Evidence Tables

Citation: Bipat S, van Leeuwen MS, Comans EF, Pijl ME, Bossuyt PM, Zwinderman AH, Stoker J. Colorectal liver metastases: CT, MR imaging, and PET for diagnosis. Meta-analysis (DARE structured abstract). Radiology 2005; 237:123-131

Design: systematic review and meta-analysis (search ended Jan 2004)
Country: the Netherlands

Aim: to perform a meta-analysis to obtain sensitivity estimates of CT, MRI, and, FDG-PET for detection of colorectal liver metastases on per-patient and per-lesion basis.

Inclusion criteria

- Articles reported in English, French or German languages
- CT, MRI, or FDG-PET were used to identify and characterise colorectal liver metastases
- Histopathological analysis (performed at surgery, biopsy, and autopsy), intra-operative observation (manual palpation or intra-operative ultrasound), and/or follow up were used as the reference standard
- Sufficient data was present to calculate the true positive and false negative valuses for imaging techniques
- When data or subsets of data were presented in more than one article, the article with the most details or the most recent article was selected.

Exclusion criteria

- If results of different imaging modalities were presented in combination and could not be differentiated for performance assessment of an individual modality.
- Review articles, letters, comments, articles that did not include raw data were not selected.

Population
61 articles fulfilled the inclusion criteria, 3187 patients in total.
Patients with colorectal cancer
Age range 12-93, age mean 61
In 57 studies the gender was reported. 1733 patients were male and 1128 were female

Interventions
CT

- Non-helical (1915 patients), helical (621 patients)
- the range of section thickness was 5-12mm, median 10mm
- the range in the amount of iodine contrast given (reported in 23 studies) was 30-60g

MRI

- 1.0T (173 patients), 1.5T (391 patients)
- the range in section thickness was 5-10mm, median 10mm
- 15 studies used gadolinium as contrast or other liver specific agents such as SPIO

FDG-PET (1058 patients)

Outcomes
Sensitivity on per patient and per lesion basis

Results

Per patient analysis	Sensitivity%	95% confidence interval	P value
Non-helical CT	60.2%	55.7%-64.6%	
Helical CT	64.7%	30.4%-88.5%	
1.5 T MRI	75.8%	55.9%-88.6%	
FDG-PET	94.6%	92.5%-96.1%	PET had highest sensitivity compared to non-helical CT P<0.001 helical CT p=0.003 1.5T MRI p<0.001

Per lesion analysis			
Non helical CT	52.3%		Nonhelical CT had lowest sensitivity compared to Helical CT p<0.017 1.0 T MRI p<0.001 1.5 T MRI p<0.001 FDG PET p<0.003
Helical CT	63.8%		
1.0 T MRI	66.1%		
1.5 T MRI	64.4%		
FDG -PET	75.9%		

Subgroup analysis 1

Helical CT	Sensitivity	
<5mm section thickness	68.2%	
>5mm section thickness	69.1%	
<45g iodine contrast	61.4%	
>45 g iodine contrast	64.0%	
One phase CT	71.4%	
two phase CT	65.7%-not significant	
1.5T MRI		
Non-enhanced	59.8%	
Gadolinium enhanced	78.2%	Higher compared to non enhanced MRI p=0.19 helical CT <45g iodine p=0.02
SPIO enhanced	73.2%	Higher compared to non enhanced MRI p<0.001 helical CT <45g iodine p<0.001

Subgroup Analysis 2

Non helical CT	sensitivity	95% confidence interval	
Lesions<1cm	25.3	15.9-37.6	
Lesions >1cm	74.3	66.5-80.9	
Helical CT			
Lesions <1cm	23.1	7.0-54.7	
Lesions >1cm	73.5	62.2-82.4	
Non enhanced MRI			
Lesions <1cm	12.6	8.0-17.5	
Lesions >1cm	65.7	56.4-73.9	
Gadolinium MRI			
Lesions <1cm	11.6	9.5-14.2	
Lesions>1cm	68.8	61.9-75.0	
SPIO MRI			
Lesions <1cm	29.3	18.2-43.6	
Lesions >1cm	90.2	87.5-92.4	Higher p<0.001

General comments

Conclusion: PET has higher sensitivity on a per patient basis but not on a per lesion basis. On a per lesion basis the modalities are comparable but all significantly more accurate than non-helical CT. Subgroup analyses showed no difference between section thickness, amount of iodine, numbers of phases for helical CT. Gadolinium and SPIO MRI however were better compared to non-enhanced MRI and helical CT with 45g or less of iodine.

References of Included Studies (For systematic reviews):

Citation: Wiering B, Krabbe PF, Jager GJ, Oyen WJ, Ruers TJ. The impact of fluor-18-deoxyglucose-positron emission tomography in the management of colorectal liver metastases: a systematic review and metaanalysis (DARE structured abstract). Cancer 2005; 104:2658-2670

Design: systematic review and meta-analysis (search ended Dec 2003)
Country: The Netherlands

Aim:

- to identify how the descriptive statistics (sensitivity and specificity) for FDG-PET compare with those for CT in the assessment of both hepatic and extra-hepatic metastases.
- To identify whether FDG-PET has a significant impact on change in management.

Inclusion criteria

- Articles that included either a description of the impact of FDG-PET on clinical management or a description of imaging results for FDG-PET.

Exclusion criteria

Population
32 articles were included

Interventions
FDG-PET
CT

Outcomes
Sensitivity and specificity of CT scanning for extra and intra hepatic disease
Sensitivity and specificity of FDG-PET for extra and intra hepatic disease
Change in management for FDG-PET.

Results

Hepatic lesions	Sensitivity and 95% CI	Specificity and 95% CI
FDG PET	88.0% (CI 88%-98%)	96.1% (CI 70.4%-?)
CT	82.7% (CI 64.2%-88.6%)	84.1% (CI 68.2%-97.0%)
Extra hepatic lesions		
FDG PET	91% (CI 84.3%-96.2%)	95% (CI 71.4%-98.4%)
CT	60.9% (CI 44.4%-68.9%)	91.1% (CI 66.0%-92.8%)

Per lesion analysis

Hepatic lesions	Sensitivity	Specificity
FDG PET	79.9%	92.3%
CT	85.8%	88.3%
Extra hepatic lesions		
FDG PET	91.2%	98.4%
CT	55.3%	95.6%

Subgroup analysis (only the 6 high quality diagnostic studies)

In this analysis it is evident that FDG PET has value in the detection of extrahepatic disease compared to CT.

On a patient basis there is a >25% change in clinical management after FDG PET. This however is attributable mostly to the detection of extra hepatic disease, which generally precludes liver resection.

General comments
Despite omissions and quality issues in the diagnostic literature the pooled sensitivity of FDG PET indicates it has added value in the workup of patients with liver metastases.

Citation: Akiyoshi T, Oya M, Fujimoto Y, Kuroyanagi H, Ueno M, Yamaguchi T, Koyama M, Tanaka H, Matsueda K, Muto T. Comparison of preoperative whole-body positron emission tomography with MDCT in patients with primary colorectal cancer. Colorectal Disease 2009; 11:464-469

Design: retrospective
Country: Japan

Aim: to evaluate the additional value of FDG PET in comparison with multidetector row CT (MDCT) in patients with primary colorectal cancer

Inclusion criteria
65 patients with histologically proven colorectal cancer
patients with suspected liver or lymph node metastases
or patients with CEA >5ng/ml
or patients with low rectal cancer awaiting pre op chemoradiotherapy to check lateral lymph node metastases.

Exclusion criteria
Not specifically mentioned.

