convenience, and faster turnarounds of reports to the referring physicians. With the widespread availability of PET scanners and the improved logistics for the delivery of (18)F radiopharmaceuticals, prior limitations to the routine use of (18)F-fluoride bone imaging have largely been overcome. The favorable imaging performance and the clinical utility of (18)F-

fluoride PET, compared with (99m)Tc-diphosphonate scintigraphy, support the reconsideration of (18)F-fluoride as a routine bone-imaging agent.

Nucl Med Commun. 2011 Mar;32(3):168-76.

^{18}F-fluoride PET/CT for assessing bone involvement in prostate and breast cancers.

Withofs N, Grayet B, Tancredi T, Rorive A, Mella C, Giacomelli F, Mievis F, Aerts J, Waltregny D, Jerusalem G, Hustinx R.
Source

University of Liège, Belgium.

Abstract
OBJECTIVE:
To evaluate the accuracy of ^{18}F-fluoride PET/computed tomography (CT) to detect bone metastases (BMs) in a breast and prostate cancer population, using magnetic resonance imaging (MRI) or thin-slice CT as a gold standard.

METHODS:
We have prospectively included 34 patients with breast (N=24) or prostate cancer (N=10) at high risk of BMs. Whole-body PET/CT (low-dose CT) and bone scintigraphy (BS) with single photon emission CT were obtained for all 34 patients and the results compared with a radiological gold standard.

RESULTS:
Out of the 386 foci detected by PET/CT, 219 (56.7%) could be verified by CT or MRI. Eighty-six additional foci were detected by BS (n=46) or seen only by CT (n=9), MRI (n=23), or both CT and MRI (n=8). The total number of verified lesions was therefore 274 (58.1%), including 119 (43.4%) benign and 155 (56.6%) BM. The sensitivity, specificity, and accuracy of ^{18}F-fluoride PET/CT were 76, 84.2, and 80%, respectively. For BS, they were 44.8, 79.2, and 60%, respectively. Sensitivity significantly decreased for the lytic lesions. The accuracy of PET/CT was significantly superior to BS for pelvic and lumbar lesions. PET/CT provided a correct diagnosis (M+/M0) in 32 of 33 patients (one false positive) compared with 28 of 33 with BS (four false positive, one false positive).

CONCLUSION:
^{18}F-fluoride PET/CT is significantly more accurate than BS for detecting BMs from breast and prostate cancers.

AJR Am J Roentgenol. 2006 Jun;186(6):1783-6.
Flare response in 18F-fluoride ion PET bone scanning.

Wade AA, Scott JA, Kuter I, Fischman AJ.
Source

Department of Radiology, Massachusetts General Hospital, 55 Fruit St., FND 216 Boston, MA 02114, USA.

Recent Results Cancer Res. 2008;170:213-24.
PET and PET/CT with F-18 fluoride in bone metastases.

Palmedo H, Grohé C, Ko Y, Tasci S.
Source

Klinik und Poliklinik für Nuklearmedizin des Universitätsklinikums Bonn, Germany.

Nuklearm,edizinertreffen November 2011
Prof. Dietlein

Tc-99m-Skelettszintigraphie für osteoblast Anteile inMetastasen
F18 Fluorid- PET osteoblast Anteile höhere Energie, hohere Sensitivität, cave FLARE Phänomen
FDG –PET: vitales tumorgewebe, lytische Anteile
Flip Flop Phänomen bei Therapieansprechen

Abe Ann Nucl Med 2005 FDG besser bei lytischen schlechter bei blastischen Läsionen

Fluor-Thymidin FLT Proliferationsmarker, Knochemarkbildgebung

Leuk Res. 2011 Mar;35(3):310-6. Epub 2010 Sep 15.
Early assessment of treatment response in patients with AML using [(18)F]FLT PET imaging.
Vanderhoek M, Juckett MB, Perlman SB, Nickles RJ, Jeraj R.
Department of Medical Physics, University of Wisconsin, Madison, WI, USA.

Assessment of treatment response in acute leukemia is routinely performed after therapy via bone marrow biopsy. We investigated the use of positron emission tomography (PET) for early assessment of treatment response in patients with acute myeloid leukemia (AML), using the proliferation marker 3'-deoxy-3'-[(18)F]fluoro-l-thymidine (FLT). Eight adult AML patients receiving induction chemotherapy underwent whole-body FLT PET/CT scans acquired at different time points during therapy. Patients who entered complete remission (CR) exhibited significantly lower FLT uptake in bone marrow than those patients with resistant disease (RD). In bone marrow, mean and maximum standardized uptake values were 0.8, 3.6 for CR and 1.6, 11.4 for RD, p<0.001. FLT PET results for CR and RD patients were independent of assessment time point, suggesting that FLT PET scans acquired as early as 2 days after chemotherapy initiation may be predictive of clinical response. This pilot study suggests that FLT PET imaging during induction chemotherapy may serve as an early biomarker of treatment response in AML.

Eur J Nucl Med Mol Imaging. 2011 Jan;38(1):166-78. Epub 2010 Jul 13.
Radionuclide imaging of bone marrow disorders.
Agool A, Glaudemans AW, Boersma HH, Dierckx RA, Vellenga E, Slart RH.
Department of Nuclear Medicine, Medical Center Twente, Hengelo, the Netherlands.
Noninvasive imaging techniques have been used in the past for visualization the functional activity of the bone marrow compartment. Imaging with radiolabelled compounds may allow different bone marrow disorders to be distinguished. These imaging techniques, almost all of which use radionuclide-labelled tracers, such as (99m)Tc-nanocolloid, (99m)Tc-sulphur colloid, (111)In-chloride, and radiolabelled white blood cells, have been used in nuclear medicine for several decades. With these techniques three separate compartments can be recognized including the reticuloendothelial system, the erythroid compartment and the myeloid compartment. Recent developments in research and the clinical use of PET tracers have made possible the analysis of additional properties such as cellular metabolism and proliferative activity, using (18)F-FDG and (18)F-FLT. These tracers may lead to better quantification and targeting of different cell systems in the bone marrow. In this review the imaging of different bone marrow targets with radionuclides including PET tracers in various bone marrow diseases are discussed.

