

I° INCONTRO AGGIORNAMENTO DEL DIPARTIMENTO ONCOLOGICO
Strategie terapeutiche nel carcinoma del colon-retto metastatico
Negrar, 11 febbraio 2014

Ruolo della PET

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NCCN Task Force Report: PET/CT Imaging

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Colorectal PET

- **Diagnosis and initial staging**
- **Key points**
 - Whole body PET scans performed for other malignancies may identify incidental colorectal cancer
 - PET scans are not routinely used in the initial staging of patients with colorectal cancer

Detection of Recurrent Colorectal Cancer

- PET scans are more accurate than CT scans in assessing suspected recurrence
- PET scans are routinely performed to rule out extrahepatic disease in patients who are considered surgical candidates for resection of isolated liver metastases
- PET scans are used to evaluate rising CEA levels when other imaging studies are negative

Response to Therapy

- There are minimal data regarding the role of PET scans in monitoring the response to chemotherapy or radiation therapy
- PET scans have been used to assess response to regional therapies of the liver where they can distinguish between necrosis and residual tumor

Summary of Recommendations

- Staging
 - PET is not routinely indicated unless initial studies suggest but are not conclusive for metastatic disease
- Detection of recurrence
 - PET scans are indicated for the evaluation of a rising CEA level or a patient with suspicious symptoms unless a CT scan has already identified metastatic disease
- PET scans are not indicated for routine surveillance for colon cancer recurrence
- Management of metastatic disease
 - PET scans are not routinely indicated to restage patients after non-surgical treatment of metastatic disease unless curative resection is considered

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

[Health Technol Assess.](#) 2011 Sep;15(35):1-192

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

Criteria for inclusion in the HTA journal series
Reports are published in the HTA journal series if they have resulted from work for the HTA programme, and they are of a sufficiently high scientific quality as assessed by the referees and editors.



Reviews in *Health Technology Assessment* are termed 'systematic' when the account of the search, appraisal and synthesis methods (to minimise biases and random errors) would, in theory, permit the replication of the review by others.

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.

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

Results:

30 studies with 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

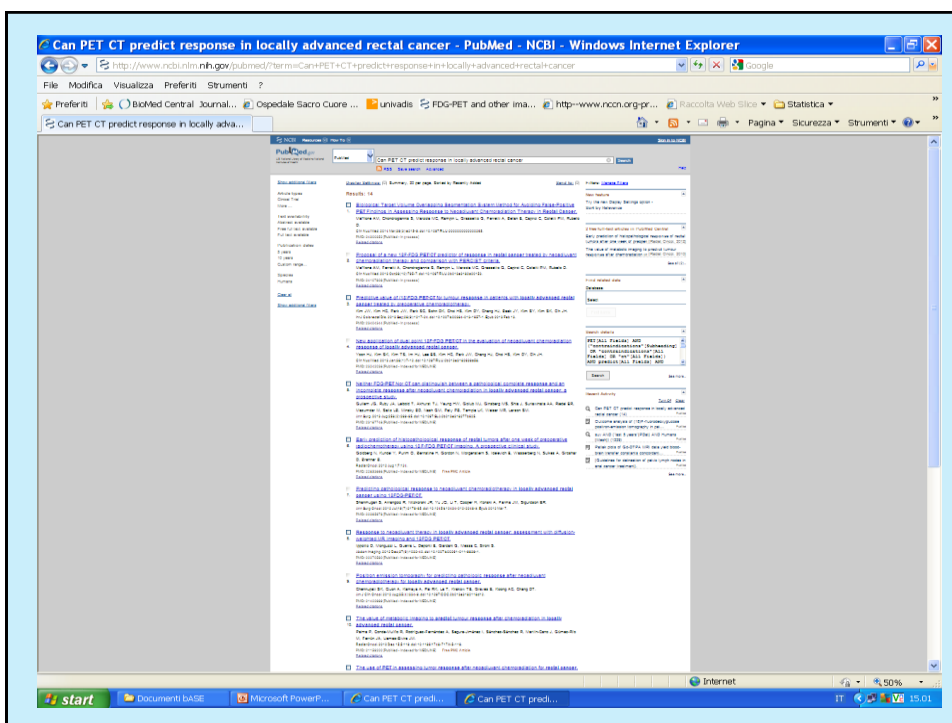
The use of FDG PET/CT for the detection of **recurrent disease** identified data from five retrospective studies from which a pooled sensitivity of 91% (95% CI 0.87% to 0.95%) and specificity of 91% (95% CI 0.85% to 0.95%) were observed.

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

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

Conclusions:

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.



Predictive value of (18)FDG PET-CT for tumour response in patients with locally advanced rectal cancer treated by preoperative chemoradiotherapy.

Kim JW et al. *Int J Colorectal Dis.* 2013 Sep;28(9):1217-24.

Center for Colorectal Cancer, Research Institute and Hospital, National Cancer Center, 809 Madu-1-dong, Ilsandong-gu, Gyeonggi-do, 410-769, Republic of Korea.

PURPOSE:

Although (18)fluorine-2-deoxy-D-glucose positron emission tomography-computed tomography ((18)FDG PET-CT) is considered a reliable modality for determining tumour response after neoadjuvant chemoradiotherapy (CRT) in locally advanced rectal cancer (LARC), the role of (18)FDG PET-CT for predicting pathologic complete response (pCR) remains unclear. The aim of this study was to evaluate whether (18)FDG PET-CT can predict tumour response after CRT in patients with LARC, in terms of downstaging and pCR.