Population
65 patients (36 men, 29 women)
characteristics as in the inclusion criteria

Interventions
MDCT
FDG PET

Outcomes
Sensitivity, specificity, PPV, NPV, Accuracy

Results

	Liver mets +	Liver mets -	total
CT +	22	1	23
CT -	0	42	42
total	22	43	65

2x2 table

Sensitivity	100% (22/22) (CI 85%-100%)
Specificity	98% (42/43) (CI 88%-100%)
PPV	96% (22/23) (CI 78%-100%)
NPV	100% (42/42) (CI 92%-100%)
Accuracy	98% (64/65) (CI 92%-100%)

	Liver mets +	Liver mets -	total
FDG PET +	20	0	20
FDG PET -	2	43	45
total	22	43	65

Sensitivity	91% (20/22) (CI 91%-99%)
Specificity	100% (43/43) (CI 92%-100%)
PPV	100% (20/20) (CI 83%-100%)
NPV	96% (43/45) (CI 85%-99%)
Accuracy	97% (63/65) (CI 89%-100%)

FDG PET failed to identify liver metatases detected by MDCT in two patients.

General comments
CT appears sufficient for detection of metastases in the liver. The strength of PET is in the ability to screen for extraheaptic metastases and this is what leads to the change in management.

Citation: Arulampalam THA. FDG-PET for the pre-operative evaluation of colorectal liver metastases. Eur.J.Surg.Oncol. 2004; 30:286-291

Design: prospective
Country: Royal Free Hospital, UK

Aim: To assess the accuracy of routine whole body FDG PET in the pre operative staging of patients with colorectal liver metastases.

Inclusion criteria
Patients referred to a single surgeon for consideration for resection of colorectal liver metastases.
Sep 1999-May 2002
Patients had both FDG PET and spiral CT.

Exclusion criteria

Population
31 patients were studied. (median age 67, range 41-82), 15 male.
28 patients had a lesion on both PET and CT. This was considered the index lesion and only these patients were considered for assessment by resection. Follow up was for 21 months (range 5-33)
No loss to follow up.

Interventions
FDG PET
CT

Outcomes

Results
Accuracy of FDG PET and CT in detecting additional metastatic lesions in 28 patients with confirmed colorectal liver metastases.

	Liver mets +	Liver mets -	total
CT +	8	1	9
CT -	9	10	19
total	17	11	28

Sensitivity	47%
Specificity	91%
PPV	89%
NPV	53%

	Liver mets +	Liver mets -	total
FDG PET +	17	1	18
FDG PET -	0	10	10
total	17	11	28

Sensitivity	100%
Specificity	91%
PPV	94%
NPV	100%

11 patients were confirmed to have solitary liver met correctly demonstrated by both modalities.
10 patients were noted to have multifocal liver mets. All were correctly diagnosed by PET. CT was only able to identify multiple lesions in the 5 patients. In 4 of these patients PET showed lesions that were not amenable to surgery. In the 5th patient laparotomy was performed. The sencond PET lesion was not found but later identified on the follow up imaging at 3 months.

There was altered patient management in 12 patients (including the extrahepatic disease results) 39%.

General comments

FDG PET greatly adds to the decision making power of the surgical oncologist.

Citation: Ashraf K. Colorectal carcinoma, preoperative evaluation by spiral computed tomography. Journal of the Pakistan Medical Association 2006; 56:149-153

Design: cross sectional prospective
Country: Pakistan

Aim: to assess the capability of spiral CT in preoperative evaluation of colorectal carcinoma. (local spread, lymph node mets and liver mets).

Inclusion criteria
Patients with biopsy proven colorectal cancer undergoing surgery
All patients must have had the CT scan within 1 month prior to surgery

Exclusion criteria
Patients that had previous treatment for colorectal cancer or had concurrent disease process which could result in false reading of the CT scan

Population
52 patients (32 male, 20 female,)
mean age was 58, range 22-87

Interventions
Spiral CT scan, 7mm, with gastrografin
1 radiologist reading the images
not blinded to the location of the primary tumour or the biopsy result.

Outcomes

Results

	Liver mets +	Liver mets -	total
CT+	16	2	18
CT -	2	32	34
total	18	34	52

Sensitivity	89% (CI 63.9%-98.1%)
Specificity	94% (CI 78.9%-99.0%)
PPV	89% (CI 63.9%-98.1%)
NPV	94% (CI 78.9%-99.0%)
Accuracy	92%

Citation: Bartolozzi C, Donati F, Cioni D, Procacci C, Morana G, Chiesa A, Grazioli L, Cittadini G, Cittadini G, Giovagnoni A, Gandini G, Maass J, Lencioni R. Detection of colorectal liver metastases: a prospective multicenter trial comparing unenhanced MRI, MnDPDP-enhanced MRI, and spiral CT. Eur.Radiol. 2004; 14:14-20

Design: prospective, multi-institutional trial
Country: Italy

Aim: to compare unenhanced MRI, MnDPDP-enhanced MRI and spiral CT in the detection of hepatic colorectal metastases.

Inclusion criteria
Adult patient with hepatic colorectal cancer metastasis
Patient scheduled for partial hepatectomy or itra operative radio frequency thermal ablation

Exclusion criteria
Pregnant or lactating woman
Severe biliary or renal insufficiency
Severe hepatic dysfunction (Child class C)
General contraindication to MRI
Inclusion in another study 7 days prior to enrollment

Population
44 consecutive patients with colorectal hepatic metastases were examined with all 3 above modalities.
3 blinded readers interpreted the images

Interventions
- unenhanced MRI
- MnDPDP-enhanced MRI
- spiral CT

Outcomes
primary endpoint
- Sensitivity

Secondary outcome
- Lesion conspicuity
- quality of lesion delineation
- confidence in diagnosis

Results

Per patient analysis

	Liver mets +	Liver mets -	total
CT+	22	3	25
CT -	19	0	19
total	41	3	44

Sensitivity	53.6%
Specificity	NA%
PPV	88.0%
NPV	NA%
Accuracy	50.0%

	Liver mets +	Liver mets -	total
MRI +	21	2	23
MRI -	21	0	21
total	42	2	44

Sensitivity	50.0%
Specificity	NA%
PPV	91.3%
NPV	NA%

Accuracy	47.7%

	Liver mets +	Liver mets -	total
MnDPDP MRI +	33	2	35
MnDPDP MRI -	9	0	9
total	42	2	44

Sensitivity	78.6%
Specificity	NA%
PPV	94.2%
NPV	NA%
Accuracy	75.0%

Per lesion analysis

	Liver mets +	Liver mets -	total
CT+	91	3?	94
CT -	37	0?	37
total	128	3?	141

Sensitivity	71%
Specificity	%
PPV	%
NPV	%
Accuracy	%

	Liver mets +	Liver mets -	total
MRI +	92	2?	
MRI -	36	0?	
total	128	2?	

Sensitivity	72%
Specificity	%
PPV	%
NPV	%
Accuracy	%

	Liver mets +	Liver mets -	total
MnDPDP MRI +	115	2?	
MnDPDP MRI -	13	0?	
total	128	2	

Sensitivity	90%
Specificity	%
PPV	%
NPV	%
Accuracy	%

Lesion size	IOUS	CT	MRI	MnDPDP MRI
<10mm	47	18(38%)	24(51%)	39(83%)
10-20mm	31	28 (90%)	24 (77%)	31(100%)
>20mm	45	45 (100%)	44 (98%)	45(100%)
All	128 (*)	91(71%)	92 (72%)	115 (90%)

* 47+31+45 = 123 not 128. this is in all the text and tables. ??? either the 128 is a typo and all their calculations of sensitivities are based on the wrong number or one of the sums is a typo.

- MnDPDP MRI is more sensitive than both CT (P=0.0007) and unenhanced MRI (P<0.0001) in the per lesion analysis.
- In the very small lesions the sensitivity difference is even more manifest.
- In the per patient analysis MnDPDP MRI sensitivity was higher than CT (p=0.0023) and unenhanced MRI (p=0.0013).

General comments

MnDPDP MRI is better than CT and unenhanced MRI.

