Evidence Tables

Citation: Choi D, Kwak J, Kim J et al (2010) Preoperative Chest Computerised Tomography in Patients with Locally Advance Mid or Low Rectal Cancer: Its Role in Staging and Impact on Treatment Strategy *Journal of Surgical Oncology* 102;6:588-592

Design: Prospective Case Series

Country: South Korea

Setting:

Aim: to evaluate the role of chest CT on preoperative staging in rectal cancer patients and to assess the impact on treatment strategy.

Inclusion criteria
Patients with biopsy proven adenocarcinoma within 12cm of the anal verge

Exclusion criteria
Patients with tumour stage T1 or T2

Sample Size
N/A

Randomisation Method
N/A

Population
N=103

Study Duration
Patients were enrolled between September 2006 and October 2008

Interventions
Abdominal CT, pelvic MRI and/or ERUS
Plain chest PA/lateral X-ray and chest CT to evaluate lung metastases

Outcomes
The outcome for the study appears to be changes in management and/or treatment strategy based on scan results.

Results
Thoracic imaging was prospectively evaluated interpreted by two radiologists who were both blinded to the local staging of rectal tumour.
Radiologists were also blinded to the results of chest x ray when interpreting the CT scans

The patient population differed at baseline with more males (70%), more tumours located in the lower rectum (60%), more T3 tumours (78.8%) and more moderately differentiated tumours (60.6%). No p values for the differences were provided.

5 patients showed metastases on Chest X-ray compared with 9 patients on Chest CT.
Of the 73 patients with negative findings in X-ray, 2 were found to have evidence of metastases and 28 had indeterminate nodules on chest CT
22 patients had benign lesions on Chest X-ray of whom 1 had evidence of definite metastases and 10 had indeterminate nodules on Chest CT.
3 patients had indeterminate nodules on chest CT 1 of whom had evidence of definite metastases on CT.

9 patients had unequivocal metastases on chest CT of who 5 were identified by chest X-ray.

Of the 4 patients whose metastases were not identified on chest X-ray, treatment strategy changed in 3 as a result of the findings on Chest CT.

40 patients had indeterminate lesions on chest CT and follow-up scans were performed in 37/40 patients at 3 to 6 months intervals.
In 4 patients the lesion had grown and/or new lesions developed indicating the presence of lung metastases that could not initially be diagnosed.
3/4 patients showed no metastases on follow-up chest X-Ray.

Histopathological results were available for 99 patients and of these, 82 (82.2%) had the correct T stage in MRI

37 patients who had follow-up CT scan because of indeterminate nodule were analysed according to nodal status and in 4/12 patients who had positive lymph nodes, the indeterminate nodules had progressed.
No change was observed in any of the patients with N0 disease (n=25).

	CT				
CXR	**Negative**	**Benign**	**Indeterminate**	**Metastasis**	**Total**
Negative	40	3	28	2	73
Benign	3	8	10	1	22
Indeterminate	0	0	2	1	3
Metastasis	0	0	0	5	5
Total	43	11	40	9	103

Comparison between Chest CT and Chest X-Ray (CXR)

General comments

Chest images were graded as negative, benign, indeterminate or metastatic.
Follow up chest CT scans were performed in the indeterminate group at 3 to 6 month intervals; policy at the institute meant that locally advanced rectal cancers were selectively treated with preoperative long course chemoradiotherapy.
In the group of patients with preoperative chemoradiotherapy, follow up chest CT scans for indeterminate nodules were performed at 3 to 6 month intervals after primary tumour resection while in the patients undergoing preoperative chemoradiotherapy, follow-up scans were performed again before primary tumour resection.
For patients with no adjuvant chemotherapy, follow-up CT's were performed once while for patients receiving adjuvant chemotherapy, follow-up CT scans were performed at 3 to 6 month intervals during chemotherapy and 1-2 more follow-up scans were performed after treatment.

This is a poor quality study with no really clear aims and outcomes. It is difficult to draw any conclusions as to the appropriateness of using chest X-ray in the preoperative staging of pulmonary metastases.

Citation: Desai D, Zervos E, Arnold M, Burak W, Mantil J, Martin E (2003) Positron Emission Tomography Affects Surgical Management in Recurrent Colorectal Cancer Patients *Annals of Surgical Oncology* 10;1:59-64

Design: Case Series

Country: USA

Aim: To determine the effect of positron emission tomography (PET) on surgical decision making in patients with metastatic or recurrent colorectal cancer.

Inclusion criteria

Exclusion criteria
Patients with underlying inflammatory bowel disease and diabetes.