METHODS:

Between March 2009 and February 2012, 151 patients with LARC treated with neoadjuvant CRT followed by radical surgery were reviewed retrospectively. Pre-CRT SUVmax (maximum standardized uptake value), post-CRT SUVmax, ΔSUVmax (difference between pre- and post-CRT SUVmax), and RI-SUV (response index) were measured before and after CRT. Univariate and multivariate analyses were used to analyse the association of PET-CT-related parameters and clinical variables, to assess downstaging and pCR.

RESULTS:

Downstaging occurred in 48 patients (31.7 %) and pCR in 19 patients (12.5 %). Univariate and multivariate analysis revealed post-CRT SUVmax as a significant factor for prediction of downstaging, with sensitivity of 60.4 %, specificity of 65.0 %, and accuracy of 55.9 %, for a cutoff value of 3.70. Regarding pCR, post-CRT SUVmax was again found as a significant parameter by univariate and multivariate analysis, with sensitivity of 73.7 %, specificity of 63.7 %, and accuracy of 64.9 %, for a cutoff value of 3.55.

CONCLUSIONS:

The results indicate that post-CRT SUVmax independently predicts downstaging and pCR. However, the predictive values of post-CRT SUVmax for tumour response after neoadjuvant CRT are too low in sensitivity and specificity to change the treatment plan for LARC.

Biological Target Volume Overlapping Segmentation System Method for Avoiding False-Positive PET Findings in Assessing Response to Neoadjuvant Chemoradiation Therapy in Rectal Cancer.

Maffione AM et al [Clin Nucl Med.](#) 2014 Mar;39(3):e215-9

*Department of Nuclear Medicine, †Medical Physics Unit, and ‡Department of Radiotherapy & Oncology, Santa Maria della Misericordia Hospital, Rovigo, Italy; and §Department of Radiology, University of Southern California, Los Angeles, CA.

PURPOSE:

FDG PET/CT has a recognized high predictive power to assess the response to neoadjuvant chemoradiation therapy (CRT) in patients affected by locally advanced rectal cancer (LARC), but a relatively high number of false-positive findings decrease its specificity: with the aim to solve this problem, a new method of imaging analysis is here proposed.

METHODS:

The new method here described, named Biological target volume (BTV) Overlapping Segmentation System (BOSS), has been applied on 24 consecutive patients with LARC that were all previously classified as nonresponders to CRT by means of the response index criterion that is adopted in our center. The BOSS method is based on the quantification of the amount of superimposition between pretreatment and posttreatment BTV. All BTVpre was down using a threshold of 60% of SUVmax in the tumor (BTV60). The results (overlap volumes and percentage of overlap volumes) were then matched up with postoperative pathology classified by the Mandard's tumor regression grade (TRG) system.

RESULTS:

Eleven patients were classified as responders (TRG1-2) and 13 as nonresponders (TRG 3-5). Among all the results obtained by BOSS method, only the percentage of overlap volume data between BTV60 and BTVpost (%Over_60) was able to correctly distinguish between responders and nonresponders. In our experience, a cutoff of 56% on the %Over_60 provided the best results in terms of true negative (11 cases), true positive (12 cases), false negative (1 case), and false positive (none).

CONCLUSIONS:

This new method, we developed, appears able to unmask the false-positive cases, improving the specificity of FDG PET/CT to predict the response to CRT patients with LARC

Proposal of a new 18F-FDG PET/CT predictor of response in rectal cancer treated by neoadjuvant chemoradiation therapy and comparison with PERCIST criteria.

Maffione AM et al. [Clin Nucl Med.](#) 2013 Oct;38(10):795-7.

From the *Nuclear Medicine Department, PET Unit, †Medical Physics Department, and ‡Radiotherapy Department, Santa Maria della Misericordia Hospital, Rovigo, Italy; and §Department of Radiology, University of Southern California, Los Angeles, CA.

PURPOSE:

The aim of this study was to correlate PERCIST criteria and a new criterion developed in our center that we named PREDIST (PET Residual Disease in Solid Tumor) with tumor regression grade (TRG) classification of pathologic response to neoadjuvant chemoradiotherapy (CRT) in patients affected by rectal cancer.

METHODS:

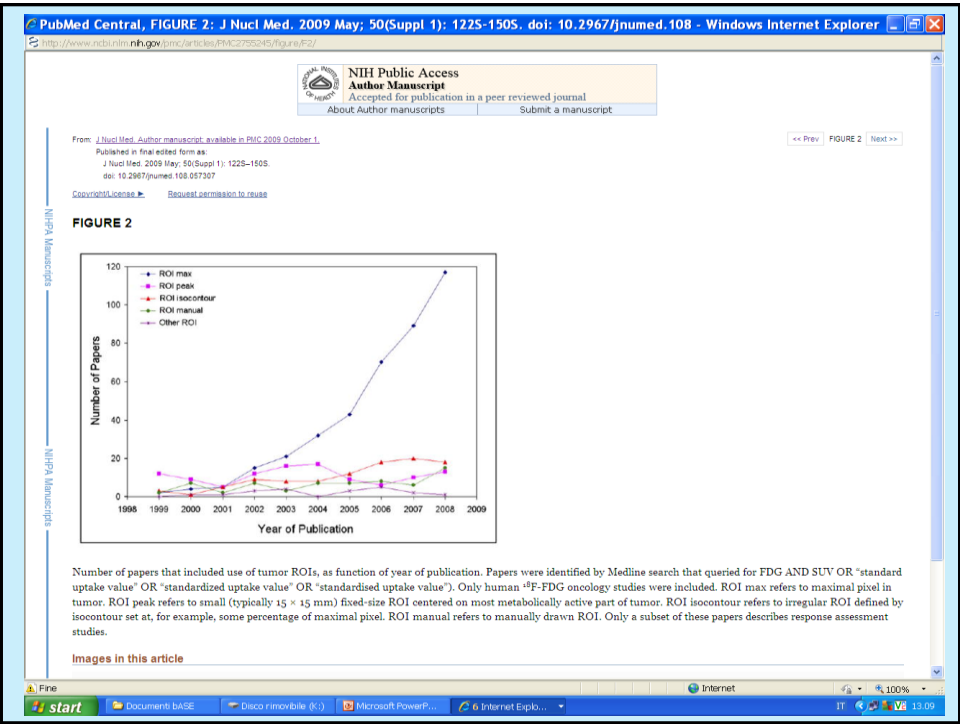
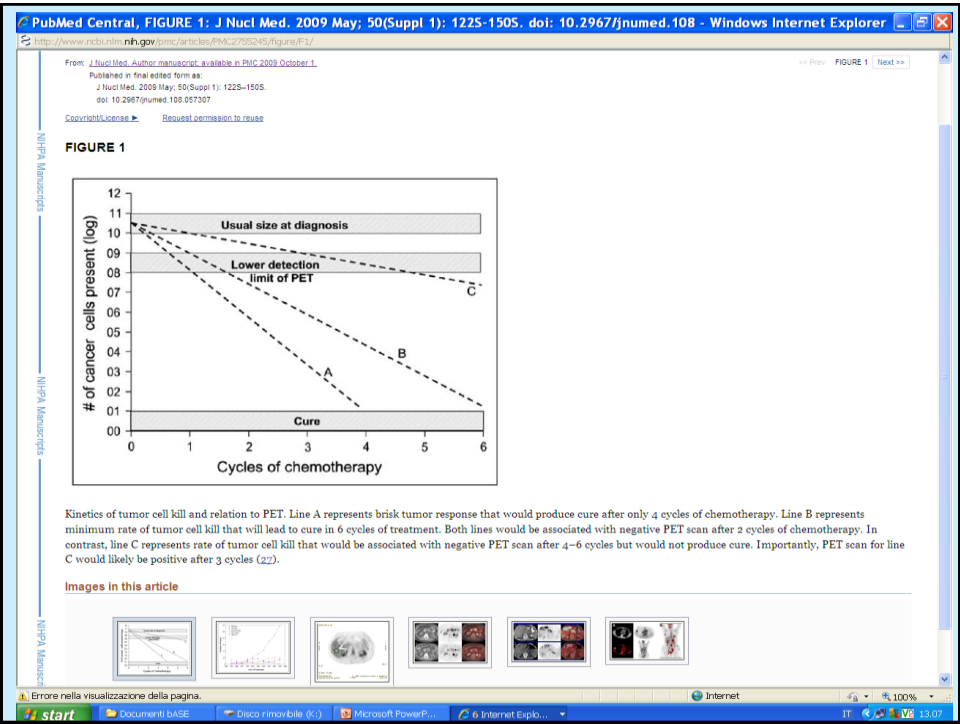
Seventy-three consecutive patients affected by locally advanced rectal cancer (LARC) were retrospectively included. FDG-PET/CT scans were performed at staging time and after the end of CRT (mean time 6.5 weeks). The analysis was performed by PERCIST criteria 1.0 and PREDIST criteria based on a new definition of residual disease. We split the TRG system into responders (TRG1-2) and nonresponders (TRG3-5). Pearson chi-square analysis by cross-tabulations was performed.

RESULTS:

PREDIST classification was statistically predictive of TRG response ($P = 0.004$, sensitivity 81.8% and specificity 54.9%). On the contrary, PERCIST criteria was not statistically correlated to TRG ($P = 0.128$) caused by a very low specificity (9.8%).

CONCLUSIONS:

FDG-PET/CT scan is an accurate tool to predict preoperatively the response to CRT in LARC patients. The novel proposed criterion (PREDIST) seems to be helpful to discriminate responder by nonresponder patients.



PubMed Central, TABLE 6: J Nucl Med. 2009 May; 50(Suppl 1): 122S-150S. doi: 10.2967/jnumed.108. - Windows Internet Explorer

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TABLE 6
Summary of Studies on Test–Retest Reproducibility of Untreated Tumors Without Interval Therapy