J Nucl Med. 2011 May;52(5):690-6. Epub 2011 Apr 15.
Predictive value of initial 18F-FLT uptake in patients with aggressive non-Hodgkin lymphoma receiving R-CHOP treatment.
Herrmann K, Buck AK, Schuster T, Junger A, Wieder HA, Graf N, Ringshausen I, Rudelius M, Wester HJ, Schwaiger M, Keller U, Dechow T.

Department of Nuclear Medicine, Technische Universitaet Muenchen, Munich, Germany. ken.herrmann@web.de
R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone)-like chemotherapy is the standard therapy in aggressive B-cell lymphoma. (18)F-FDG PET has high prognostic implications at treatment completion but is limited as an early predictor. Here, we present the results of a prospective study correlating the initial uptake of the in vivo proliferation marker 3'-deoxy-3'-(18)F-fluorothymidine ((18)F-FLT) with the clinical outcome of patients with aggressive non-Hodgkin lymphoma treated with R-CHOP. Sixty-six eligible patients were evaluated prospectively with (18)F-FLT PET before R-CHOP. PET was performed 45 min after injection of 300-370 MBq of (18)F-FLT. Mean and maximum standardized uptake values (SUVs) were calculated on a lesion-by-lesion basis. Response was assessed at the end of therapy. International Prognostic Index (IPI) scores and clinical parameters (Ann Arbor stage, lactate dehydrogenase, performance status, extranodal disease) were determined in all patients. Response was assessed according to revised response criteria after the end of therapy. After treatment, patients were followed in intervals from 4 wk to 6 mo (mean follow-up, 23.1 mo [range, 1-63 mo]), and progression-free and overall survival were determined. All lymphoma lesions identified by a reference method ((18)F-FDG PET/CT or multislice CT of the trunk) showed increased focal tracer uptake (mean (18)F-FLT SUV, 7.3 ± 2.5). Response assessment revealed progressive disease in 4, partial response in 3, and complete response (CR) in the remaining 55 patients. The IPI score was predictive for achieving CR (P = 0.034). Importantly, initial mean SUV was also significantly higher in patients who showed progressive disease and partial response than in patients who achieved CR (P = 0.049). In addition, we found a significant correlation between IPI score and initial (18)F-FLT uptake. Taken together, high (18)F-FLT uptake is a negative predictor of response to R-CHOP treatment in aggressive B-cell non-Hodgkin lymphoma and correlates with the IPI score. Thus, (18)F-FLT PET may represent a useful tool for implementing risk-adapted treatment in these patients.

F-18 FLT PET: a noninvasive diagnostic tool for visualization of the bone marrow compartment in patients with aplastic anemia: a pilot study.

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Department of Nuclear Medicine and Molecular Imaging, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands.
A discordant relationship between bone marrow cellularity and peripheral blood findings is regularly noticed in patients with aplastic anemia (AA). Therefore, the feasibility of 3-F-18 fluoro-3-deoxy-L-thymidine (F-18 FLT PET was tested as a noninvasive tool to visualize the total distribution of the hematopoietic bone marrow compartment in AA at presentation or after treatment. In vivo scanning was performed

with F-18 FLT PET in AA patients (n = 17), including patients upfront (n = 11) and following treatment (n = 6), in addition to peripheral blood cell counts and a bone marrow biopsy. A striking abnormal F-18 FLT scan was observed in all patients upfront treatment, in particular a reduced uptake of the pelvis was shown, the area that is biopsied for the bone marrow biopsy. Following treatment, the number of solitary lesions with increased proliferative activity outside the pelvis was noticed in patients with partial response, whereas patients with a complete remission showed a homogenous uptake throughout the skeleton. This pilot study demonstrates that F-18 FLT scan provides a highly distinctive overview of the bone marrow compartment in AA that might be helpful for making a proper diagnosis and monitoring treatment response of AA patients.

Clin Cancer Res. 2011 May 15;17(10):3304-15. Epub 2011 Mar 1.
Changes in 18F-fluorodeoxyglucose and 18F-fluorodeoxythymidine positron emission tomography imaging in patients with non-small cell lung cancer treated with erlotinib.
Mileshkin L, Hicks RJ, Hughes BG, Mitchell PL, Charu V, Gitlitz BJ, Macfarlane D, Solomon B, Amler LC, Yu W, Pirzkall A, Fine BM.
Peter MacCallum Cancer Centre, East Melbourne, The University of Melbourne, Parkville, Australia. linda.mileshkin@petermac.org
Assessing clinical activity of molecularly targeted anticancer agents, especially in the absence of tumor shrinkage, is challenging. To evaluate on- treatment 18F-fluorodeoxyglucose (FDG) and/or 18F-fluorodeoxythymidine (FLT) positron emission tomography (PET) for this purpose, we conducted a prospective multicenter trial assessing PET response rates and associations with progression-free (PFS) and overall survival (OS) in 2nd/3rd-line non-small-cell lung cancer patients treated with erlotinib. PET/computed tomography (CT) scans were conducted at baseline, day (d)14 and d56 after the first daily erlotinib dose, with diagnostic CT at baseline and d56 (all scans centrally reviewed). PET partial metabolic response (PMR) was defined as a mean decrease (in ≤ 5 lesions/patient) of 15% or more maximum standardized uptake value. PFS was investigator-determined. Of 74 erlotinib-treated patients, 51 completed all imaging assessments through d56; 13 of 51 (26%) FDG-evaluable patients had PMR at d14, as did 9 of 50 (18%) FLT-evaluable patients. Four (7.8%) showed partial responses (PR) by d56 CT; all 4 had PMR by d14 FDG-PET with 3 PMRs by d14 FLT-PET. Three of the 4 patients with CT PR had evaluable archival tumor tissue; all 3 had epidermal growth factor receptor mutations. D14 and d56 PMRs by FDG or FLT were associated with improved PFS; HRs for PET responders versus nonresponders were 0.3 to 0.4. D14 FDG-PET PMR was associated with improved OS (P = 0.03) compared with FDG-PET nonresponders. Early (d14) FDG-PET PMR is associated with improved PFS and OS, even in the absence of subsequent Response Evaluation Criteria in Solid Tumors response. These data support inclusion of FDG-PET imaging in clinical trials testing novel targeted therapies, particularly those with anticipated cytostatic effects.