Population
N=114
N=89 with presumed recurrent colorectal cancer + N=25 with presumed isolated liver metastases.

Interventions
CT scan of the abdomen + whole body PET scan

Outcomes

Results
PET/CT Negative Correlation
42/114 patients had presumably resectable recurrences on CT scan. 17/42 patients had presumed isolated liver metastases by CT scan but had evidence of additional, extrahepatic disease rendering them unresectable on PET scan. PET scan found extrahepatic disease in the abdomen or chest in 14 patients, retroperitoneal disease in 2 as well as bilobar liver involvement in 3 patients.

PET/CR Positive Correlation
PET and CT were in agreement for 25 patients with no evidence of disease found in 13, 7 with isolated liver metastases and 5 with isolated foci of recurrent disease in the abdomen.

Patients with isolate liver disease by CT
25 patients had presumed isolated liver metastases on CT scan. PET findings correlated with CT in 7 patients, found additional disease in 17 patients and PET was negative in 1 patient with a positive CT.

Therapeutic decision making was altered in 17 of 42 potentially operable patients with information obtained from PET scans allowing surgery to be avoided in patients it could not help.

Information provided by PET scans complements that which is provided by CT scan.

General comments
All CT and PET scans were performed within 2 months of each other
Patients were evaluated by a single surgeon and PET scans were interpreted by two nuclear radiologists with PET expertise and who knew the results of the previous CT scan.

Citation: Imdahl A, Reinhardt MJ, Nitzche EU, Mix M, Dingeldey A, Einert A, Baier P, Farthmann EH (2000) Imapct of ^{18}F-FDG-positron emission tomography for decision making in colorectal cancer recurrences. *Langenbeck's Archives of Surgery* 385;129-134

Design: Prospective Case Series

Country: Germany

Aim: to evaluate the clinical impact of whole body ^{18}F-FDG-PET for the detection and localisation of tumour recurrence and tumour spread in patients with colorectal cancer.

Inclusion criteria
Patients suspected of having a tumour recurrence or metastases either due to imaging or raised CEA levels.

Exclusion criteria
Patients with elevated fasting blood glucose level or diabetes

Population
N=71 with suspected tumour recurrence or metastases either due to raised CEA level or to imaging methods.

Interventions
All patients received ^{18}F-FDG-PET, one received three investigations and three patients received two investigations.

Outcomes
Sensitivity
Specificity
Positive predictive value (PPV)
Negative predictive value (NPV)

Results
^{18}F-FDG-PET was performed in 14 patients due to raised CEA level, for suspicion of local recurrence or metastases in 33 patients and for staging in 24 patients. Results of ^{18}F-FDG-PET resulted in a change in the treatment strategy in 16 patients. The results for each patients group are not provided therefore it is not possible to determine the sensitivity and specificity of FDG-PET in relation to those patients with suspected metastases only.

Pulmonary metastases were demonstrated in 16 of 76 investigations (21%) while chest x-ray demonstrated pulmonary metastases in 9 of 69 (13%) patients but failed in 5 of 69 patients (7.2%). FDG-PET demonstrated pulmonary metastases in 5 patients with negative chest x-rays and missed a pulmonary lesion in one patient. CT scan was performed only in patients in whom a chest x-ray or FDG-PET was indicative of pulmonary metastases.

	FDG-PET (performed in 71 patients)	Chest X-Ray (performed in 69 patients)	CT (performed in 21 patients)
Sensitivity	0.94 (94%)	0.64 (64%)	1 (100%)
Specificity	1 (100%)	0.98 (98%)	1 (100%)
PPV	1 (100%)	0.9 (90%)	1 (100%)
NPV	0.98 (98%)	0.92 (92%)	1 (100%)

Table: Comparison of FDG-PET, CT and chest X-ray for the detection of pulmonary metastases

Note: the paper reports there to be 77 investigations and 17 pulmonary metastases however the numbers do not add up.

General comments
The paper is not solely concerned with the best imaging method for the detection of extra-hepatic metastases, the result reflect only the data that are related to the PICO in some way.

Care should be taken when interpreting the results of this study as CT scan was used as a confirmation procedure for patients showing evidence of metastases on FDG-PET or chest X-ray thus giving 100% sensitivity and specificity which is misleading.