Study	Pts/lesions	No. and time between PET scans	Imaging and reconstruction parameters	Variables and ROIs	Major findings
Minn 1993	10 pts; 10 lesions; primary lung cancer ≥ 2 cm	2 scans; mean 1.8 ± 1.8 d	PET alone/ ^{68}Ge AC; dynamic acquisition $\times 60$ min; 3.4-mm slice thickness ($n = 8$); 6.75-mm slice thickness ($n = 2$); 128×128 matrices; FBP 0.3 Hanning filter; 8 mm FWHM; axial resolution not given	Maximal SUL $1.2 \times 1.2 \times 1.2$ cm; ROI 4 $\times 4$ pixels ("peak")	Test–retest mean percentage difference between scans; correlation (SUL): $10\% \pm 7\%$ (0.987); KI: $10\% \pm 8\%$ (0.969); SUL glucose correction: $6\% \pm 6\%$ (0.993); K ₁ : $24\% \pm 13\%$ (0.812); K ₂ : $42\% \pm 31\%$ (0.0765); K ₃ : $24\% \pm 13\%$ (0.953)
Weber 1999	16 pts; 30 lesions; various cancers; tumor volume $0.8\text{--}111$ mL	2 scans; mean 3 ± 3 d	PET alone/ ^{68}Ge AC; dynamic acquisition $\times 70$ min; 3.4-mm slice thickness; 128×128 matrices (4×4 mm); FBP 0.4 Hanning filter; 8 mm FWHM; axial resolution ~ 5 mm	SUV bw in 50% threshold around maximal ^{18}F -FDG ROI (mean diameter 32 ± 36 mm, range 12–60 mm)	Mean percentage difference in SUV for test–retest is $\sim 10\%$; 0.9 SUV unit required for significant change; greater variability in smaller lesions; glucose correction, no significant differences
Nakamoto 2002	10 pts; lung cancer	2 scans; within 1 wk	Reassessment of Minn data; same parameters for image acquisition and reconstruction	Maximal SUL in 1×1 pixel anywhere in tumor; highest average SUL in 4×4 pixels in tumor; effective glycolytic volume (SUL $\times$ volume)	Mean percentage difference between scans (maximal SUL: $11.3\% \pm 8\%$; mean SUL: $10.1\% \pm 8.2\%$; effective glycolytic volume: $10.1\% \pm 8\%$; mean percentage differences slightly reduced with glucose correction)
Krak 2003	11 pts; 29 lesions; NSCLC; median volume ~ 9 cm ³	2 scans; 2 consecutive days	PET alone/ ^{68}Ge AC; dynamic acquisition $\times 60$ min; 2.5-mm slice thickness; 128×128 matrices; FBP 0.3 Hanning filter; OSEM (2 iterations, 16 subsets); ~ 7 mm FWHM; axial resolution not given	FBP vs. OSEM; SUL ROIs (manual: 13 mm fixed; 50%, 75% threshold; single pixel maximum)	Test–retest reproducibility similar for FBP vs. OSEM; mean percentage differences of SUV between 2 scans ($8\%\text{--}10\%$ for manual and 13-mm fixed ROI; $12\%\text{--}14\%$ for 50%–75% threshold methods; $13\% \pm 11\%$ for single-pixel SUV max); mean percent differences of ROI volume ($23\% \pm 20\%$ for 50% threshold; $53\% \pm 25\%$ for 75% threshold); ICC highest for 13-mm fixed ROI (0.93); ICC for threshold/single-pixel SUV max 0.89–0.91
Nahmias 2008	26 pts; 26 lesions; various cancers	2 scans; mean 1.5 ± 0.4 d	PET/CT (CT AC); static acquisition; 90 min; offset frame acquisition; 0.2 mm slices	Manual ROI definition in axial slices with most ^{18}F -FDG uptake	Mean SUV (large manual ROI) test–retest: high correlation ($r = 0.99$, 95% confidence interval (CI) 0.95–1.00); mean difference 0.01 ± 0.04 SUV

http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2755245/pdf/nihms121494.pdf - Windows Internet Explorer

http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2755245/pdf/nihms121494.pdf

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TABLE 4
Response Definitions for Clinical Trials: Lymphoma Response (33)

Response	Definition	Nodal masses	Spleen, liver	Bone marrow
CR	Disappearance of all evidence of disease	(a) ^{18}F -FDG-avid or PET-positive before therapy must be PET-negative after therapy; mass of any size is permitted if PET is negative; (b) variably ^{18}F -FDG-avid or PET-negative; regression to normal size on CT	Not palpable, nodules disappeared	Infiltrate has cleared on repeated biopsy; if indeterminate by morphology, immunohistochemistry should be negative for CR
PR	Regression of measurable disease and no new sites	$\geq 50\%$ decrease in SPD of up to 6 largest dominant masses; no increase in size of other nodes; (a) ^{18}F -FDG-avid or PET-positive before therapy; one or more PET-positive at previously involved site; (b) variably ^{18}F -FDG-avid or PET-negative; regression on CT	$\geq 50\%$ decrease in SPD of nodules (for single nodule in greatest transverse diameter), no increase in size of liver or spleen	Irrelevant if positive before therapy; cell type should be specified
SD	Failure to attain CR/PR or PD	(a) ^{18}F -FDG-avid or PET-positive before therapy; PET positive at prior sites of disease and no new sites on CT; (b) variably ^{18}F -FDG-avid or PET-negative; no change in size of previous lesions on CT		
Relapsed disease or PD	Any new lesion or increase of previously involved sites by $\geq 50\%$ from nadir	Appearance of new lesions > 1.5 cm in any axis, $\geq 50\%$ increase in SPD of more than one node, or $\geq 50\%$ increase in longest diameter of previously identified node > 1 cm in short axis; lesions PET-positive if ^{18}F -FDG-avid lymphoma or PET-positive before therapy	$> 50\%$ increase from nadir in SPD of any previous lesions	New or recurrent involvement

CR = complete remission; PR = partial remission; SPD = sum of product of diameters; SD = stable disease; PD = progressive disease.

New application of dual point 18F-FDG PET/CT in the evaluation of neoadjuvant chemoradiation response of locally advanced rectal cancer.