Ann Surg Oncol. 2011 May 3. [Epub ahead of print]

Molecular Imaging of Proliferation and Glucose Utilization: Utility for Monitoring Response and Prognosis after Neoadjuvant Therapy in Locally Advanced Gastric Cancer.

Ott K, Herrmann K, Schuster T, Langer R, Becker K, Wieder HA, Wester HJ, Siewert JR, Büschenfelde CM, Buck AK, Wilhelm D, Ebert MP, Peschel C, Schwaiger M, Lordick F, Krause BJ.
Department of Surgery, University of Heidelberg, Heidelberg, Germany.

Metabolic imaging of gastric cancer is limited due to the 30% of primary tumors that are not (18)F-fluorodeoxyglucose (FDG) avid. In contrast, the proliferation marker (18)F-fluorothymidine (FLT) has been shown to visualize also non-FDG-avid gastric tumors. In this study we tested whether FLT-positron emission tomography (PET) can improve the predictive potential of molecular imaging for assessing response to neoadjuvant therapy in gastric cancer compared with FDG-PET. 45 patients with gastric cancer underwent FDG- and FLT-PET before and 2weeks after initiation of chemotherapy. FDG/FLT-PET findings and Ki67 immunohistochemistry were correlated with clinical and histopathological response and survival. 14 patients had non-FDG-avid tumors, whereas all tumors could be visualized by FLT-PET. No significant association of clinical or histopathological response with any of the analyzed metabolic parameters [initial standardized uptake value (SUV), SUV after 2 weeks, change of SUV for FDG/FLT] was found. Univariate Cox regression analysis for Ki67 and metabolic parameters revealed significant prognostic impact for survival only for FLT SUV(mean) day 14 ($p = 0.048$) and Ki67 ($p = 0.006$). Multivariate Cox regression analysis (including clinical response, Lauren type, ypN category, and FLT SUV(mean) day 14) revealed Lauren type and FLT SUV(mean) day 14 as the only significant prognostic factors ($p = 0.006$, $p = 0.002$). FLT uptake 2 weeks after initiation of therapy was shown to be the only imaging parameter with significant prognostic impact. Neither FLT-PET nor FDG-PET were correlated with histopathological or clinical response. However, these data must be interpreted with caution due to the single-center trial study design, relatively short follow-up, poor response rates, and unfavorable prognosis.

F-Mizo Hypoxiebildgebung Strahlentherapie

Phys Med Biol. 2011 Apr 7;56(7):2045-57. Epub 2011 Mar 8.
Modelling and simulation of [18F]fluoromisonidazole dynamics based on histology-derived microvessel maps.
Mönnich D, Troost EG, Kaanders JH, Oyen WJ, Alber M, Thorwarth D.
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Hypoxia can be assessed non-invasively by positron emission tomography (PET) using radiotracers such as [(18)F]fluoromisonidazole (Fmiso) accumulating in poorly oxygenated cells. Typical features of dynamic Fmiso PET data are high signal variability in the first hour after tracer administration and slow formation of a consistent contrast. The purpose of this study is to investigate whether these characteristics can be explained by the current conception of the underlying microscopic processes and to identify fundamental effects. This is achieved by modelling and simulating tissue oxygenation and tracer dynamics on the microscopic scale. In simulations, vessel structures on histology-derived maps act as sources and sinks for oxygen as well as tracer molecules. Molecular distributions in the extravascular space are determined by reaction- diffusion equations, which are solved numerically using a two-dimensional finite element method. Simulated Fmiso time activity curves (TACs), though not directly comparable to PET TACs, reproduce major characteristics of clinical curves, indicating that the microscopic model and the parameter values are adequate. Evidence for dependence of the early PET signal on the vascular fraction is found. Further, possible effects leading to late contrast formation and potential implications on the quantification of Fmiso PET data are discussed.

Radiother Oncol. 2011 Aug 26. [Epub ahead of print]
Hypoxia imaging with [F-18] FMISO-PET in head and neck cancer: Potential for guiding intensity modulated radiation therapy in overcoming hypoxia-induced treatment resistance.
Hendrickson K, Phillips M, Smith W, Peterson L, Krohn K, Rajendran J.
Department of Radiation Oncology, University of Washington Medical Center, Seattle, WA, USA.
Positron emission tomography (PET) imaging with [F-18] fluoromisonidazole (FMISO) has been validated as a hypoxic tracer [1,2]. Head and neck cancer exhibits hypoxia, inducing aggressive biologic traits that impart resistance to treatment. Delivery of modestly higher radiation doses to tumors with stable areas of chronic hypoxia can improve tumor control [3]. Advanced radiation treatment planning (RTP) and delivery techniques such as intensity modulated radiation therapy (IMRT) can deliver higher

doses to a small volume without increasing morbidity. We investigated the utility of co-registered FMISO-PET and CT images to develop clinically feasible RTPs with higher tumor control probabilities (TCP). FMISO-PET images were used to determine hypoxic sub-volumes for boost planning. Example plans were generated for 10 of the patients in the study who exhibited significant hypoxia. We created an IMRT plan for each patient with a simultaneous integrated boost (SIB) to the hypoxic sub-volumes. We also varied the boost for two patients. A significant (mean 17%, median 15%) improvement in TCP is predicted when the modest additional boost dose to the hypoxic sub-volume is included. Combined FMISO-PET imaging and IMRT planning permit delivery of higher doses to hypoxic regions, increasing the predicted TCP (mean 17%) without increasing expected complications.