Citation: Metser U, You J, McSweeny S et al (2010) Assessment of Tumour Recurrence in Patients with colorectal cancer and elevated carcinoembryonic antigen level: FDG PET/CT versus contrast enhanced 64-MDCT of the chest and abdomen *AJR* 194;766-771

Design: Retrospective case series

Country: Canada

Setting:

Aim: to compare the detection of tumour recurrence with FDG-PET/CT with detection with contrast enhanced 64-MDCT of the chest, abdomen and pelvis in patients with colorectal cancer and elevated CEA levels.

Inclusion criteria
History of colorectal cancer
Elevated or increasing CEA levels and conventional imaging did not reveal an unequivocal explanation for the raised CEA levels.

Exclusion criteria
None given

Sample Size
N/A

Randomisation Method
N/A

Population
N= 50

Study Duration
Recruitment occurred over a 30 month period

Interventions
FDG PET/CT
ceCT
Histopathologic exam (reference)

Outcomes
Sensitivity
Specificity

Results
50 patients with 55 PET/CT scans available for review underwent CECT of the chest, abdomen and pelvis within 60 days of PET/CT (mean=22days).
In 18 cases ceCT followed PET/CT and in 37 cases the PET/CT was performed before ceCT.
All patients were followed up for at least 6 months (median 12 months, range 6-31 months)

All PET/CT images were reviewed by two expert reviewers with all sites of abnormal FDG uptake recorded and graded as definite or equivocal for tumour. Abnormalities observed in the unenhanced CT portion of the PET/CT that were consistent with or equivocal for tumour recurrence were recorded.

Reviewers were aware of the patient history of colorectal cancer and elevated CEA levels but were blinded to patients' outcome clinical outcome, results of surgery or biopsy and subsequent imaging findings.

Event based analysis

19/55 events of CEA level had not recurred by final analysis; in 6 of these events, lesions identified with at least 1 technique were benign and 13 events, both PET/CT and ceCT showed no tumour. These patients underwent follow-up (clinical and imaging) for a mean period of 18 months (average, 18.5 months, range 6-31 months) without evidence of recurrence.
36/55 events had confirmed metastatic disease or recurrence.

For PET/CT and ceCT the sensitivities were 97.3% (95% CI, 85-99) and 70.3% (95% CI, 53-84) respectively (p=0.002) and the specificities were 94.4% (95% CI, 72-99) and 94.4% (72-99) respectively (p=1.0).

Tumour Site Based Analysis
61 suspicious tumour sited were identified on either PET/CT or ceCT, 54 of which were true positive for recurrent or metastatic colorectal cancer.

All tumour sites found at PET/CT were associated with abnormal FDG uptake apart from 2 metastatic lung lesions which were identified on the CT portion and on ceCT.

Sensitivity for PET/CT and ceCT was 98.1% (95% CI, 52-78%) respectively (p<0.0001) and the specificities were 75% (95% CI, 34-96%) and 62.5% (95% CI, 24-91) respectively (p=0.56).

General comments
This is a poor quality study with little to add to the overall body of evidence.

Citation: Potter KC, Husband JE, Houghton SL, Brown G (2009) Diagnostic accuracy of serial CT/Magnetic resonance imaging review vs. positron emission tomography/CT in colorectal cancer patients with suspected and known recurrence *Diseases of the Colon and Rectum* 52;2:253-259

Design: Case Series

Country: UK

Aim: to examine the sensitivity and specificity of CT/magnetic resonance imaging serial review compared to FDG-PET/CT to optimise colorectal cancer follow-up

Inclusion criteria
Patients undergoing follow-up for colorectal cancer via FDG-PET/CT imaging within 40 days of CT and/or MRI.
Patients referred for PET/CT to evaluate findings initially deemed to be equivocal on CT/MRI, to investigate unexplained CEA elevation or to exclude any further sites of recurrence prior to surgical resection of recurrence.

Exclusion criteria
Patients undergoing PET/CT for the evaluation of treatment
Patients whose imaging results were unavailable

Population
N=50

Interventions
FDG-PET/CT
CT/MRI

Outcomes
Accuracy
Sensitivity
Specificity

Results
FDG-PET/CT was performed in 20 patients to evaluate findings considered equivocal on CT/MRI, in 17 patients to investigate CEA levels and in 13 patients to exclude further sites of recurrence prior to potentially curative surgery.

There was no significant difference between FDG-PET/CT and CT/MRI in relation to accuracy, sensitivity or specificity (table).