Yoon HJ et al. Clin Nucl Med. 2013 Jan;38(1):7-12.

Department of Nuclear Medicine, and Center for Colorectal Cancer, Research Institute and Hospital, National Cancer Center, Goyang, Republic of Korea.

PURPOSE:

FDG PET/CT has been suggested as the most reliable modality to predict pathological tumor responses after neoadjuvant chemoradiotherapy (CRT) in locally advanced rectal cancer (LARC). However, several confounding factors including radiation-induced inflammation could not be easily avoided with the commonly used single-point FDG PET/CT. Our aim was to evaluate the accuracy of a dual-point PET/CT protocol in LARC response prediction to CRT.

PATIENTS AND METHODS:

Sixty-one LARC patients were enrolled and treated with neoadjuvant CRT. PET/CT was performed before and after CRT. Dual-point acquisition was applied to post-CRT PET/CT. Post-CRT SUVmax (postSUV), pre/post-CRT SUVmax change (RI), and dual-point index (DI) of post-CRT PET/CT were compared with the Dworak tumor regression grade (TRG) as a gold standard. Univariate and multivariate analyses, as well as receiver operating characteristic curve analysis, were used to evaluate the predictive ability of demographic, clinical, and metabolic PET parameters.

RESULTS:

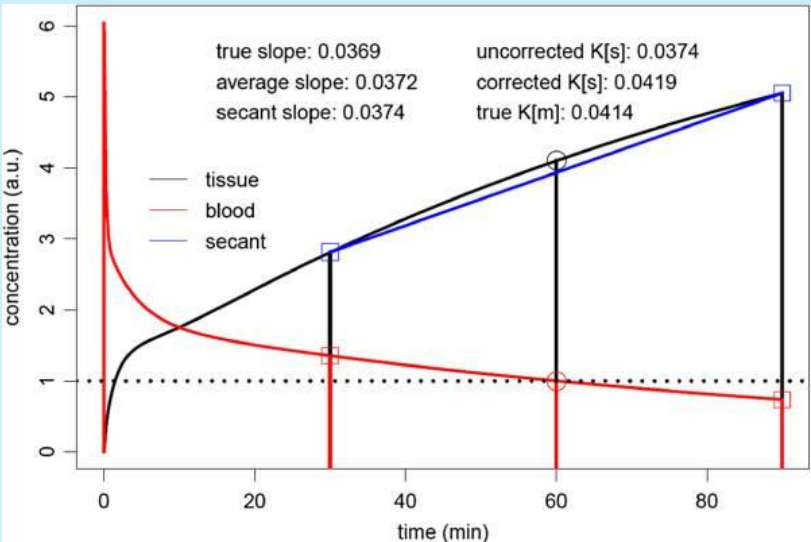
Fifteen patients of TRG3-4 were defined as pathological responders, and 46 patients of TRG1-2 were nonresponders. The resulting response index (RI) ranged from -13 to 94.8% (59.1±22.0%), and delay index (DI) ranged from -45.2 to 25.0% (-9.1±12.1%). Univariate analysis resulted in PET parameters (postSUV, RI, and DI) as significant predictors (P=0.004, P<0.001, P<0.0001). According to multivariate analysis, RI and DI remained as significant predictors (P=0.04 and P=0.0004). Receiver operating characteristic analysis showed that DI had significantly higher area under the curve compared with RI (0.906 vs 0.696, P=0.018). Delay index had 86.7% sensitivity, 87.0% specificity, 68.4% positive predictive value, 95.2% negative predictive value, and 86.9% accuracy.

CONCLUSIONS:

Dual-point post-CRT PET/CT can predict pathological tumor response better than conventional single time point pre- and post-CRT PET/CT.

New application of dual point 18F-FDG PET/CT in the evaluation of neoadjuvant chemoradiation response of locally advanced rectal cancer.

Yoon HJ et al. Clin Nucl Med. 2013 Jan;38(1):7-12.



New application of dual point 18F-FDG PET/CT in the evaluation of neoadjuvant chemoradiation response of locally advanced rectal cancer.

Yoon HJ et al. *Clin Nucl Med*. 2013 Jan;38(1):7-12.

$$K_m = K_s + V_r \tau_a = m_t c a_0 + V_r \tau_a$$

with
 $K_s = m_t c a_0$,

where m_t is the secant (or average) TRF slope in the chosen time interval centered at t_0 and $c a_0 = c a(t_0)$ (see Figure [Figure 11](#)).

The rate K_s defined by Equation 2 (i.e., the ratio between the TRF slope and AIF level at time t_0) can be determined from measurements during the late phase alone. Contrary to the Patlak method, knowledge of the full AIF is not required. To the extent that $K_s V_r \tau_a$, K_s might directly serve as an (negatively biased) approximation of K_m . Moreover, to the extent that V_r can be replaced by a suitable constant value V_r , K_s differs from K_m only by a τ_a -dependent offset that can be added to K_s to obtain a corrected value

$$K_s(c) = K_s + K_0 = K_s + V_r \tau_a$$

Neither FDG-PET Nor CT can distinguish between a pathological complete response and an incomplete response after neoadjuvant chemoradiation in locally advanced rectal cancer: a prospective study.

Guillem JG et al. *Ann Surg*. 2013 Aug;258(2):289-95

Department of Surgery, Memorial Sloan-Kettering Cancer Center, New York, NY 10065, USA.
 guillemj@mskcc.org

OBJECTIVE:

To prospectively compare the ability of fluorodeoxyglucose-positron emission tomography (FDG-PET) and computed tomography (CT) to identify a pathological complete response (pCR) in patients with rectal cancer treated by chemoradiation.