Citation: Bhattacharjya S. B. Prospective study of contrast-enhanced computed tomography, computed tomography during arterioportography, and magnetic resonance imaging for staging colorectal liver metastases for liver resection. Br.J.Surg. 2004; 91:1361-1369

Design: prospective
Country: UK

Aim: To compare the value of contrast-enhanced CT, CT during arterioportography, and magnetic resonance imaging for staging patients with colorectal liver metastases.

Inclusion criteria
Consecutive patients between January 1996 – December 2001 with known or suspected colorectal liver metastases.

Exclusion criteria

- Pulmonary metastases
- Intra-abdominal extrahepatic disease

All patients without evidence of extrahepatic disease on imaging underwent laparotomy.
Diagnostic laparoscopy was performed before the laparotomy in 54 patients. Suspicious nodules were biosied and sent for frozen section.confirmation of extrahepatic disease contraindicated liver resection.

- Local recurrence or metachronous primaries (all patients had colonoscopy to exclude this)
- Medical contraindications to MRI (pacemaker, claustrophobia)
- Medical contraindication to surgery

Population
120 patients with known or suspected colorectal liver metastases.
64 men / 56 women mean age 62 (29-74)
31 synchronous metastases – 89 metachronous metastases
85 patients had all three modalities and were finally included in the study population.
120 patients referred for consideration for resection.
120 had CT chest abdo pelvis
13 excluded after CT as either unfit for surgery or have pulmonary mets
15 do not have an MRI due to contraindications
92 have MRI.
54 of the 107 patients that had a CT and were fit for surgery proceed to have laparoscopy (as part of another study being carried out in the unit)
7 are excluded because of peritoneal mets
100 patients proceed to laparotomy, bimanual palpation and IOUS.
11 were opened and closed as they either had positive lymph nodes (4 – included in the study) or additional mets or unfavourable positioned mets.
89 patients went on to have liver resection

Interventions
Spiral contrast-enhanced CT (dual phase)
Contrast-enhanced MRI (gadolinium)
CTAP
MRI and CTAP were performed within 3 weeks of CT.
Gold standard: intraoperative ultrasound IOUS, bimanual palpation, histology of resected specimen.

The films were reviewed by one of two consultant hepatobiliary radiologists. They were blinded to the clinical history, the surgical and the pathological findings. The IOUS was performed by surgeons competent in this imaging modality and they were aware of the pre-operative findings. The pathologist that performed the histology of the resected specimens was blinded

Outcomes
Per lesion basis analysis

- Sensitivity
- Specificity
- Positive predictive value

Per patient basis analysis

Results
The results for CTAP have been excluded from this summary as not relevant to our PICO.

It has also not been possible to extract all the information for the 2x2 tables but the summary diagnostic values have been presented.

Per lesion analysis

	Liver mets +	Liver mets -	total
CT+	176	20	196
CT -	65		
total	241		

Sensitivity	73%
Specificity	96.5%
PPV	89.8%
NPV	%
Accuracy	%

	Liver mets +	Liver mets -	total
GAD MRI+	154	22	176
GAD MRI-	34		
total	188		

Sensitivity	81.9%
Specificity	93.2%
PPV	87.5%
NPV	%
Accuracy	%

Lesion size	TOTAL	CT	GAD MRI
<10mm	42	22 of 42 (52%)	16 of 28 (57%)
>10mm	199	154 of 199 (77.4%)	138 of 150 (92%)
All	241	176 of 241 (73%)	154 of ? (86.3%)

Per patient analysis

	Liver mets +	Liver mets -	total
CT+		16	
CT -	21		
total			85?

Sensitivity	73.0%
Specificity	%
PPV	%
NPV	%
Accuracy	Area under ROC curve 0.73

	Liver mets +	Liver mets -	total
GAD MRI+		18	103
GAD MRI-	16		
total	101		85?

Sensitivity	82%
Specificity	%
PPV	%
NPV	%
Accuracy	Area under ROC curve 0.82

Detection of liver metastases by various imaging modalities on an individual patient basis stratified by number of lesions.

Modality	No of patients examined	No correctly identified	No understaged	No overstaged
Solitary liver met				
CT	40	35	1	4
MRI	41	28	1	2
2 liver mets				
CT	28	24	3	1

MRI	22	19	1	2
3 liver mets				
CT	16	8	4	4
MRI	16	14	1	1
4 liver mets				
CT	7	4	0	3
MRI	7	3	2	2
5 liver mets				
CT	2	1	1	0
MRI	2	1	1	0
≥ 6 liver mets				
CT	7	1	6	0
MRI	7	4	3	0

Based on these results MRI is significantly superior to spiral CT (p=0.043) in staging colorectal cancer liver metastases on an individual patient basis once the number of metastases exceeds 4.

No single modality diagnosed all hepatic metastases and a multimodal imaging approach is recommended.

General comments

The diagnostic accuracy of these modalities is similar.

Citation: Cantwell CP, Setty BN, Holalkere N, Sahani DV, Fischman AJ, Blake MA. Liver Lesion Detection and Characterization in Patients With Colorectal Cancer: A Comparison of Low Radiation Dose Non-enhanced PET/CT, Contrast-enhanced PET/CT, and Liver MRI. J.Comput.Assist.Tomogr. 2008; 32:738-744

Design: retrospective
Country: Boston,USA

Aim: To compare low-radiation dose non-enhanced FDG-PET/CT, contrast-enhanced FDG-PET/CT and gadolinium-enhanced liver MRI for the detection and characterisation of liver lesions in patients with colorectal cancer.

Inclusion criteria
Patients with colorectal cancer who had a gadolinium-enhanced MRI within 6 weeks of the PET/CT scan.
The follow up diagnosis of the liver lesion must have been established either through histology of resected specimen or through imaginf follow up of at least 6 months for lesion stability or growth.
Patient should have at least 1 but no more than 10 liver lesions

Note: previous hepatic resection and previous chemotherapy was allowed.

Exclusion criteria
More than 10 liver lesions (possibility of lesion overlap).

Population
33 non-consecutive patients (22 men, 11 women, mean age 63 years)
retrospective review of imaging database of patients with colorectal cancer with suspected liver metastases from one institution in Boston Massachusetts from Jan 2004 to Dec 2005

Interventions
low-radiation dose non-enhanced FDG-PET/CT
contrast-enhanced FDG-PET/CT
gadolinium-enhanced liver MRI

Data were analysed by 2 radiologists. Patient demographic data was blinded as was clinical data. All data was interpreted in consensus.

Outcomes
Sensitivity
Specificity
accuracy

Results

Per lesion analysis

	Liver mets +	Liver mets -	total
Gad MRI +	98	0	98
Gad MRI -	2	10	12
total	100	10	110

Sensitivity	98%
Specificity	100%
PPV	100%
NPV	83%
Accuracy	98%

	Liver mets +	Liver mets -	total
PET CT+	85	0	85
PET CT -	15	10	25
total	100	10	110

Sensitivity	85%
Specificity	100%
PPV	100%
NPV	40%
Accuracy	86%

	Liver mets +	Liver mets -	total
Ne PET CT+	67	4	71
Ne PET CT -	33	6	39
total	100	10	110

Sensitivity	67%
Specificity	60%
PPV	94%
NPV	15%
Accuracy	66%

- No statistical significant difference in lesion detection was found between enhanced PET CT and MRI.
- Both PET CT and MRI had a higher detection rate than non-enhanced PET-CT.
- For lesion characterisation MRI was significantly more accurate than PET CT enhanced and non-enhanced. In turn enhanced was better than non-enhanced PET-CT.

General comments

Contrast enhanced PET CT is better than unenhanced PET CT.
MRI and contrast enhanced PETCT are comparable in their detection rate
MRI is better than contrast enhanced PETCT with regard to lesion characterization.

Citation: Chua SC, Groves AM, Kayani I, Menezes L, Gacinovic S, Du Y, Bomanji JB, Ell PJ. The impact of F-18-FDG PET/CT in patients with liver metastases. European Journal of Nuclear Medicine and Molecular Imaging 2007; 34:1906-1914

Design: retrospective
Country: UCLH London, UK

Aim: To assess the performance of PETCT versus contrast enhanced CT in the detection of colorectal liver disease.