	FDG-PET/CT		CT/MRI		
	N (%)	95% CI	N (%)	95% CI	P value
Accuracy	46/50 (92%)	81%-98%	46/50 (92%)	81%-98%	0.999
Sensitivity	20/23 (87%)	66%-97%	19/23 (83%)	61%-95%	0.999
Specificity	26/27 (96%)	81%-100%	27/27 (100%)	87%-100%	0.999

Table: Accuracy, sensitivity and specificity of FDG-PET/CT and CT/MRI

A significant difference was found in accuracy and sensitivity between the three individual readers of the CT/MRI scans, but no significant difference in specificity. Reader 1 and 2 h ad good agreement while reader 3 had poorer agreement with both reader 1 and reader 2.

	Reader 1		Reader 2		Reader 3		
	N (%)	95% CI	N (%)	95% CI	N (%)	95% CI	P value
Accuracy	44/50 (92)	76-95	43/50 (86)	73-94	35/50 (70)	55-82	0.012
Sensitivity	19/23 (83)	61-95	19/23 (83)	61-95	13/23 (57)	34-77	0.011
Specificity	25/27 (93)	76-99	24/27 (89)	71-98	22/27 (81)	62-94	0.556

Table: Accuracy, sensitivity and specificity among independent readers for CT/MRI

37 of 50 patients underwent FDG-PET/CT for apparently unexplained elevated CEA or equivocal CT or MRI results and careful reviewing of serial images using defined protocol enabled a definitive diagnosis to be made in 24 of the 37 patients.

7 false negative diagnoses were made on consensus imaging review and comprised 3 pelvic recurrences, a peritoneal recurrence, a patient with lung, liver and retroperitoneal lymph node recurrence and a patient with lung

metastasis. 2 of the three patients with pelvic recurrence had no pelvic MRI available for review which would have provided improved soft-tissue contrast and is more sensitive in identifying pelvic pathology.
No false positives were diagnosed on consensus serial imaging review although individual readers did make false positive errors.
There were 3 false-negative diagnoses on FDG-PET/CT, a patient with small lung metastases that were visible on serial CT/MRI imaging, a patient with peritoneal disease shown on CT and a patient with a large mucinous pelvic recurrence visible on MRI that did not show any activity on FDG-PET/CT.
There was one false positive diagnosis of pelvic recurrence on FDG-PET/CT, conventional CT and MRI were negative in this patient.

Citation: Schmidt GP, Baur-Melnyk A, Haug A, Utzschneider S, Becker CR, Tiling R, Reiser MF, Hermann KA (2009) Whole-body MRI at 1.5 T and 3 T compared with FDG-PET-CT for the detection of tumour recurrence in patients with colorectal cancer.

Design: Retrospective Case Series

Country: Germany

Aim: To compare the diagnostic potential of FDG-PET-CT and WB-MRI at 1.5 T and 3 T in patients with colorectal cancer and suspected tumour recurrence.

Inclusion criteria

Exclusion criteria
To avoid bias in diagnostic accuracy of PET-CT due to suppressed metabolic activity, patients receiving chemotherapy or radiotherapy immediately before or between examinations were excluded from statistical analysis.

Population
N=24 patients with a history of colorectal cancer.

Interventions
Whole body MRI at 1.5 T and at 3 T

FDG-PET-CT

Outcomes
Sensitivity
Specificity
Accuracy
Location, extension and number of suspected malignant legions

Results

Only results relating to distant metastases are presented.

A total of 83 distant lesions were observed from PET-CT and WB-MRI, 46 malignant and 37 benign. PET-CT detected 37 of the 46 malignant lesions while WB-MRI detected 36 of 46.

	PET-CT	WB-MRI
Sensitivity	80% (37/46)	78% (36/46)
Specificity	95% (35/37)	95% (35/37)
Accuracy	87% (72/83)	86% (71/83)

Table: Diagnostic accuracy, sensitivity and specificity for PET-CT and WB-MRI for the detection of distant metastases.

PET-CT revealed more lung metastases and was more sensitive to detecting peritoneal spread. WB-MRI revealed more metastases of the bone and when considering the full field of view of WB-MRI examination (covering the body from head to calves) additional metastatic disease was found in the brain in one patient.

General comments
Two certified radiologists read the MRI examinations and a third radiologist and a nuclear medicine physician read the PET-CT images; each group was blinded to the other investigation and had no knowledge of previous or current diagnostic imaging results.

The standard of reference was the confirmation of local recurrent tumour, node involvement and distant metastatic disease using radiological follow-up within at least five months.