BACKGROUND:

A major obstacle in pursuing nonoperative management in patients with rectal cancer after chemoradiation is the inability to identify a pCR preoperatively.

METHODS:

A total of 121 patients with rectal cancer were prospectively enrolled. FDG-PET scans and helical CT scans were obtained before and after neoadjuvant chemoradiation. Consensus readings of PET and CT scans were used to classify certainty of disease (5-point confidence rating scale). The ability of PET and CT scans to accurately distinguish a pCR (ypT0) from an incomplete response (ypT1-4) was estimated using the area under the receiver operating characteristic curve (AUC).

RESULTS:

Of the 121 patients, 26 (21%) had a pCR. PET and CT scans were equally inadequate at distinguishing a pCR from an incomplete response (AUC = 0.64 for both, $P = 0.97$). Among the 26 patients with a pCR, 14 (54%) and 5 (19%) were classified as complete responders on PET and CT scans, respectively. Among the 95 patients with an incomplete pathological response, 63 (66%) and 90 (95%) were classified as incomplete responders on PET and CT scans, respectively. None of the individual PET parameters, including visual response score, mean standard uptake value (SUVmean), maximum SUV (SUVmax), and total lesion glycolysis, accurately distinguished a pCR (AUCs = 0.57-0.73).

CONCLUSIONS:

Neither PET nor CT scans have adequate predictive value to be clinically useful in distinguishing a pCR from an incomplete response and, therefore, should not be obtained for the purpose of attempting to predict a pCR after neoadjuvant chemoradiation for rectal cancer

Early prediction of histopathological response of rectal tumors after one week of preoperative radiochemotherapy using 18 F-FDG PET-CT imaging. A prospective clinical study.

Goldberg N et al. [Radiat Oncol](#). 2012 Aug 1;7:124.
Institute of Oncology, Beilinson Hospital, Petah Tiqva, Israel.

BACKGROUND:

Preoperative radiochemotherapy (RCT) is standard in locally advanced rectal cancer (LARC). Initial data suggest that the tumor's metabolic response, i.e. reduction of its 18 F-FDG uptake compared with the baseline, observed after two weeks of RCT, may correlate with histopathological response. This prospective study evaluated the ability of a very early metabolic response, seen after only one week of RCT, to predict the histopathological response to treatment.

METHODS:

Twenty patients with LARC who received standard RCT regimen followed by radical surgery participated in this study. Maximum standardized uptake value (SUV-MAX), measured by PET-CT imaging at baseline and on day 8 of RCT, and the changes in FDG uptake (Δ SUV-MAX), were compared with the histopathological response at surgery. Response was classified by tumor regression grade (TRG) and by achievement of pathological complete response (pCR).

RESULTS:

Absolute SUV-MAX values at both time points did not correlate with histopathological response. However, patients with pCR had a larger drop in SUV-MAX after one week of RCT (median: -35.31% vs -18.42%, $p=0.046$). In contrast, TRG did not correlate with Δ SUV-MAX. The changes in FDG-uptake predicted accurately the achievement of pCR: only patients with a decrease of more than 32% in SUV-MAX had pCR while none of those whose tumors did not show any decrease in SUV-MAX had pCR.

CONCLUSIONS:

A decrease in Δ SUV-MAX after only one week of RCT for LARC may be able to predict the achievement of pCR in the post-RCT surgical specimen. Validation in a larger independent cohort is planned.

Predicting pathological response to neoadjuvant chemoradiotherapy in locally advanced rectal cancer using 18FDG-PET/CT.

Shanmugan S et al. [Ann Surg Oncol](#). 2012 Jul;19(7):2178-85

Department of Surgery, Temple University, Philadelphia, PA, USA. sshanmug@temple.edu

BACKGROUND:

Pathologic complete response (pCR) after neoadjuvant chemoradiation (CRT) has been observed in 15-30% of patients with locally advanced rectal cancer (LARC). The objective of this study was to determine whether PET/CT can predict pCR and disease-free survival in patients receiving CRT with LARC.

METHODS:

This is a retrospective review of patients with EUS-staged T3-T4, N+rectal tumors treated with CRT, who underwent pre/post-treatment PET/CT from 2002-2009. All patients were treated with CRT and surgical resection. Standardized uptake value (SUV) of each tumor was recorded. Logistic regression was used to analyze the association of pre-CRT SUV, post-CRT SUV, %SUV change, and time between CRT and surgery, compared with pCR. Kaplan-Meier estimation evaluated significant predictors of survival.

RESULTS:

Seventy patients (age 62 years; 42M:28F) with preoperative stage T3 (n=61) and T4 (n=9) underwent pre- and post-CRT PET/CT followed by surgery. The pCR rate was 26%. Median pre-CRT SUV was 10.8, whereas the median post-CRT SUV was 4 ($P=0.001$). Patients with pCR had a lower median post-CRT SUV compared with those without (2.7 vs. 4.5, $P=0.01$). Median SUV decrease was 63% (7.5-95.5%) and predicted pCR ($P=0.002$). Patients with a pCR had a greater time interval between CRT and surgery (median, 58 vs. 50 days) than those without ($P=0.02$). Patients with post-CRT SUV<4 had a lower recurrence compared with those without ($P=0.03$). Patients with SUV decrease $\geq$ 63% had improved overall survival at median follow-up of 40 months than those without ($P=0.006$).