Inclusion criteria
All patients that presented to one institution with suspected metastatic disease who underwent both PETCT and CT within 6 weeks of each other were retrospectively analysed covering a 5 year period.

Exclusion criteria

Population
131 patients
67 men, 64 women
mean age 62 (range 30-85 years)
75 had primary CRC
56 had other malignancies
patients were either pre chemotherapy or minimum 6 weeks post chemo

Interventions
CECT (contrast enhanced CT)
FDG PET CT

Outcomes
Sensitivity, specificity, PPV, NPV
Subgroup analysis for those patients that had undergone chemotherapy (as this has the potential to alter the PET CT results

Results
Colorectal malignancy results only

Per patient analysis

	Liver mets +	Liver mets -	total
PET CT+	63	2	65
PET CT -	4	6	10
total	67	8	75

Sensitivity	94% (CI 85%-98%)
Specificity	75% (CI 34%-96%)
PPV	97% (CI 89%-99%)
NPV	60% (CI 26%-87%)
Accuracy	%

	Liver mets +	Liver mets -	total
ceCT+	61	6	67
ceCT -	6	2	8
total	67	8	75

Sensitivity	91% (CI 81%-96%)
Specificity	25% (CI 3%-65%)
PPV	91% (CI 81%-96%)
NPV	25% (CI 3%-65%)
Accuracy	%

Subgroup analysis for patients that had and didn't have chemotherapy prior to PETCT scanning.

Sensitivity -chemo	89% (CI 51%-99%)
Sensitivity – no chemo	95% (CI 85%-98%)

Specificity - chemo	100% (CI 29%-100%)
Specificity – no chemo	60% (CI 14%-94%)
PPV - chemo	100% (CI 63%-100%)
PPV – no chemo	97% (CI 87%-99%)
NPV - chemo	75% (CI 19%-99%)
NPV – no chemo	50% (CI 11%-88%)
Accuracy	%

Chemotherapy did not statistically significantly impact on the diagnostic accuracy of FDG PET CT p=0.178

General comments

FDG PETCT is more accurate than ceCT in the detection of metastatic liver disease both from colorectal cancer and from other malignancies. (only colorectal results presented here.)

When the detection of extrahepatic disease was also taken into account there was a change in management from the use of PETCT of about 25% (33 patients).

Citation: Coenegrachts K, De GF, ter BL, Walgraeve N, Bipat S, Stoker J, Rigauts H. Comparison of MRI (including SS SE-EPI and SPIO-enhanced MRI) and FDG-PET/CT for the detection of colorectal liver metastases. Eur.Radiol. 2009; 19:370-379

Design: pprospective
Country: Belgium and the Netherlands

Aim: To prospectively compare the FDG-PET/CT and MRI in 24 consecutive patients suspected of having colorectal liver metastases.

Inclusion criteria
USS shows new non-cyctic focal lesion
And / or CEA >3.4ng/ml for non-smokers, >4.3 ng/ml for smokers
ALT>41 U/L for males, >31 U/L for females
ALP >129 u/l
And /or bilirubin >1.2mg/dl
Time interval between MRI and FDG PET/CT was at most 3 weeks.

Note: patients that had previously received chemotherapy for their colorectal malignancy were included including those in which the treatment was within a month of the PET.

Exclusion criteria
Contraindications to MRI e.g. pacemaker,metalic implants

Population
14 men, 10 women with suspected colorectal cancer liver metastases
mean age 65.3 +/- 10.8 years
consecutive presentation between Oct 2005-Jan 2008

Interventions
FDG-PET/CT
MRI
All patient data were blinded. Blinded evaluations were done by 2 radiologists independently. In case of disagreement a consensus opinion was reached.

Reference standard: for lesions that were operated on intraoperative ultrasound scan and the histology result
For lesions that were not operated on follow up was with repeat MRI.

Outcomes
Sensitivity (per lesion and per patient analysis)
Positive Predictive Value PPV (per lesion and per patient analysis)

Results

Per patient analysis

	Liver mets +	Liver mets -	total
EPI MRI+	24	0	24
EPI MRI -	0	0	0
total	24	0	24

Sensitivity	100%
Specificity	na
PPV	100%
NPV	na
Accuracy	100%

	Liver mets +	Liver mets -	total
SPIO MRI +	24	0	24
SPIO MRI -	0	0	0
total	24	0	24

Sensitivity	100%
Specificity	na
PPV	100%

NPV	na
Accuracy	100%

	Liver mets +	**Liver mets -**	**total**
PET CT +	23	0	23
PET CT -	1	0	1
total	24	0	24

Sensitivity	96%
Specificity	na
PPV	100%
NPV	na
Accuracy	96%

Per lesion analysis

MRI and PETCT concordant in 9 patients

MRI identified more liver mets than PETCT

	Liver mets +	**Liver mets -**	**total**
EPI MRI+	77	0	77
EPI MRI -	0	0	0
total	77	0	77

Sensitivity	100%
Specificity	na
PPV	100%
NPV	na
Accuracy	100%

	Liver mets +	**Liver mets -**	**total**
SPIO MRI +	69	0	69
SPIO MRI -	8	0	8
total	77	0	77

Sensitivity	90%
Specificity	na
PPV	100%
NPV	na
Accuracy	90%

	Liver mets +	**Liver mets -**	**total**
PET CT +	47	0	47
PET CT -	30	0	30
total	77	0	77

Sensitivity	61%
Specificity	na
PPV	100%
NPV	na
Accuracy	61%

Citation: Kim HJ, Kim KW, Byun JH, Won HJ, Shin YM, Kim PN, Lee MS, Lee MG. Comparison of mangafodipir trisodium- and ferucarbotran-enhanced MRI for detection and characterization of hepatic metastases in colorectal cancer patients. AJR.American journal of roentgenology. 2006; 186:1059-1066

Design: block randomisation trial
Country: South Korea

Aim: to evaluate the validity of mangafodipir trisodium versus ferucarbotran-enhanced MRI in the detection and characterisation of hepatic lesions in colorectal cancer patients.

Inclusion criteria
Patients known to have or suspected of having hepatic metastases form colorectal cancer on the basis of prior helical CT examinations
Patients scheduled to have laparotomy for their hepatic mets or an intervention such as ablation.

Exclusion criteria
Multiple (>5) hepatic metastases on CT
Known contraindications to MRI (pacemaker or aneurysm clip)

Population
41 patients
48 patients between June 2003 – Feb 2004 enrolled. 7 patients further excluded for multiple mets or histology confirming hepatocellular or chalangiocarcinoma.

Interventions
1.5 T MRI with either

- mangafodipir trisodium (a type of liver specific contrast like gadolinium)
- ferucarbotran (a type of SPIO MRI)

Outcomes

Results

PER LESION ANALYSIS

	Liver mets +	Liver mets -	total
MT MRI +	37	2	39
MT MRI -	1	0	1
total	38	2	40

Sensitivity	*97%*
Specificity	*NA*
PPV	*95%*
NPV	*NA*
Accuracy	37/40= 93%

	Liver mets +	Liver mets -	total
SPIO MRI+	31	0	31
SPIO MRI -	1	0	1
total	32	0	32

Sensitivity	*97%*
Specificity	*NA*
PPV	*100%*
NPV	*NA*
Accuracy	31/32= 97%

Citation: Koh DM, Brown G, Riddell AM, Scurr E, Collins DJ, Allen SD, Chau I, Cunningham D, Desouza NM, Leach MO, Husband JE. Detection of colorectal hepatic metastases using MnDPDP MR imaging and diffusion-weighted imaging (DWI) alone and in combination. Eur.Radiol. 2008; 18:903-910

Design: prospective
Country: Royal Marsden Oncology Hospital, UK

Aim: To compare the diagnostic accuracy of MnDPDP MRI and diffusion weighted MRI alone and in combination.