Citation: Selzner M, Hany T, Wildbreet P, McCormack L, Zakiyah K, Clavien PA (2004) Does the novel PET/CT imaging modality impact on the treatment of patients with metstatic colorectal cancer of the liver *Annals of Surgery*240;6:1027-1036

Design: Prospective case series

Country: Switzerland

Aim: To compare the diagnostic value of contrast enhanced CT (ceCT) and 2-[18-F]-fluoro-2-deoxyglucose-PET/CT in patients with metastatic colorectal cancer to the liver

Inclusion criteria
Patients evaluated for resection of liver metastases from colorectal cancer

Exclusion criteria
Cases with synchronous metastases

Population
N=76

Interventions
Conventional work-up including ceCT of the chest and abdomen.
PET/CT

Outcomes
The primary outcome was to assess how PET/CT may change the indications for surgery compared with conventional radiology.

Secondary outcomes included the ability of ceCT and PET/CT to detect extrahepatic disease

Results
The presence of extrahepatic metastases was identified by ceCT and PET/CT in 24/76 (31%) and 34/76 (45%) patients respectively though the difference was not statistically significant (p=0.13).

In 66 patients with documented liver metastases, extrahepatic metastases were present in 36; ceCT failed to diagnose extrahepatic metastases in 13/36 (36%) (sensitivity 64%) whereas PET/CT failed to diagnose extrahepatic lesions in only 4/36 (11%) sensitivity 89%; p=0.02).

Lung metastases were present in 18 patients and all were correctly identified by PET/CT (sensitivity 100%) whereas ceCT detected only 14 (sensitivity 78%, p=0.1).
Portal and para-aortic lymph node metastases were present in 13 patients; PET/CT detected 10 (sensitivity 77%) and ceCT failed to identify lesions in 7 patients (sensitivity 46%, p=0.4).
Bone metastases were identified in 4 patients and PET/CT missed 1 while ceCT missed 2.

Extrahepatic metastases were identified in 9 of 18 patients with recent chemotherapy (within 1 month prior to PET). No FDG uptake was noted in 3 of the 9 patients (sensitivity 66%). In comparison, 27 of the remaining 58 patients without recent chemotherapy were identified with extrahepatic metastases. FDG uptake was negative in 1 patient (sensitivity 96%, p=0.05).

General comments
The primary focus of the study was not to compare imaging modalities in relation to their ability to detect extra-hepatic metastases; however as this was a secondary outcome the relevant data only have been presented here.

Each patient was evaluated for respectability of liver metastases and received a ceCT and a PET/CT within a period of two weeks.

Citation: Squillaci E, Maneti G, Mancino S, Ciccio C, Calabria F, Danieli R, Schillaci O, Simonetti G (2008) Staging of colon cancer: whole body MRI vs. whole body PET-CT – initial clinical experience *Abdom Imaging* 33:676-688

Design: case series

Country: Italy

Aim: to define the potential role of WB-MRI in staging and follow-up of patients diagnosed with CRC compared to morphological and functional findings of PET-CT.

Inclusion criteria
Patients with previously undiagnosed colorectal cancer

Exclusion criteria
Exclusion criteria were based on contraindications to MR imaging including the presence of a pacemaker, metallic implants in critical organs, severe claustrophobia and lack of willingness or ability to sign informed consent.

Population
N=20

Interventions
WB MRI
WB PET-CT

Outcomes

Results

WB MRI detected 19 pulmonary metastases in five patients, the smallest of which was 4mm in diameter. PET-CT detected 25 pulmonary metastases in 7 patients.
Nine bone metastases were detected on WB MRI in 3 patients.
One spine lesion was missed on PET-CT while a rib lesion was missed on WB MRI.
Peritoneal metastatic involvement was detected in two patients by both PET-CT and WB MRI.
No brain metastases were detected on WB MRI or PET-CT.

	PET-CT	WB-MRI
Brain	0	0
Lung	25	19
Bone	9	9
Other	5	5

Table: Number of extrahepatic metastases by site and imaging modality

General comments
The morphological and functional results obtained by PET-CT analysis were considered as the reference standard for the correct assessment of malignancy presence in the definitive interpretation of WB-MRI and relative diagnostic value.

WB-MRI exam was performed within 10 following PET-CT.

Both imaging modalities were performed without adverse effects in all patients.

Citation: Tanaka T, Kawai Y, Kanai M, Taki Y, Nakamoto Y, Takabayashi A (2002) Usefulness of FDG-positron emission tomography in diagnosing peritoneal recurrence of colorectal cancer. *The American Journal or Surgery* 184;433-436

Design: Case Series

Country: Japan

Aim: To compare sensitivity and accuracy of FDG-PET and CT in the diagnosis of peritoneal metastases of colorectal cancer.