Br J Radiol. 2011 Mar 22. [Epub ahead of print]
Positron emission tomography (PET) imaging approaches for external beam radiation therapies: current status and future developments.
Price PM, Green MM.
Department of Academic Radiation Oncology, The University of Manchester, The Christie Hospital NHS Foundation Trust, Manchester M20 4BX, UK. In an era in which it is possible to deliver radiation with high precision, there is a heightened need for enhanced imaging capabilities to improve tumour localisation for diagnostic, planning and delivery purposes. This is necessary to increase the accuracy and overall efficacy of all types of external beam radiotherapy (RT), including particle therapies. Positron emission tomography (PET) has the potential to fulfil this need by imaging fundamental aspects of tumour biology. The key areas where PET may support the RT process include: improving disease diagnosis and staging; assisting tumour volume delineation; defining tumour phenotype or biological tumour volume; assessment of treatment response; and in-beam monitoring of radiation dosimetry. The role of PET and its current developmental status in these key areas are overviewed here, highlighting its advantages and drawbacks.

Radiother Oncol. 2011 Jan;98(1):109-16. Epub 2010 Nov 4.
Simultaneous positron emission tomography (PET) assessment of metabolism with 1␣F-fluoro-2-deoxy-d-glucose (FDG), proliferation with 1␣F-fluoro-thymidine (FLT), and hypoxia with 1␣fluoro-misonidazole (F-miso) before and during radiotherapy in patients with non-small-cell lung cancer (NSCLC): a pilot study.
Vera P, Bohn P, Edet-Sanson A, Salles A, Hapdey S, Gardin I, Ménard JF, Modzelewski R, Thiberville L, Dubray B.
Department of Nuclear Medicine, Henri Becquerel Cancer Center and Rouen University Hospital, France. pierre.vera@rouen.fnclcc.fr

To investigate the changes in tumour proliferation (using FLT), metabolism (using FDG), and hypoxia (using F-miso) during curative (chemo-) radiotherapy (RT) in patients with non-small-cell lung cancer (NSCLC). Thirty PET scans were performed in five patients (4 males, 1 female) that had histological proof of NSCLC and were candidates for curative-intent RT. Three PET-CT (Biograph S16, Siemens) scans were performed before (t(0)) and during (around dose 46 Gy, t(46)) RT with minimal intervals of 48 h between each PET-CT scan. The tracers used were (18)fluoro-2deoxyglucose (FDG) for metabolism, (18)fluorothymidine (FLT) for proliferation, and (18)F-misonidasole (F-miso) for hypoxia. The 3 image sets obtained at each time point were co-registered (rigid: n=9, elastic: n=1, Leonardo, TrueD, Siemens) using FDG PET-CT as reference. VOIs were delineated (40% SUV(max) values were used as a threshold) for tumours and lymph nodes on FDG PET-CT, and they were automatically pasted on FLT and F-miso PET-CT images. ANOVA and correlation analyses were used for comparison of SUV(max) values. Four tumours and twelve nodes were identified on initial FDG PET-CT images. FLT SUV(max) values were significantly lower ($p<0.0006$) at t(46) in both tumours and nodes. The decrease in FDG SUV(max) values had a trend towards significance ($p=0.048$). F-Miso SUV(max) values were significantly higher in tumours than in nodes ($p=0.02$) and did not change during radiotherapy ($p=0.39$). A significant correlation was observed between FLT and FDG uptake ($r=0.56$, $p<10(-4)$) when all data were pooled together, and they remained similar when the before and during RT data were analysed separately. FDG and F-miso uptakes were significantly correlated ($r=0.59$, $p=0.0004$) when all data were analysed together. The best fit was obtained after adjusting for lesion type (tumour vs. node). This correlation was observed for the SUV(max) measured during RT ($r=0.70$, $p=0.008$) but not for the pre-RT data ($r=0.19$, $p=0.35$). The weak correlation between FLT and F-miso uptakes only became significant ($r=0.66$, $p=0.002$) when the analysis was restricted to the data acquired during RT. Three different PET acquisitions can be performed quasi-simultaneously (4-7 days) before and during radiotherapy in patients with NSCLC. Our results at 46 Gy suggest that a fast decrease in the proliferation of both tumours and nodes exists during radiotherapy with differences in metabolism (borderline significant decrease) and hypoxia (stable).

Ann Nucl Med. 2011 Jul 1. [Epub ahead of print] **18F-fluoromisonidazole positron emission tomography before treatment is a predictor of radiotherapy outcome and survival prognosis**
in patients with head and neck squamous cell carcinoma.
Kikuchi M, Yamane T, Shinohara S, Fujiwara K, Hori SY, Tona Y, Yamazaki H, Naito Y, Senda M. Department of Otolaryngology, Head and Neck Surgery, Kobe City Medical Center General Hospital, 4-6 Minatojima-Nakamachi, Chuo-ku,
Kobe, 650-0046, Japan, kikuchan0414@gmail.com.
To evaluate the usefulness of [(18)F]fluoromisonidazole ([(18)F]FMISO)-positron emission tomography (PET) prior to the treatment of head and neck squamous cell

carcinoma. Seventeen patients with untreated HNSCC underwent pretreatment [(18)F]FMISO PET. Six of them underwent definitive surgery and the remaining 11 definitive (chemo-)radiotherapy. We evaluated 30 lesions from the 17 patients. SUVmax and tumor-to- muscle ratios (TMR) were measured as hypoxia indicators. Tumors equal to or above the median value were defined as tumor with high uptake of [(18)F]FMISO and those below as tumor with low uptake of [(18)F]FMISO in both indicators. Local control rates with radiotherapy, event- free survival and disease-specific survival (DSS) rates with radiotherapy or operation were compared. [(18)F]FMISO-PET imaging of 30 lesions resulted in a SUVmax median value of 2.3 and a TMR median value of 1.3. Local control rates with radiotherapy (20-month median follow-up duration) were significantly lower in the tumor group with high uptake of [(18)F]FMISO compared to the tumor group with low uptake of [(18)F]FMISO using either SUVmax or TMR as the hypoxic indicator (P = 0.02 and 0.04, respectively). DSS rate with radiotherapy or operation (21-month median follow-up duration) was significantly lower in the patient group with high uptake of [(18)F]FMISO compared to the patient group with low uptake of [(18)F]FMISO defined by SUVmax (P = 0.04), but was not by TMR (P = 0.57). Radiotherapy outcome and survival prognosis (radiotherapy or operation) in HNSCC may be predicted by carrying out [(18)F]FMISO PET before treatment.