Inclusion criteria
Consecutive patients with suspected colorectal liver metastatic disease
Pathologically proven adenocarcinoma of the colon or rectum
At least one liver lesion detected on CT scan or ultrasound that was diagnostic or suspicious of liver metastasis
Patients candidates for liver resection (i.e disease sparing at least two contuguous liver segments)

Exclusion criteria
Contraindication to MRI
Previous history of other malignancies.

In 5 patients no metastatic disease was diagnosed on MRI nor at follow up hence these patients were excluded from the analysis.

Population
38 consecutive patients originally referred for consideration into the study
5 patients had no evidence of metastatic disease at MRI or follow up so they were excluded.
33 patients were the final study population.
23 males, 10 females.
Mean age 57 years old (range 45-67)

Interventions

- MnDPDP MRI (liver contrast MRI)

- DWI MRI (diffusion weighted imaging)

DWI is sensitive to the molecular diffusion of water in biological tissues and recent advancements have enabled high quality DWI images of the liver to be obtained. Breath-hold single shot echo planar diffusion weighted (SS-EPI-DWI) MRI has been shown to be superior to SPIO liver contrast enhanced MRI.

- The combination of both MnDPDP and DWI MRI

Outcomes
ROC curve analysis with summary sensitivity and specificity.

Results
Average sensitivity and specificity from two observers reading the images of the different modalities.

	Sensitivity	specificity
MnDPDP MRI	81.3%	93%
DWI MRI	78.3%	95%
MnDPDP + DWI MRI	92.2%	97%

	Accuracy as Area under curve from observer 1	Accuracy as Area under curve from observer 2
MnDPDP MRI	Az=0.92 (0.86-0.96)	Az=0.88 (0.82-0.93)
DWI MRI	Az=0.83 (0.76-0.89)	Az=0.90 (0.84-0.95)
MnDPDP + DWI MRI	Az 0.94 (0.89-0.98)	Az=0.96 (0.91-0.99)

There was no significant difference in the averaged sensitivities between MnDPDP and DWI
For the combined MnDPDP + DWI the sensitivity was better compared to MnDPDP (p=0.01)
And there was a trend of improved sensitivity compared to DWI (p=0.06)

Accuracy was good but significantly improved for observer 2 who was more experienced in reading DWI images.

General comments
Combination of MnDPDP and DWI improved sensitivity without loss of specificity.

Citation: Kong G, Jackson C, Koh DM, Lewington V, Sharma B, Brown G, Cunningham D, Cook GJR. The use of F-18-FDG PET/CT in colorectal liver metastases-comparison with CT and liver MRI. European Journal of Nuclear Medicine and Molecular Imaging 2008; 35:1323-1329

Design: Retrospective
Country: Royal Marsden, UK

Aim: to compare FDG-PET/CT with liver MRI (Mn-DPDP) for the presence and number of liver metastases in patients with colorectal liver metastases being considered for surgery.

Inclusion criteria
Patients that had colorectal cancer and known or suspicion of liver mets that were thought operable from 2004-2006
Had PETCT and MRI with median time between studies <1month

Exclusion criteria
Patients with chemotherapy <3months before PETCT (lesions that are responding to treatment wont be detected on PET.

Population
65 patients (42 men) median age 65 years with colorectal cancer and known or suspicion of liver metastases retrospective identification of patients from 2004-2006 that presented to the Royal Marsden Hospital

Interventions
PETCT
MRI (Mn-DPDP)
Proof of metastases in the lesions operated came from histopathology reports or for those not operated from follow up MRI.

Outcomes
Per patient and per lesion analysis
Sensitivity
Specificity
False positives

Results
Per patient analysis:

	Liver mets +	Liver mets -	total
MnDPDP MRI+	60	0	60
MnDPDP MRI -	1	4	5
total	61	4	65

	Mn-DPDP MRI
Sensitivity	98%
Specificity	100%

	Liver mets +	Liver mets -	total
PET CT+	60	0	60
PET CT -	1	4	5
total	61	4	65

	PET CT
Sensitivity	98%
Specificity	100%

Per lesion analysis

	Liver mets +	Liver mets -	total
MnDPDP MRI+	163	0	163
MnDPDP MRI -	2	6	8
total	165	6	171

	Mn-DPDP MRI
Sensitivity	99%
Specificity	100%

	Liver mets +	Liver mets -	total
PET CT+	155	0	155
PET CT -	10	6	16
total	165	6	171

	PETCT
Sensitivity	94%
Specificity	100%

MRI and PETCT Concordant 85% of lesions
MRI and PETCT Discordant 15% of lesions
MRI detected total 30 lesions / mean 3.8 per patient
PETCT detected 20 lesions / mean 2.5 per patient
The lesions not detected by PETCT were all <1cm apart from 1
PETCT correctly identified more mets than MRI in 1 case and confirmed mets in an equivocal MRI lesion.

General comments
PETCT has high sensitivity and specificity for the presence of liver metastases and should be included early in the initial pre surgical evaluation and could potentially guide the use of MRI. However MRI is superior for small liver mets and remains a prerequisite for surgical planning in patients with confined liver mets.

Citation: Liu YN, Huang MX, An Q, Wei JM. The Impact of PET/CT on Therapeutic Strategy of Patients with Colorectal Cancer Metastasis. Hepatogastroenterology. 2009; 56:968-970

Design: prosepctive
Country: China

Aim: to assess the impact of the PETCT on the therapeutic strategy of patients with colorectal cancer metastases.

Inclusion criteria
Patients that had suspicion of liver metastases on CT scan and CEA after resection for colorectal cancer.

Exclusion criteria

Population
15 patients that all had contrast enhanced CT scan and CEA and had suspicion of liver metastasis
7 men, 8 women

Interventions
Contrast enhanced CT
PET CT

Outcomes
Sensitivity
Specificity
Change in therapeutic management

Results

	Liver mets +	**Liver mets -**	**total**
PETCT+	5 patients 9 lesions	0	5 patients 9 lesions
PETCT -	0	10 patients	10 patients
total	5 patients 9 lesions	10 patients	15 patients / 9 lesions

	PETCT
Sensitivity	100%
Specificity	100%

	Liver mets +	**Liver mets -**	**total**
CT+	4 patients 6lesions	0	4 patients 6 lesions
CT -	1 patient 3 lesions	10 patients	11patients 3 lesions
total	5 patients 9 lesions	10 patients	15 patients / 9 lesions

	PETCT
Sensitivity	80%
Specificity	100%

PET CT is statistically more sensitive than CT p=0.0009 - SIGNIFICANT

General comments
PETCT is more sensitive than contrast enhanced CT in detecting liver metastases from colorectal cancer. Taking into account the extrahepatic disease as well the results of which are not presented in this review there is a change in therapeutic strategy in 40% of patients based on the results of the PETCT.

Citation: Nanashima A, Taheshita H, Sawai T, Sumida Y, Abo T, Tanaka K, Nonaka T, Sengyoku H, Hidaka S, Yasutake T, Nagayasu T. Preoperative Assessment of Liver Metastasis Originating from Colorectal Carcinoma: Is Super Paramagnetic Iron Oxide Particles-Magnetic Resonance Imaging (SPIO-MRI) Useful for Screening? Hepatogastroenterology. 2008; 55:1750-1753

Design: retrospective
Country: Japan

Aim: To retrospectively examine the accuracy of diagnosis for metastatic lesions per patient and per lesion by enhanced CT and SPIO-MRI in one institution in Japan over a 7 year period.

Inclusion criteria
Data of 47 consecutive patients with metastatic liver carcinoma who underwent hepatectomy between 2000 and June 2007 were collected retrospectively. During this period enhanced CT and SPIO-MRI were performed routinely 2 weeks before hepatic resection.

The reference standard was intraoperative ultrasound scan or palpation and histological findings in the resected specimen.