Inclusion criteria

Exclusion criteria

Population
N=23

Interventions
FDG-PET
CT

Outcomes
Sensitivity
Accuracy

Results
Overall sensitivity and accuracy of FDG-PET were 95% and 93% respectively as compared with those of CT, sensitivity 83% and accuracy 83%.

Peritoneal Metastases
Peritoneal metastases were suspected in 9 sites of six patients with 8 of the 9 suspected lesions confirmed benign in 5 patients. Sensitivity and accuracy for CT and FDG-PET for the detection of peritoneal metastases is outlined in the table below.

	True Positive	False Positive	True Negative	False Negative	Sensitivity	Specificity	Accuracy
CT	3	0	1	5	3/8 (38%)	0/1 (0%)	4/9 (44%)
FDG-PET	7	1	0	1	7/8 (88%)	1/1 (100%)	7/9 (78%)

Table: Comparison of CT and FDG-PET for the detection of peritoneal metastases

FDG PET detected lesions 15mm in diameter whereas CT did not detect anything smaller than 30mm. In all of the 5 patients proved to have peritoneal metastases, FDG-PET identified at least some of the metastases in all patients compared to CT which detected metastases in only 2 of the 5 patients.

General comments
FDG-PET scanning was performed at an interval of at least six months following first operation.
All patients underwent CT scan within a month of the PET scan.
The PET and CT images were interpreted independently by at least two experienced radiologists.

Authors Conclusion: FDG-PET may be superior to CT in the detection of peritoneal metastases.

Citation: Valk P, Abella-Culmna E, Haseman M, Pounds T, Tesar R, Myers R, Greiss H, Hofer G (1999) Whole-body PET Imaging with [F^{18}] Fluorodeoxyglucose in Management of Recurrent Colorectal Cancer *Arch. Surg.* 134;503-511

Design: Prospective Case Series

Country: USA

Aim: To demonstrate the accuracy of PET in patients with known or suspected recurrent colorectal cancer.

Inclusion criteria

Exclusion criteria
Six patients with less than 1 year of follow-up after studies with negative findings.
Six patients lost to follow-up
Five patients died without validation of sites of tumour involvement
Four patients treated by radiation or chemotherapy without further validation of findings

Population
N=115

Interventions
FDG-PET
CT

Outcomes
Sensitivity
Specificity

Results
115 patients underwent both PET and CT and validation procedures established a diagnosis of recurrent tumour at 157 sites in 101 patients and no tumour recurrence in 14 patients.
Validated recurrence was found 149 of 171 sites that were abnormal PET, CT or both and at 8 sites that were normal by both modalities.
A final diagnosis of no recurrence was established at 22 sites of image abnormality, 17 of which were abnormal by CT only, 3 abnormal by PET only and 2 abnormal by both.
5 patients without recurrence and who had a normal PET and CT scan remained clinically disease free for more than 1 year after imaging.

104 sites were true positive for both PET and CT
48 sites were false negative by CT, 42 (88%) of these were true positive by PET
11 sites were false negative by PET, 5 (45%) of these were true positive by CT

PET was more sensitive than CT at all locations apart from the lungs (and liver though liver data have not been included due to not being relevant to this particular question).
PET was more specific that CT at all sites apart from the retopritoneum, though the only statistically significant difference was in the lungs.

Site	PET Scan (%)	CT Scan (%)	Difference % (95% CI)
Pelvis	30/31 (97)	21/31 (68)	11 (-1 to 22)
Abdomen	22/28 (79)	13/28 (46)	29 (9 to 49)
Retroperitoneum	12/12 (100)	7/12 (58)	33 (11 to 54)
Lungs	16/17 (94)	16/17 (94)	42 (10 to 74)
Other	12/12 (100)	4/12 (33)	0 (-19 to 19)
Total	92/100 (92)	61/100 (61)	31 (18 to 42)

Table: Sensitivity of PET and CT by site

Site	PET Scan (%)	CT Scan (%)	Difference % (95% CI)
Pelvis	81/84 (96)	76/84 (90)	6 (-2 to 13)
Abdomen	87/87 (100)	85/87 (98)	2 (-2 to 6)
Retroperitoneum	103/103 (100)	103/103 (100)	0 (0 to 0)
Lungs	97/98 (99)	94/98 (96)	3 (1 to 5)
Other	103/104 (99)	101/104 (98)	1 (-1 to 1)
Total	471/476 (99)	459/476 (96)	3 (1 to 4)

Table: Specificity of PET and CT by site

The positive predictive value of PET was 97% on a site by site basis and 97% patient by patient basis while the positive predictive value of CT was 85% (109/128) on a site by site basis and 93% (79/85) on a patient by patient basis.
The negative predictive value of PET was 69% (11/16) on a patient by patient basis, while for CT it was 24% (7/29).