Neuro-PET/CT Neurodegenerative Erkrankungen, Alzheimerdiagnostik

J Am Geriatr Soc. 2011 Aug 24. doi: 10.1111/j.1532-5415.2011.03539.x. [Epub ahead of print]

Value of Neuropsychological Tests, Neuroimaging, and Biomarkers for Diagnosing Alzheimer's Disease in Younger and Older Age Cohorts.

Schmand B, Eikelenboom P, van Gool WA; the Alzheimer's Disease Neuroimaging Initiative.

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To examine the influence of age on the value of four techniques for diagnosing Alzheimer's disease (AD). Observational cohort study.mAlzheimer's Disease Neuroimaging Initiative. Individuals with mild cognitive impairment (MCI; n=179),

individuals with AD (n=91), and normal controls (n=105). Neuropsychological tests, structural magnetic resonance imaging (MRI), amyloid-beta and tau in cerebrospinal fluid (CSF), and [18F]fluorodeoxyglucose positron emission tomography (FDG-PET) for the diagnosis of MCI or AD. MCI was defined according to subjective memory complaints corroborated by an informant and an abnormal score on the delayed paragraph recall subtest of the Wechsler Memory Scale-Revised, a Mini-Mental State Examination score greater than 23, and a Clinical Dementia Rating score of 0.5. Participants with AD satisfied National Institute of Neurological and Communicative Diseases and Stroke/Alzheimer's Disease and Related Disorders Association criteria of probable AD. Neuropsychological tests and MRI were the most informative techniques, with 84% and 82% correct classifications, respectively, and areas under the receiver operating characteristic curve (AUCs) of 0.93 (90% confidence interval (CI)=0.91-0.95) and 0.88 (90% CI=0.85-0.91). FDG-PET and CSF assessments had 76% and 73% correct classifications, respectively, (AUC=0.77, 90% CI=0.71-0.83; AUC=0.77, 90% CI=0.73-0.82). These figures increased slightly when the techniques were combined. All analyses were repeated for the younger (<75) and older (≥75) halves of the sample. FDG-PET and CSF assessment were substantially less informative in the older cohort, and they did not add diagnostic information when all techniques were combined. Structural MRI and neuropsychological assessment are diagnostic methods of first choice if AD is suspected. CSF and FDG-PET add little to these diagnostic techniques, especially in older adults.

Neurology. 2011 Aug 23;77(8):e47.
Teaching NeuroImages: Brain MRI and FDG-PET in malformations of cortical development and hippocampal hypoplasia.
Renard D, Castelnovo G, Daubin D, Collombier L, Briere C, Labauge P.
Source
Department of Neurology, CHU Nîmes, Hôpital Caremeau, Place du Pr Debré, 30029 Nîmes Cedex 4, France

Arch Neurol. 2011 Jul 11. [Epub ahead of print]
Using Positron Emission Tomography and Florbetapir F 18 to Image Cortical Amyloid in Patients With Mild Cognitive Impairment or Dementia Due to Alzheimer Disease.
Fleisher AS, Chen K, Liu X, Roontiva A, Thiyyagura P, Ayutyanont N, Joshi AD, Clark CM, Mintun MA, Pontecorvo MJ, Doraiswamy PM, Johnson KA, Skovronsky DM, Reiman EM.
Chen, Ayutyanont, and Reiman, Ms Liu, and Messrs Roontiva and Thiyyagura), Arizona Alzheimer's Consortium (Drs Fleisher, Chen, and Reiman), Department of Psychiatry, University of Arizona College of Medicine (Dr Reiman), Neurogenomics Division, Translational Genomics Research Institute, Phoenix (Dr Reiman), and Department of Mathematics, Arizona State University, Tempe (Dr Chen); Department

of Neurosciences, University of California, San Diego (Dr Fleisher); Avid Radiopharmaceuticals (Drs Clark, Mintun, Pontecorvo, and Skovronsky and Mr Joshi) and University of Pennsylvania School of Medicine, Philadelphia (Drs Clark and Skovronsky); Washington University School of Medicine, St Louis, Missouri (Dr Mintun); Department of Neurology, Brigham and Women's Hospital, Harvard Medical School, and Departments of Neurology and Radiology, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts (Dr Johnson); and Departments of Psychiatry, Duke University Medical Center, Durham, North Carolina (Dr Doraiswamy).
To characterize quantitative florbetapir F 18 (hereafter referred to as simply florbetapir) positron emission tomographic (PET) measurements of fibrillar β-amyloid (Aβ) burden in a large clinical cohort of participants with probable Alzheimer disease (AD) or mild cognitive impairment (MCI) and older healthy controls (OHCs). Cerebral-to-whole-cerebellar florbetapir standard uptake value ratios (SUVRs) were computed. Mean cortical SUVRs were compared. A threshold of SUVRs greater than or equal to 1.17 was used to reflect pathological levels of amyloid associated with AD based on separate antemortem PET and postmortem neuropathology data from 19 end-of-life patients. Similarly, a threshold of SUVRs greater than 1.08 was used to signify the presence of any identifiable Aβ because this was the upper limit from a separate set of 46 individuals 18 to 40 years of age who did not carry apolipoprotein E (APOE) ε4. Multiple research imaging centers. A total of 68 participants with probable AD, 60 participants with MCI, and 82 OHCs who were 55 years of age or older. Main Outcome Measure Florbetapir-PET activity. All of the participants (ie, those with probable AD or MCI and those who were OHCs) differed significantly in mean (SD) cortical florbetapir SUVRs (1.39 [0.24], 1.17 [0.27], and 1.05 [0.16], respectively; P < 1.0 × 10(-7)), in percentage meeting levels of amyloid associated with AD by SUVR criteria (80.9%, 40.0%, and 20.7%, respectively; P < 1.0 × 10(-7)), and in percentage meeting SUVR criteria for the presence of any identifiable Aβ (85.3%, 46.6%, and 28.1%, respectively; P < 1.0 × 10(-7)). Among OHCs, the percentage of florbetapir positivity increased linearly by age decile (P = .05). For the 54 OHCs with available APOE genotypes, APOE ε4 carriers had a higher mean (SD) cortical SUVR than did noncarriers (1.14 [0.2] vs 1.03 [0.16]; P = .048). The findings of our analysis confirm the ability of florbetapir-PET SUVRs to characterize amyloid levels in clinically probable AD, MCI, and OHC groups using continuous and binary measures of fibrillar Aβ burden. It introduces criteria to determine whether an image is associated with an intermediate-to-high likelihood of pathologic AD or with having any identifiable cortical amyloid level above that seen in low-risk young control