Exclusion criteria

Population
32 male, 15 female, mean age 61.4 years (24-85)
10 synchronous liver metastases (same time as primary colorectal tumour)
35 metachronous liver metastases

Interventions
Enhanced CT (dual phase multi detector)
SPIO-MRI

Outcomes
Accuracy
Sensitivity
Positive predictive value
Negative predictive value

Results
Per patient analysis:
40 of 47 patients with liver metastases were accurately diagnosed by both modalities.
Sensitivity 85% CT and SPIO-MRI
Positive predictive value 100% CT and SPIO-MRI
Negative predictive value 100% CT and SPIO-MRI
The 7 patients that were missed had small liver metastases 5-8mm.

Per lesion analysis
Comparison of diagnosis of liver metastases between enhanced CT and SPIO-MRI in patients with liver metastases undergoing liver resection.

		Histology	Histology
		Liver mets (-)	Liver mets (+)
Enhanced CT	**Liver mets (-)**	15	3
Enhanced CT	**Liver mets (+)**	18	92
SPIO-MRI	**Liver mets (-)**	17	1
SPIO-MRI	**Liver mets (+)**	12	98

	Enhanced CT	SPIO-MRI
Sensitivity	92/110 (84%)	98/110 (89%) p=0.32
Positive predictive value PPV	92/92 (99%)	98/99 (99%)
Negative predictive value NPV	15/18 (83%)	17/18 (94%) p=0.6

Undetectable liver mets by CT in 18 lesions included 4 lesions of 5mm, 5 of 6mm, 5 of 7mm, 3 of 8mm, 1 of 9mm.
Undetectable liver mets by SPIO-MRI in 12 lesions included 4 lesions of 5mm, 4 of 6mm, 2 of 7mm, 2 of 8mm.

Conclusions Undetectable cases had small tumours less than 8mm In the per lesion analysis SPIO-MRI appears superior to CT but this is not statistically significant. In the per-patient analysis there was no difference between the two modalities.
General comments

Citation: Orlacchio A, Schillaci O, Fusco N, Broccoli P, Maurici M, Yamgoue M, Danieli R, D'Urso S, Simonetti G. Role of PET/CT in the detection of liver metastases from colorectal cancer. Radiol.Med.(Torino). 2009; 114:571-585

Design: prospective
Country: Italy

Aim: to compare the diagnostic accuracy of FDG PET versus CT verus PET-CT in the detection of liver metastases during tumour staging in patients suffering from colorectal cancer for the purposes of correct surgical planning and follow up.

Inclusion criteria

Exclusion criteria

Population
467 patients from April 2005 to Dec 2007.
With diagnosis of colorectal cancer and suspected liver metastases.
301 men, 166 women
mean age 64.4 +/-10.2 years

Interventions
CT
FDG PET
PET CT

Outcomes

Results
426 cases (91.2%) there was concordance among the three modalities

	Liver mets +	Liver mets -	total
CT+	336	6	342
CT -	30	95	125
total	366	101	467

Sensitivity	91.07% (CI 88.02%-94.12%)
Specificity	95.42% (CI 91.84%-99.0%)
PPV	98.08% (CI 96.55%-99.6%)
NPV	80.65% (CI 74.43%-86.86%)
Accuracy	92.29% (CI 89.87%-94.71%)

	Liver mets +	Liver mets -	total
PET+	336	11	347
PET -	20	100	120
total	356	111	467

Sensitivity	94.05% (CI 91.52%-96.58%)
Specificity	91.6% (CI 86.85%-96.35%)
PPV	96.64% (CI 94.68%-98.59%)
NPV	85.71% (CI 79.92%-91.51%)
Accuracy	93.36% (CI 91.10%-95.62%)

	Liver mets +	Liver mets -	total
PETCT+	336	3	339
PETCT -	7	121	128
total	343	124	467

Sensitivity	97.92% (CI 96.39%-99.44%)
Specificity	97.71% (CI 95.15%-100%)
PPV	99.10% (CI 98.08%-100%)

NPV	94.81% (CI 91.07%-98.56%)
Accuracy	97.86%(CI 96.55%-99.17%)

There is statistically significant difference between the sensitivity, specificity and accuracy of PET CT v PET (P<0.05). There is also statistically significant difference between the sensitivity and accuracy of PET CT v CT (P<0.05). There is no difference between PET and CT.

General comments

PET CT offers excellent diagnostic performance. It may modify a patients treatment protocol. The all in one examination may lead to considerable cost savings.

Citation: Rappeport ED, Loft A, Berthelsen AK, von der Recke P, Larsen PN, Mogensen AM, Wettergren A, Rasmussen A, Hillingsoe J, Kirkegaard P, Thomsen C. Contrast-enhanced FDG-PET/CT vs. SPIO-enhanced MRI vs. FDG-PET vs. CT in patients with liver metastases from colorectal cancer: A prospective study with intraoperative confirmation. Acta Radiol. 2007; 48:369-378

Design: prospective
Country: Denmark

Aim: To compare PET/CT with SPIO-MRI, PET, CT in the detection of liver metastases and extrahepatic tumour from colorectal cancer.

Inclusion criteria

Exclusion criteria
Diabetes
Contraindications to MRI imaging
Timing of imaging not feasible before surgery
Extrahepatic metastases confirmed on histology

Population
35 consecutive patients with suspected liver metastases from colorectal cancer
patients referred between March 2004 and Nov 2005 for surgery for suspected or verified mets
16 men, 19 women
median age 62 (range 33-74)

Interventions
PET/CT
SPIO-MRI
PET
CT

Readers of the imaging studies were blinded to the results of other imaging studies but were informed of the date for the primary colorectal cancer surgery.

Reference standard was intraoperative ultrasound scan and histological result of the resected specimen.

Outcomes
Sensitivity (true positives/[true positives+false negatives]
Specificity (true negatives/[true negatives+false positives]
Accuracy (true positives +true negatives)/all lesions
Positive predictive value PPV(true positives/[true positives +false positives])
Negative predictive value NPV (true negatives /[true negatives+false negatives])

Results

Per patient

	Liver mets +	Liver mets -	total
CT+	28	2	30
CT -	0	1	1
total	28	3	31

Sensitivity	100% (CI %)
Specificity	33% (CI %)
PPV	93% (CI %)
NPV	100% (CI %)
Accuracy	94% (CI %)

	Liver mets +	Liver mets -	total
PET+	23	0	23

PET -	5	3	8
total	28	3	31

Sensitivity	82% (CI %)
Specificity	100% (CI %)
PPV	100% (CI %)
NPV	38% (CI %)
Accuracy	84% (CI %)

	Liver mets +	**Liver mets -**	**total**
PETCT+	26	0	28
PETCT -	2	3	3
total	28	3	31

Sensitivity	93% (CI %)
Specificity	100% (CI %)
PPV	93% (CI)
NPV	100% (CI %)
Accuracy	94%

	Liver mets +	**Liver mets -**	**total**
SPIO MRI+	28	2	30
SPIO MRI -	0	1	1
total	28	3	31

Sensitivity	100% (CI %)
Specificity	33% (CI%)
PPV	93% (CI%)
NPV	100% (CI%)
Accuracy	94

Per lesion analysis

	Liver mets +	**Liver mets -**	**total**
CT+	43	25	68
CT -	28	50	78
total	71	75	146

Sensitivity	61% (CI %)
Specificity	67% (CI %)
PPV	72% (CI %)
NPV	86% (CI %)
Accuracy	77% (CI %)

	Liver mets +	**Liver mets -**	**total**
PET+	38	1	39
PET -	33	74	107
total	71	75	146

Sensitivity	54% (CI %)
Specificity	99% (CI %)
PPV	97% (CI %)
NPV	69% (CI %)
Accuracy	77% (CI %)

	Liver mets +	**Liver mets -**	**total**
PETCT+	47	1	48
PETCT -	24	74	98
total	71	75	146

Sensitivity	66% (CI %)
Specificity	99% (CI %)
PPV	98% (CI %)
NPV	76% (CI %)

Accuracy	83% (CI %)

	Liver mets +	Liver mets -	total
SPIO MRI+	58	14	72
SPIO MRI -	13	61	74
total	71	75	146

Sensitivity	82% (CI %)
Specificity	81% (CI %)
PPV	81% (CI %)
NPV	82% (CI %)
Accuracy	82% (CI %)

Both CT and SPIO MRI were significantly more sensitive than PET alone. P<0.0001, p<0.0001 respectively and PET CT p<0.001, p<0.05 respectively.
There was no difference between SPIO MRI and CT

All modalities were more sensitive in detecting liver metastases larger than 1cm compared to liver metastases of up to 1cm. Of the 19 liver metastases that were less than 1cm in size PET diagnosed 1, PETCT 5, SPIO MRI 10 and CT 13.