The largest number of false negative CT findings occurred in the abdomen, retroperitoneum and pelvis with 30 of 71 disease sites (42%) not detected. 21 of these missed sites were positive on PET.

General comments
The interval between CT and PET ranged from 0 to 56 days, with a median interval of 22 days.

The diagnosis was established histologically at 103 sites, surgically at 93 sites and by needle biopsy at 10 sites. Abnormal imaging findings were validated by demonstration of progression or no progression at a second CT imaging. Clinical evidence of tumour progression was accepted as positive evidence at 20 sites of imaging abnormality. Clinical evidence of absence of disease was accepted as negative evidence at 13 sites of imaging abnormality and in 5 patients with normal PET and CT findings.

Citation: Votrubova J, Belohlavek O, Jaruskova M, Oliverius M, Lohynska R, Trskova K, Sedlackova E, Lipska L, Stahalova V (2006) The role of FDG-PET/CT in the detection of recurrent colorectal cancer *Eur J Nucl Med Mol Imaging* 33;779-784

Design: Retrospective Case Series

Country: Czech Republic

Aim: To compare the value of FDG-PET and PET/CT in the detection of colorectal cancer recurrence subsequent to colonic resection or rectal amputation.

Inclusion criteria
None given

Exclusion criteria
None given

Population
N=84

Interventions
FDG-PET/CT

Outcomes
Sensitivity
Specificity

Results
Intra-abdominal extra-hepatic recurrence (including metastases to the peritoneum)
33 patients had proven intra-abdominal extra-hepatic recurrence. 27 showed focally increase FDG uptake while 6 showed no pathological FDG uptake (false negative). 4/6 false negative results showed no pathological signs on CT scan.
Of the 51 patients with no recurrence, 45 had no signs of focally increased FDG uptake.
The sensitivity, specificity and accuracy of FDG uptake were 82%, 88% and 86% respectively.
The sensitivity, specificity and accuracy of integrated FDG-PET/CT for the detection of intra-abdominal extrahepatic recurrence were 88%, 94% and 92% respectively.

Extra-abdominal and/or hepatic recurrence
Extra-abdominal and/or hepatic recurrence was detected in 19 patients, with 14/19 patients showing increased FDG uptake.
The sensitivity, specificity and accuracy of focal FDG uptake were 74%, 88% and 85% respectively.
The sensitivity, specificity and accuracy of PET/CT were 95%, 100% and 99% respectively.
Integrated FDG-PET/CT achieved significantly higher specificity and accuracy in the diagnosis of extra-abdominal and/or hepatic recurrence of colorectal cancer and in the diagnosis of any form of colorectal cancer recurrence ($p<0.05$).

	Intra-abdominal extrahepatic	Extra-abdominal and/or hepatic	Any recurrence
Sensitivity			
FDG uptake	82% (27/33)	74% (14/19)	80% (36/45)
PET/CT	88% (29/33)	95% (18/19)	89% (40/45)
Specificity			
FDG uptake	88% (45/51)	88% (57/65)	69% (27/39)
PET/CT	94% (48/51	100% (65/65)	92% (36/39)
Accuracy			
FDG uptake	86% (72/84)	85% (71/84)	75% (63/84)
PET/CT	92% (77/84)	99% (83/83)	90% (76/84)

Table: Sensitivity, specificity and accuracy of FDG uptake and combined PET/CT

General comments
All patients underwent FDG-PET/CT no earlier than 1 month following surgery.

Final diagnosis was based on histology and/or follow-up information. The histological confirmations were obtained within 4 weeks of FDG-PET/CT and patients without histological confirmation were followed-up for a mean period of 6.5 months.

The data in this study are combined and it is not possible to elucidate sensitivity and specificity for specific extra-hepatic metastases alone, therefore the evidence from this study should be interpreted with caution when discussing the benefits of FDG-PET versus FDG-PET/CT.

Citation: Wiering B, Krabbe P, Jager G, Oyen W, Ruers T (2005) The impact of fluor-18-deoxyglucose-poitron emission tomography in the management of colorectal liver metastases; a systematic review and meta-analysis *Cancer* 104;12:2658-2670

Design: Systematic Review and meta-analysis

Country: Conducted in the Netherlands, studies included from various countries

Aim: To assess the usefulness of FDG-PET for the selection of patients to undergo resection for colorectal liver metastases.