Int J Geriatr Psychiatry. 2011 Jul 1. doi: 10.1002/gps.2749. [Epub ahead of print] **Biomarkers in dementia with Lewy bodies: a review.** Sinha N, Firbank M, O'Brien JT.
Institute for Ageing and Health, Newcastle University, Wolfson Research Centre, Campus for Ageing and Vitality, Newcastle upon Tyne, NE4 5PL, UK.

namrta.sinha@ntw.nhs.uk. Dementia with Lewy bodies (DLB) shares common clinical, neuropsychological and pathological features with other dementia subtypes, such as Alzheimer's disease (AD), making it difficult to differentiate in clinical practice. Despite the development of consensus diagnostic criteria, many cases are missed, and biomarkers to assist with diagnosis would represent important advances. Our aim was to review the literature to identify potential biomarkers that may distinguish DLB from other dementia subtypes, especially AD. The literature search was performed using Medline up to October 2010 for imaging studies [single-photon emission computed tomography (SPECT), positron emission tomography (PET), magnetic resonance imaging (MRI) and amyloid imaging] and cerebrospinal fluid (CSF) markers in DLB. Individual articles were examined for additional references. The abstracts of the identified articles were read to determine the most relevant papers, which became the basis for this review. The most robust evidence available was for striatal dopamine transporter activity visualised by (123) I-labelled N-(3-fluoropropyl)-2β-carbomethoxy-3β-(4-iodophenyl)nortropane ((123) I-FP-CIT) SPECT. Several other imaging techniques have also reported promising results, such as [(18) F]fluorodopa PET, which assesses nigrostriatal integrity; [(18) F]fluorodeoxyglucose PET, which assesses metabolic deficits; and meta-iodobenzylguanidine imaging, which assesses sympathetic cardiac denervation. Data from studies using CSF measures of amyloid and tau, occipital hypoperfusion on SPECT and preservation of medial temporal lobe structures on MRI suggest that they may offer less diagnostic discrimination. Several potential biomarkers have shown good diagnostic accuracy for DLB, but apart from FP-CIT SPECT, there is now a need for larger clinical multi-site studies, as well as for studies with pathological verification of diagnosis, before their use could be recommended for routine clinical practice

Neurology. 2011 Jun 14;76(24):e114.
Teaching NeuroImages: primary progressive aphasia: PET demonstration.
Tarlaci S, Savas R, Kocacelebi K.
Source
Ege Sag Iık Hastanesi, Department of Neurology, Alsancak, Đzmir, Turkey. info@kuantumbeyin.coms.

FDG-PET and MRI features in multiple system atrophy.
Seok HY, Eun MY, Park KW, Yu SW.
Department of Neurology, Korea University College of Medicine, Republic of Korea.

Cholinergic dysfunction after traumatic brain injury: preliminary findings from a PET study.
Östberg A, Virta J, Rinne JO, Oikonen V, Luoto P, Någren K, Arponen E, Tenovuo O.
Department of Neurology, University of Turku and Turku University Central Hospital, Turku, Finland.
There is evidence that the cholinergic system is frequently involved in the cognitive consequences of traumatic brain injury (TBI). We studied
whether the brain cholinergic function is altered after TBI in vivo using PET. Cholinergic function was assessed with [methyl-(11)C]N-
methylpiperidyl-4-acetate, which reflects the acetylcholinesterase (AChE) activity, in 17 subjects more than 1 year after a TBI and in 12 healthy
controls. All subjects had been without any centrally acting drugs for at least 4 weeks. The AChE activity was significantly lower in subjects with
TBI compared to controls in several areas of the neocortex (-5.9% to -10.8%, p=0.053 to 0.004). Patients with chronic cognitive symptoms after

Parkinsonism Relat Disord. 2011 Mar;17(3):160-5. Epub 2010 Dec 31.
Amyloid and glucose imaging in dementia with Lewy bodies and multiple systems atrophy.
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Multiple Systems Atrophy (MSA) and Dementia with Lewy bodies (DLB) can present with both REM behavior disorder and severe autonomic
dysfunction. In rare occasions, patients with MSA progress to cognitive impairment and even dementia. Positron emission topography (PET)
imaging using both the amyloid ligand Pittsburgh Compound B (11C-PiB) and 18 flurodeoxyglucose (18F-FDG) was used to ascertain the
presence of amyloid and pattern of glucose metabolic derangement in both disorders. Patients diagnosed with probable DLB or MSA, with
clinical symptoms of either REM Behavior Disorder (RBD), Parkinsonism, or dysautonomia were prospectively identified. All underwent both
11C-PiB and 18F-FDG PET imaging. Statistical comparison between DLB, MSA, and normal controls was performed. Six patients, 3 with DLB,
2 with Parkinson predominant MSA (MSA-P), and 1 with cerebellar predominant MSA (MSA-C) were identified. Increased level of PiB
retention was noted in all patients diagnosed with DLB, but was absent in MSA. In those with DLB, glucose hypometabolism corresponded with
regions of amyloid presence, and included prefrontal, parietotemporal, occipital and primary visual cortex regions. MSA patients were
distinguished by cerebellar glucose hypometabolism. These findings emphasize the distinguishing characteristics between the alpha-synuclein
related disorders of DLB and MSA. The absence of amyloid in the cases of MSA is a possible distinguishing characteristic of the disorder.