There were four patients that had chemotherapy less than 1 month prior to PETCT. Even when these patients were excluded from the analysis CT and SPIO were significantly more sensitive than PET. (p=0.001)

General comments

PET alone was significantly less sensitive than CT and SPIO MRI in the detection of LM. This is in contradiction to the conclusions from meta-analyses. Only some of the studies reported in the meta-analysis reported lesion by lesion sensitivity.
PET CT equaled MRI imaging in accuracy for liver metastasis detection.

Citation: Regge D, Campanella D, Anselmetti GC, Cirillo S, Gallo TM, Muratore A, Capussotti L, Galatola G, Floriani I, Aglietta M. Diagnostic accuracy of portal-phase CT and MRI with mangafodipir trisodium in detecting liver metastases from colorectal carcinoma. Clin.Radiol. 2006; 61:338-347

Design: prospective
Country: Italy

Aim: to compare the diagnostic accuracy of single section spiral CT and MRI with and without tissue specific contrast agent MnDPDP in the detection of colorectal liver metastases.

Inclusion criteria
Consecutive patients referred to one institution undergoing surgery for primary and / or metastatic colorectal cancer.
>18 years of age
Histologically confirmed diagnosis of CRC
Surgical indication for either resection of the primary and/or liver resection of metastases according to colonoscopy and CT chest/abdo
Life expectancy of at least 12 weeks
Normal renal function (creatinine <1.5mg/dl)

Exclusion criteria
Pregnancy or lactation
Contraindication to CT, MRI, laparoscopic surgery
CT-MRI interval > 4 weeks
CT or MRI imaging of poor quality due to movement artefact

Population
125 consecutive patients from one institution considered (Dec 2000-Mar 2003)
61 men (48.8%)
Median age 64.4 (41-86)
82/125 had resection of primary
19/82 also had synchronous metastases
43/125 had resection of metachronous metastases
19/125 had received neoadjuvant chemotherapy prior to inclusion in the study.

Interventions
Dual phase spiral single section CT with contrast. (Triple phase (delayed phase – done only when required by radiologist to differentiate between slowly filling haemangioma and metastasis.)

MRI with and without MnDPDP contrast.

Reference Standard: IOUS combined with palpation and surgical inspection together with histopathologic reliefs (intra operative frozen section histology when needed and histology on resected specimens).

2 radiologists assessed CT images and 2 the MRI images. Disagreement between readers was resolved by consensus re-evaluation. The readers were aware that the patient had CRC but were unaware of the result of other investigations and of the other readers. IOUS was performed by 1 of 2 radiologists and they were aware of the results of the CT and MRI.

Outcomes
Primary outcome

- sum of TP, sum of TN for all patients for CT, unenhanced MRI, MnDPDP MRI (per patient analysis)

TP = when the procedure detected the same metastases as the reference standard
TN = when the procedure correctly diagnosed no metastases.

Secondary outcome

- Sensitivity / specificity - per patient basis
- Sensitivity / PPV – per lesion basis

- The level of diagnostic confidence
- Inter-observer agreement

Per-patient basis analysis definitions

Sensitivity = number of TP cases / number of patients with at least one metastasis.

Specificity = number of TN cases / all cases in whom the reference standard did not detect any metastases.

Results

- MnDPDP MRI is more accurate than CT on a per patient basis. There is no difference between CT and MRI and only a trend of higher accuracy for MnDPDP MRI compared to unenhanced MRI.
- MnDPDP MRI has a significantly higher sensitivity on a per lesion basis than both CT (OR 2.6; 95% CI 1.44, 4.92) and unenhanced MRI (OR 2.1; 95% CI 1.11, 3.84). (multiple logistic model accounting for lesion dimensions and intra-patient variability)
- Kappa for inter-observer variability was 0.85 for CT, 0.77 for both enhanced and unenhanced MRI. Overall Kappa was 0.75 suggesting excellent agreement.
- Diagnostic confidence levels have not been included in this evidence table as not a relevant outcome to our PICO.
- No serious side effects were reported from any of the investigations.

	CT	MRI	MnDPDP MRI	CT v MRI	CT v MnDPDP MRI	MRI v MnDPDP MRI
Per patient analysis						
Accuracy	91/125(72.8%)	98/125(78.4%)	103/125(82.4%)	p=0.071	p=0.005	P=0.059
Sensitivity	30/62(48.4%)	36/62(58.1%)	41/62(66.1%)	p=0.083	p=0.004	p=0.059
Specificity	61/63(96.8%)	62/63(98.4%)	62/63(98.4%)			
Per lesion analysis						
Sensitivity	137/191(71.7%)	143/191(74.9%)	158/191(82.7%)			
Sensitivity per lesion size						
≤ 10mm	31/65(47.7%)	35/65(53.8%)	44/65(67.7%)			
11-20mm	39/53(73.6%)	40/53(75.5%)	46/54(86.8%)			
>20mm	67/73(91.8%)	68/73(93.2%)	68/73(93.2%)			
PPV	137/163(84%)	143/149(96%)	158/165(95.8%)			

Per patient analysis

	Liver mets +	Liver mets -	total
MnDPDP MRI+	41	1	42
MnDPDP MRI -	21	62	83
total	62	63	125

Sensitivity	66.1%
Specificity	98.4%
PPV	97.6%
NPV	74.7%
Accuracy	82.4%

	Liver mets +	Liver mets -	total
MRI+	36	1	37
MRI -	26	62	88
total	62	63	125

Sensitivity	58.1%
Specificity	98.4%
PPV	97.3%
NPV	70.5%
Accuracy	78.4%

	Liver mets +	Liver mets -	total
CT+	30	2	32
CT -	32	61	93

total	62	63	125

Sensitivity	48.4%
Specificity	96.8%
PPV	94%
NPV	66%
Accuracy	72.8%

There was no difference between CT and MRI
MnDPDP MRI was more accurate and more sensitive than CT
There was a higher accuracy and sensitivity tendency for MnDPDP MRI v unenhanced MRI but not statistically significant.

Per lesion analysis

	Liver mets +	**Liver mets -**	**total**
MnDPDP MRI+	158	7	165
MnDPDP MRI -	33	67	100
total	191	74	265

Sensitivity	82.7%
Specificity	90.5%
PPV	95.8%
NPV	67.0 %
Accuracy	84.9%

	Liver mets +	**Liver mets -**	**total**
MRI+	143	6	149
MRI -	48	68	116
total	191	74	265

Sensitivity	74.9%
Specificity	91.9%
PPV	96%
NPV	58.6%
Accuracy	79.6%

	Liver mets +	**Liver mets -**	**total**
CT+	137	26	163
CT -	54	48	102
total	191	74	265

Sensitivity	71.7%
Specificity	64.9%
PPV	84%
NPV	47.1%
Accuracy	69.8%

CT and unenhanced MRI showed no difference in sensitivity in the per lesion analysis (OR 1.3, CI 0.73-2.27)
The sensitivity of MnDPDP MRI was significantly higher than both CT (OR 2.6 CI 1.44-4.92), and unenhanced MRI (OR 2.1 CI 1.11-3.84)

General comments

On a per patient basis MnDPDP MRI is significantly more accurate and sensitive than CT in the detection of colorectal liver metastases. Specificity was similar. However MnDPDP MRI failed to be more accurate and sensitive than unenhanced MRI for both comparisons. There was no difference between CT and unenhanced MRI.