Inclusion criteria
Articles concerning recurrent liver metastases and PET imaging from Medline and EMBASE up to January 2004. Articles were included only if they provided a description of the impact of FDG-PET results in patients with recurrent colorectal carcinoma or a description of the impact on clinical management of patients.

Exclusion criteria
Systematic review articles as the individual studies were included in the review.

Population
N=32 studies included in the systematic analysis with all selected articles scored according to a weighting procedure.

Interventions
FDG-PET
CT

Outcomes
Sensitivity
Specificity

Results

	FDG-PET (95% CI)	CT (95% CI)
Pooled Sensitivity	91.5% (84.3 to 96.2)	60.9% (44.4 to 68.9)
Pooled Specificity	95.4% (71.4 to 98.4)	91.1% (66 to 92.8)

Table: pooled sensitivity and specificity for FDG-PET and CT for extra-hepatic metastases

	FDG-PET (95% CI)	CT (95% CI)
Pooled Sensitivity	91.2% *From 4 studies*	55.3% *From 3 studies*
Pooled Specificity	98.4% *From 4 studies*	95.6% *From 3 studies*

Table: pooled sensitivity and specificity for FDG-PET and CT for extra-hepatic metastases using only data from the 6 highest scoring articles to be included in the review.

General comments
The main focus of the review was to address the usefulness of FDG-PET in determining best management for patients with recurrent liver metastases, part of which addressed the effectiveness of FDG-PET in detecting extra-hepatic metastases. Only data relating to extrahepatic metastases are presented here.

The authors devised a system to compare, weight and summarise the data from different studies. This was done in a stepwise process:

1) A panel of experts consisting of a hepatic surgeon, a nuclear medicine physician, a methodologist and a radiologist constructed a concept study containing all items that should be included and weighted. The experts identified 5 different domains, each containing several items (detailed in the paper).
2) Every item in a domain was weighted (5-very significant to 1-not significant) by each individual member of the team and a consensus was achieved on the final weight factor of each item.
3) All articles were screened for the presence of the selected items. When an item was not available no points were awarded, in articles in which an item was covered partially 0.5 points were awarded and in articles where an item was present and reported 1 point was awarded.
4) The awarded points for each item were multiplied by the weight factor to achieve a final value per item and a total number of points per domain were calculated.

The scoring system was not designed to assess the quality of the individual studies, merely the contribution a given study made in addressing the usefulness of FDG-PET, that said there were no randomised trials with which to answer the question and therefore the studies included were of a generally low quality (prospective or retrospective case series) with small numbers (smallest study n=8, largest study n=115).

Several gaps in the literature were identified including a lack of randomised controlled trials. The included studies also failed to include a number of relevant items of information such as xo-morbidities, patient selection criteria and characteristics of primary tumour.

Author Conclusion: Despite apparent omissions in the literature, the pooled results indicate FDG-PET is useful in the diagnostic workup of patients with potentially resectable hepatic metastases from colorectal carcinoma, particularly in the detection of extrahepatic metastases which would preclude liver resection.

References of Included Studies (For systematic reviews):
A total of 32 studies were included in the review the citations for the six highest scoring studies (as determined by the authors) are:

Fong Y, Saldinger PF, Akhurst T, et al. (1999) Utility of 18F-FDG positron emission tomography scanning on selection of patients for resection of hepatic colorectal metastases *Am J Surg* 178;282-287

Imdahl A, Reinhardt MJ, Nitzsche EU, et al. (2000) Impact of 18F-FDG-positron emission tomography scanning for decision making in colorectal cancer recurrences. *Langenbecks Arch Surg* 385;129-134

Lai DT, Fulham M, Stephen MS, et al. (1996) The role of whole body positron emission tomography with [18F]fluorodeoxyglucose in identifying operable colorectal cancer metastases to the liver.

Langenhoff BS, Oyen WJ, Jager GJ, et al. (2002) Efficacy of fluorine-18-deoxyglucose positron emission tomography in detecting tumour recurrence after local ablative therapy for liver metastases: a prospective study *J Clin Oncol* 20;4453-4458

Ruers TJ, Langenhoff BS, Neeleman N, et al. (2002) Value of positron emission tomography with [F-18]fluorodeoxyglucose in patients with colorectal liver metastases: a prospective study *J Clin Oncol* 20;388-395

Valk P, Abella-Culmna E, Haseman M, et al (1999) Whole-body PET imaging with [F^{18}] fluorodeoxyglucose in management of recurrent colorectal cancer *Arch. Surg.* 134;503-511