F-DOPA Parkinsondiagnostik

Mov Disord. 2011 Apr 25. doi: 10.1002/mds.23672. [Epub ahead of print]
A new diagnostic test to distinguish tremulous Parkinson's disease from advanced essential tremor.
Muthuraman M, Hossen A, Heute U, Deuschl G, Raethjen J.
Department of Neurology, University of Kiel, Kiel, Germany.
Clinical distinction between advanced essential tremor and tremulous Parkinson's disease can be difficult. In selected power spectra of accelerometric postural tremor recordings on the more affected side of 41 patients with essential tremor and 39 patients with tremulous Parkinson's disease being indistinguishable by tremor frequency, peak power or number of harmonic peaks, waveform asymmetry (autocorrelation decay), and mean peak power of all harmonic peaks were computed. Cutoff for essential tremor-Parkinson's disease distinction was determined by receiver operating characteristics. Diagnostic yield was tested in 12 clinically unclear patients with monosymptomatic tremor, subsequently definitively diagnosed with essential tremor (n = 2) or Parkinson's disease (n = 10) by 123-I FP-CIT-single-photon emission computed tomography, fluorodopa-positron emission tomography, or clinical course. By autocorrelation decay 64%, by mean harmonic peak power 94% (Parkinson's disease > essential tremor) of patients with a definite clinical diagnosis, and 11 of 12 clinically unclear patients were classified correctly. Mean harmonic power is a useful measure to separate clinically difficult cases of advanced essential tremor from tremulous Parkinson's disease. © 2011 Movement Disorder Society.

Neurology. 2011 Apr 12;76(15):1296-301. Epub 2011 Apr 6.
Reduced uptake of [1␣F]FDOPA PET in asymptomatic welders with occupational manganese exposure. Criswell SR, Perlmutter JS, Videen TO, Moerlein SM, Flores HP, Birke AM, Racette BA. Department of Neurology, Washington University School of Medicine, 660 South Euclid Ave., Box 8111, St. Louis, MO 63110, USA.
Welding exposes workers to manganese (Mn) fumes, but it is unclear if this exposure damages dopaminergic neurons in the basal ganglia and predisposes individuals to develop parkinsonism. PET imaging with 6-[(18)F]fluoro-l-dopa (FDOPA) is a noninvasive measure of nigrostriatal dopaminergic neuron integrity. The purpose of this study is to determine whether welding exposure is associated with damage to nigrostriatal neurons in asymptomatic workers. We imaged 20 asymptomatic welders exposed to Mn fumes, 20 subjects with idiopathic Parkinson disease (IPD), and 20 normal controls using FDOPA PET. All subjects were examined by a movement disorders specialist. Basal ganglia volumes of interest were identified for each subject. The specific uptake of FDOPA, K(i), was generated for each region using

graphical analysis method. Repeated measures general linear model (GLM) analysis demonstrated a strong interaction between diagnostic group and region ($F(4,112) = 15.36$, $p < 0.001$). Caudate K(i)s were lower in asymptomatic welders (0.0098 + 0.0013 minutes(-1)) compared to control subjects (0.0111 + 0.0012 minutes(-1), $p = 0.002$). The regional pattern of uptake in welders was most affected in the caudate > anterior putamen > posterior putamen. This uptake pattern was anatomically reversed from the pattern found in subjects with IPD. Active, asymptomatic welders with Mn exposure demonstrate reduced FDOPA PET uptake indicating dysfunction in the nigrostriatal dopamine system. The caudate K(i) reduction in welders may represent an early (asymptomatic) marker of Mn neurotoxicity and appears to be distinct from the pattern of dysfunction found in symptomatic IPD.

Mov Disord. 2011 Mar;26(4):614-20. doi: 10.1002/mds.23503. Epub 2011 Mar 29.
Rate of 6-[18F]fluorodopa uptake decline in striatal subregions in Parkinson's disease.
Gallagher CL, Oakes TR, Johnson SC, Chung MK, Holden JE, Bendlin BB, McLaren DG, Xu G, Nickles RJ, Pyzalski R, DeJesus O, Brown WD.
William S. Middleton Memorial Veterans Hospital, Madison, Wisconsin 53792, USA. gallagher@neurology.wisc.edu
Rate of decline in 6-L-[(18)F]fluorodopa (FDOPA) uptake within the striatum has been reported as showing regional differences in Parkinson's disease (PD). We acquired longitudinal brain FDOPA positron emission tomography (PET) studies in 26 PD subjects and 11 controls over 4.5 years. We analyzed both spatially normalized voxel-wise maps of radiotracer influx (Kocc) and average Kocc values for six non-overlapping volumes of interest (VOIs) encompassing the striatum. The voxel-wise analysis showed that in PD, FDOPA Kocc decline spanned the striatum but was greatest in the posterior putamen ipsilateral and anterior putamen contralateral to initial symptoms. The VOI approached showed that absolute rates of Kocc decline were significantly greater in PD than control subjects, but that the slope of decline did not differ between subregions. In PD, ratios of uptake between subregions did not change during the study with the exception of the ipsilateral putamen/caudate ratio. Decline rates were marginally greater during earlier time segments. Both male gender and advancing age were associated with lower baseline FDOPA uptake, but no difference in decline rates. VOI Kocc values were significantly correlated with disease duration, but only moderately correlated with clinical measures.We conclude that FDOPA uptake in subregions of the striatum is strongly correlated with disease duration and age, and declines approximately equally from symptom onset in PD. This implies that in idiopathic PD, relative preservation of uptake in the anterior striatum reflects a delay in pathologic involvement of nigrostriatal projections to this region.