CONCLUSIONS:

PET/CT can predict response to CRT in patients with LARC. Posttreatment SUV, %SUV decrease, and greater time from CRT to surgery correlate with pCR. Post-CRT, SUV<4, and SUV decrease $\geq$ 63% were predictive of recurrence-free and overall survival.

The value of metabolic imaging to predict tumour response after chemoradiation in locally advanced rectal cancer.

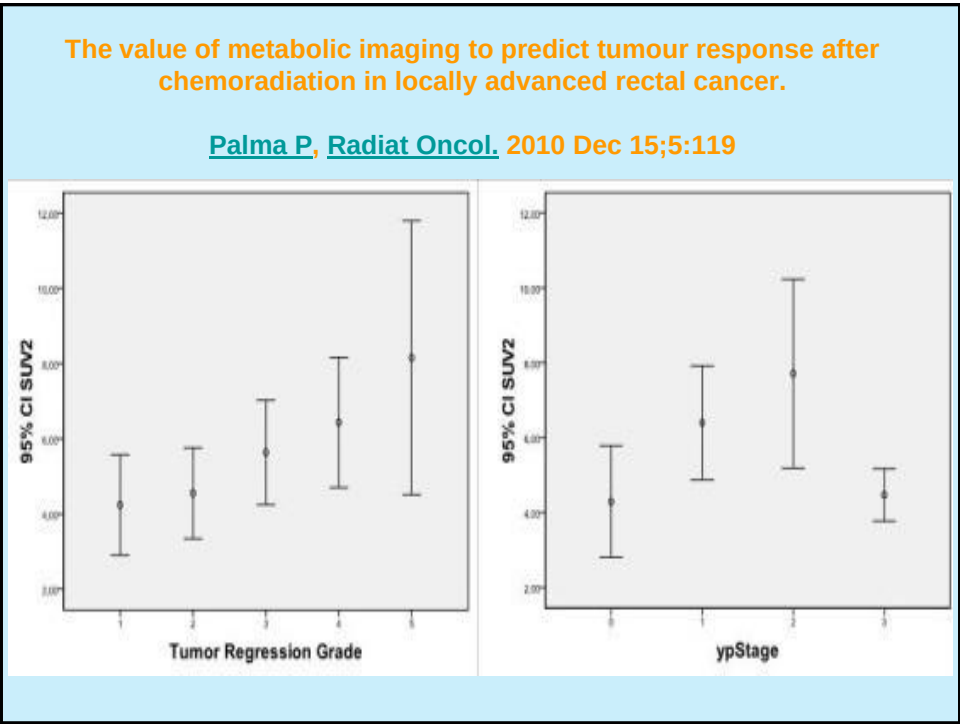
[Palma P, Radiat Oncol. 2010 Dec 15;5:119.](#)
Division of Colon & Rectal Surgery - Department of Surgery, HUVN Granada, Spain.
pablopalma@andaluciajunta.es

BACKGROUND:
We aim to investigate the possibility of using 18F-positron emission tomography/computer tomography (PET-CT) to predict the histopathologic response in locally advanced rectal cancer (LARC) treated with preoperative chemoradiation (CRT).

METHODS:
The study included 50 patients with LARC treated with preoperative CRT. All patients were evaluated by PET-CT before and after CRT, and results were compared to histopathologic response quantified by tumour regression grade (patients with TRG 1-2 being defined as responders and patients with grade 3-5 as non-responders). Furthermore, the predictive value of metabolic imaging for pathologic complete response (ypCR) was investigated.

RESULTS:
Responders and non-responders showed statistically significant differences according to Mandard's criteria for maximum standardized uptake value (SUVmax) before and after CRT with a specificity of 76,6% and a positive predictive value of 66,7%. Furthermore, SUVmax values after CRT were able to differentiate patients with ypCR with a sensitivity of 63% and a specificity of 74,4% (positive predictive value 41,2% and negative predictive value 87,9%); This rather low sensitivity and specificity determined that PET-CT was only able to distinguish 7 cases of ypCR from a total of 11 patients.

CONCLUSIONS:
We conclude that 18-F PET-CT performed five to seven weeks after the end of CRT can visualise functional tumour response in LARC. In contrast, metabolic imaging with 18-F PET-CT is not able to predict patients with ypCR accurately.



Has PET/CT a role in the characterization of indeterminate lung lesions on staging CT in colorectal cancer? A prospective study

Jess P et al. [Eur J Surg Oncol](#). 2014 Jan 15

Department of Surgery, Roskilde University Hospital, Denmark; Faculty of Health Sciences, University of Copenhagen, Denmark. Electronic address: pjss@regionsjaelland.dk.

PURPOSE:

CT has been found superior to chest x-ray to detect lung malignancies. However, indeterminate lung lesions (ILL) are found in 4-42% by using CT in staging colorectal cancer (CRC) patients. Our aim was to examine the frequency of ILL on staging CT and the rate of the ILL being malignant, and to investigate if PET/CT was useful in pointing out the malignant cases.

METHODS:

A prospective analysis of 238 consecutive patients operated for CRC followed median 24 months. All the patients had a preoperative staging CT. Patients with ILL had a PET/CT scan performed 3 months postoperatively and low dose chest CT performed 6, 12, 18 and 24 months postoperatively.