Neuroimage. 2011 Jun 1;56(3):1463-8. Epub 2011 Mar 17.
Progression of monoaminergic dysfunction in Parkinson's disease: a

longitudinal 18F-dopa PET study.
Pavese N, Rivero-Bosch M, Lewis SJ, Whone AL, Brooks DJ.
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Post-mortem and neuroimaging studies in Parkinson's disease (PD) have shown involvement of the brain serotoninergic, noradrenergic and
cholinergic pathways alongside the characteristic degeneration of nigrostriatal dopamine neurons. The rate of progression of the degenerative
process in these extrastriatal areas is still unclear. We used (18)F-dopa PET, a marker of aromatic aminoacid decarboxylase activity in
monoaminergic neurons, to assess longitudinal changes in tracer uptake in brain noradrenergic, serotoninergic and extrastriatal dopaminergic
structures over a 3-year period in a group of early PD patients. Ten PD patients had (18)F-dopa PET twice: at baseline and again after 37.1±21.5
months follow up. A standard object map was used to extract tracer influx constants (Ki) in 11 striatal and extrastriatal regions. Progressive
decreases in (18)F-dopa Ki occurred over the follow-up period in the majority of the investigated areas, the fastest annual declines occurring in
putamen (8.1%), locus coeruleus (7.8%), and globus pallidus interna (7.7%). Caudate and hypothalamus showed 6.3% and 6.1% annual Ki
declines, respectively. At baseline, some structures showed increased levels of (18)F-dopa uptake in PD compared to controls (internal pallidum,
locus coeruleus), indicating possible compensatory upregulation of monoamine turnover. These increased levels had normalised (globus pallidus
interna) or become subnormal (locus coeruleus) at follow-up suggesting exhaustion of these mechanisms within the first years of disease. Loss of
monoaminergic function in extrastriatal regions, as reflected by(18)F-dopa PET, is delayed and occurs independently from nigrostriatal
degeneration. When assessing the efficacy of novel neuroprotective agents on nigrostriatal dysfunction in PD, (18)F-dopa PET could provide
supplementary information concerning function of extrastriatal monoaminergic structures.

Rev Esp Med Nucl. 2011 Mar-Apr;30(2):88-93. Epub 2011 Feb 19.
[Dual time point 18F-FDOPA PET as a tool for characterizing brain tumors].
[Article in Spanish]
González-Forero M, Prieto E, Domínguez I, Vigil C, Peñuelas I, Arbizu J.
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(18)F-FDOP A is an amino acid analogue used to evaluate presynaptic dopaminergic activity, which has aroused great interest in neuro-oncology.
We have evaluated five (18)F-FDOPA PET studies of patients referred for study of parkinsonian syndrome. Two subjects had previously treated
high-grade brain tumors, one nonspecific brain injury, and 2 subjects presented unexpected tumoral lesions. For all lesions SUVmax, time to

SUVmax and tumor-to-normal grey matter SUVmax rate (T/N) were calculated, and 90 minutes (18)F-FDOPA kinetics were analyzed. Tumor
lesions corresponded to three malignant neurocytomas, one meningioma, one pineocytoma and one intrasinusal hemangioma. Both malignant and
benign tumors exhibited high uptake of (18)F-FDOPA well above the normal cortex. However, the analysis of the curve uptake displayed
characteristic patterns that facilitate the characterization of tumor lesions. A dual phase maximum uptake was observed, with an early 10 minutes
uptake in malignant lesions, and a late 60 to 90 minutes uptake in benign or low grade lesions.

Cardio-PET/CT

Eur J Nucl Med Mol Imaging. 2011 Jan;38(1):201-12.
Hybrid cardiac imaging: SPECT/CT and PET/CT. A joint position statement by the European Association of Nuclear Medicine (EANM), the European Society of Cardiac Radiology (ESCR) and the European Council of Nuclear Cardiology (ECNC).
Flotats A, Knuuti J, Gutberlet M, Marcassa C, Bengel FM, Kaufmann PA, Rees MR, Hesse B; Cardiovascular Committee of the EANM, the ESCR and the ECNC.
Nuclear Medicine Department, Hospital de la Santa Creu i Sant Pau, Universitat Autònoma de Barcelona, Sant Antoni M. Claret, 167, 08025, Barcelona, Spain. aflotats@santpau.cat
Improvements in software and hardware have enabled the integration of dual imaging modalities into hybrid systems, which allow combinedacquisition of the different data sets. Integration of positron emission tomography (PET) and computed tomography (CT) scanners into PET/CTsystems has shown improvement in the management of patients with cancer over stand-alone acquired CT and PET images. Hybrid cardiac imaging either with single photon emission computed tomography (SPECT) or PET combined with CT depicts cardiac and vascular anatomical abnormalities and their physiologic consequences in a single setting and appears to offer superior information compared with either stand-alone or side-by-side interpretation of the data sets in patients with known or suspected coronary artery disease (CAD). Hybrid systems are also advantageous for the patient because of the single short dual data acquisition. However, hybrid cardiac imaging has also generated controversy with regard to which patients should undergo such integrated examination for clinical effectiveness and minimization of costs and radiation dose, and if software-based fusion of images obtained separately would be a useful alternative. The European Association of Nuclear Medicine (EANM), the European Society of Cardiac Radiology (ESCR) and the European Council of Nuclear Cardiology (ECNC) in this paper want to present a

position statement of the institutions on the current roles of SPECT/CT and PET/CT hybrid cardiac imaging in patients with known or suspected CAD.