RESULTS:

Twenty percent of the patients had ILL. Four of these patients (8.5%) had lung metastases detected median 9 months postoperatively, while 2 (4.3%) had other lung malignancies. One patient had TB. In patients with normal staging chest CT 10 of the 185 patients (5.4%) developed lung metastases detected median 16 months postoperatively. This was significantly later than in patients with ILL ($p < 0.001$), but with regard to the number of patients developing lung metastases no significant difference was found between the groups ($p = 0.12$).

CONCLUSIONS:

Even though a relative low number of ILL turn out to be malignant it seems advisable to use PET/CT scan in the follow-up to detect lung metastases as early as possible to better the prognosis. For the same reason all CRC patients should have chest CT included in their follow-up 6-12 months postoperatively.

Current Approaches and Challenges for Monitoring Treatment Response in Colon and Rectal Cancer.

McKeown E et al. [J Cancer](#). 2014 Jan 1;5(1):31-43.

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Abstract

Introduction: With the advent of multidisciplinary and multimodality approaches to the management of colorectal cancer patients, there is an increasing need to define how we monitor response to novel therapies in these patients. Several factors ranging from the type of therapy used to the intrinsic biology of the tumor play a role in tumor response. All of these can aid in determining the ideal course of treatment, and may fluctuate over time, pending down-staging or progression of disease. Therefore, monitoring how disease responds to therapy requires standardization in order to ultimately optimize patient outcomes. Unfortunately, how best to do this remains a topic of debate at

single best approach. The challenges to monitoring conducted utilizing PubMed

Sono necessari passi avanti, probabilmente la combinazione di molteplici modalità potrebbe consentire l'adeguata stima dei risultati di terapia

metastases, neoadjuvant therapy, rectal cancer, imaging modalities, CEA, down-staging, tumor response, and biomarkers. Directed searches of the embedded references from the primary articles were also performed in selected circumstances. **Results:** Pathologic examination of the post-treatment surgical specimen is the gold standard for monitoring response to therapy. Endoscopy is useful for evaluating local recurrence, but not in assessing tumor response outside of the limited information gained by direct examination of intra-luminal lesions. Imaging is used to monitor tumors throughout the body for response, with CT, PET, and MRI employed in different circumstances. Overall, each has been validated in the monitoring of patients with colorectal cancer and residual tumors. **Conclusion:** Although there is no imaging or serum test to precisely correlate with a tumor's response to chemo- or radiation therapy, these modalities, when used in combination, can aid in allowing clinicians to adjust medical therapy, pursue operative intervention, or (in select cases) identify complete responders. Improvements are needed, however, as advances across multiple modalities could allow appropriate selection of patients for a close surveillance regimen in the absence of operative intervention

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Table 1
Comparison of Imaging Modalities for Evaluation of Response of Rectal Cancer Following Neoadjuvant CRT.

Author/Year	Modality	Protocol	Data	Conclusions
Chennupati, 2012 ^{44A}	PET	All patients who received both pre- and post-CRT PET scans. Compared PET results to TRG	35 patients; No correlation between SUV, metabolic tumor volume between pathologic responders versus non-responders	Changes on PET have limited value in predicting pathologic response of rectal cancer after neoadjuvant CRT
MERCURY, 2007 ^{44B}	MRI	MRI preoperatively at an average of 23 days before surgery. Only short duration radiotherapy included.	679 patients with rectal cancer; MRI vs. pathological examination of extramural depth	MRI and histopathologic assessment of tumor spread correlated within 0.3mm
Brown, 2004 ⁴²	ERUS, DRE, MRI	Each of three modalities performed at baseline and repeated two weeks prior to surgery. Both early stage rectal cancers and those receiving nCRT included. Compared each to final pathology. Assessed favorability (invasion, nodal involvement)	98 patients undergoing TME; MRI 94% agreement with pathology; DRE 63% agreement with pathology; ERUS 69% agreement with pathology;	MRI is a better predictor of tumor response
Wieder, Geinitz, 2007 ^{44A}	PET-FLT	PET prior to CRT, two weeks after initiation of CRT, & 3-4 weeks after chemotherapy but before resection	10 patients; Poor correlation with pathologic specimen.	PET uptake of FLT decreased steadily. Did not correlate to tumor regression.
Pastor C, 2011 ⁵⁹	ERUS	4 - 6 weeks after neoadjuvant CRT; Goal of the study was to validate ERUS as a predictor pathologic response. Correlated to pathologic specimen	235 patients; 20% misclassified as uNo; 75% correct regarding LNs; Overall, over-staging in 37%	ERUS is not accurate in identification of positive nodes.
Denecke, 2005 ²⁸	MRI, CT, and PET	Each patient received one of the modalities before neoadjuvant CRT and 2-4 weeks after neoadjuvant CRT. Compared with ERUS and pathology.	23 patients with T3 or 4 rectal cancer after CRT; FDG PET: 100% (sens), 60% (spec); CT 54% (sens), 80% (spec); MR 71% (sens), 67% (spec)	PET is superior to CT and MRI predicting response to CRT

Legend: PET: Positron Emission Tomography; CRT: Chemoradiotherapy; SUV: Standardized uptake value; TRG: Tumor regression grade; MRI: Magnetic Resonance; Imaging;
ERUS: Endoscopic rectal ultrasound; DRE: Digital rectal exam; TME: Total mesorectal excision; PET-FLT: Fluoro-L-Thymidine; LN: Lymph node; CT: Computed tomography;

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Carcinosi peritoneale in progressa eteroplasia del colon dx