Citation: Ruers TJM. Improved selection of patients for hepatic surgery of colorectal liver metastases with 18F-FDG PET: A randomized study. J.Nucl.Med. 2009; 50:1036-1041

Design: randomised phase III multicentre trial
Country: the Netherlands

Aim: to investigate whether the addition of FDG PET to conventional CT-based the preoperative screening of colorectal liver metastases is beneficial and reduces the number of futile laparotomies.

Inclusion criteria
Histologically documented colorectal cancer treated by R0 resection
1-4 suspected potentially resectable liver metastases
No evidence of extrahepatic metastatic disease (except up to a maximum of 2 resectable lung mets on CT)
No evidence of recurrent or second colorectal carcinoma on barium enema or colonoscopy
WHO performance status of 0-2
Age 18 - 75

Exclusion criteria
Previous malignancies (except in situ carcinoma of the cervix, non-melanoma cancer of the skin, or a cancer where there had been a disease-free interval of at least 10 years)
Liver dysfunction (bilirubin, ALP x3 times upper limit if normal)
Active infection
Poorly regulated diabetes mellitus

Population
150 patients with colorectal liver metastases selected for surgical treatment by CT
Multicentre
Between May 2002 and February 2006.

Interventions
FDG PET and CT
Versus
CT only

Outcomes
Primary
Number of futile laparotomies (defined as any laparotomy that did not result in complete tumour treatment, that revealed benign disease, or that did not result in disease-free survival period longer than 6 months.
Secondary
Disease-free survival (DFS)
Overall survival (OS)

Results

Futile laparotomies

Variable	Control arm (no PET) n=75	Experimental arm (PET) n=75
No laparotomy	0	5 (7%)
Confirmed benign disease	-	2
Confirmed extrahepatic disease	-	3
laparotomy	75 (100%)	70(93%)
Futile laparotomy	34 (45%)	21(28%)
Extra hepatic disease at laparotomy – not resectable	6	2
Too extensive liver disease at laparotomy – not resectable	8	3
Benign disease at laparotomy	3	2
Benign disease after resection	1	1
Disease recurrence in <6 months	16	13

- A significantly higher proportion of patients underwent futile laparotomies in the control-no PET arm than in the experimental arm (45% v 28%) p=0.042
- The relative risk reduction was 38% (CI 4%-60%)
- The absolute difference of 17% means that 6 patients need to undergo PET to avoid 1 futile laparotomy.
- Futile laparotomy was not found to be associated with other prognostic factors as measured by the Fong score (p=0.539)

Survival
All patients were followed up for at least 3 years after randomization. For all patients randomized

3 year survival	Control arm (no PET)	Experimental arm (PET)
Overall survival OS	65.8%	61.3%
Disease free survival DFS	29.8%	35.5%

Both OS and DFS were not significantly different between the experimental and the control groups.

General Comments:
The introduction of PET in the preoperative work up of patients with suspected liver metastases from colorectal cancer significantly reduces the number of futile laparotomies due to unexpected unresectable disease.

Citation: Schwartz L, Brody L, Brown K, Covey A, Tuorto S, Mazumdar M, Riedel E, Jarnagin W, Getrajdman G, Fong Y. Prospective, blinded comparison of helical CT and CT arterial portography in the assessment of hepatic metastasis from colorectal carcinoma. World J.Surg. 2006; 30:1892-1901

Design: prospective
Country: Memorial Sloan Kettering Cancer Centre - USA

Aim: To compare helical CT with helical CT with arterial portography aimed at detecting liver metastases from colorectal carcinoma.

Cannot obtain 2X2 table as only ROC curve presented.

Inclusion criteria

Exclusion criteria
Patients with evidence of extrahepatic disease on imaging (37 patients)

Population
87 consecutive patients between April 1999 and April 2001 with suspected colorectal liver metastases .
all imaging done at a single institution
no evidence of extrahepatic disease (final population analysed n=50)

Interventions
Helical CT
Helical CTAP – results not presented as not relevant to PICO

Outcomes
Sensitivity from ROC curve

Results
Only CT results are presented as they are relevant to the PICO.

	CT using cutt-off 1 **0-1 benign 2-3-4 malignant**	**CT using cutt-off 2** **0-1-2 benign 3-4 malignant**
Sensitivity	76%	69%
Specificity	56%	82%
PPV	61%	78%
NPV	73%	75%
Accuracy	65%	76%

Citation: Selzner MK, Hany TF, Wildbrett P, McCormack L, Kadry Z, Clavien PA. Does the novel PET/CT imaging modality impact on the treatment of patients with metastatic colorectal cancer of the liver? Ann.Surg. 2004; 240:1027-1036

Design: prospective
Country: Switzerland

Aim: To compare the diagnostic value of contrast enhanced CT with that of FDG PETCT in patients with metastatic colorectal cancer to the liver.

Inclusion criteria
All patients referred for consideration for liver resection between Jan 2002 and July 2003.
CT and PETCT must have occurred within 2 weeks of each other.

Exclusion criteria
Synchronous metastatic lesions (i.e. metastatic liver disease at the same time as the primary colon cancer diagnosed)

Population
76 patients
52 men, 24 women
median age of 63 years (range 35-78)
62 patients received chemotherapy after their initial bowel resection
Median interval between chemo and PETCT = 3 months (range 7 days to 15 months)
Median follow up 16 months (range 6 months to 3 years)

Interventions
Contrast enhanced CT
FDG PET CT

Follow up was at 3 and 6 months for those patients that did not proceed to surgery.
Separate CT radiologist and PET radiologist. Both blinded to the results of other findings.

Outcomes
Primary outcome
Does PETCT alter the indications for surgery compared to CT.

Secondary outcome
True positive/negatives, false positive/negatives for PETCT
The diagnostic ability of the modality in patients with a previous hepatectomy
The influence of previous chemotherapy on the detection of tumours by PETCT

Results

Per patient analysis

	Liver mets +	Liver mets -	total
CT+	63	3	66
CT -	3	7	10
total	66	10	76

Sensitivity	95%
Specificity	70%
PPV	95%
NPV	70%
Accuracy	92%

	Liver mets +	Liver mets -	total
PETCT+	60	1	61
PETCT -	6	9	15
total	66	10	76

Sensitivity	91%
Specificity	90%

PPV	98%
NPV	60%
Accuracy	91%

No difference between CT and PETCT with regard to specificity p=0.58

General comments

Comparable results between PETCT and CT with regard to the diagnosis of hepatic metastases.
Management is latered by PETCT but purely on the identification of extrahepatic disease.
PETCT is also better at diagnosing recurrent liver disease in patient with prior hepatectomy.

Citation: Truant S, Huglo D, Hebbar M, Ernst O, Steinling M, Pruvot FR. Prospective evaluation of the impact of 18Ffluoro 2 deoxy D glucose positron emission tomography of resectable colorectal liver metastases. The British journal of surgery 2005; 92:362-369

Design: prospective double blind
Country: France

Aim: to assess the additional value of information provided by FDG PET over that provided by CT in patients with respectable liver metastases from colorectal cancer.

Inclusion criteria
Oct 2001-Nov 2002
Those patients that on CT were thought to be eligible for liver resection
If the PET was discordant with the CT this did not alter the decision to proceed to laparotomy.

Exclusion criteria

Population
All 53 patients underwent laparotomy
40 men, 13 women
mean age 63, range 44-78
27 patients presented with synchronous liver metastases., 26 had metachronous liver metastases.

Interventions
FDG PET
Helical CT, dual phase, 5mm slices, with iodinated contrast
Mean time between PET and CT was 24 days (range 0-61 days)
All PET scan performed within 2 months of laparotomy

Outcomes

Results

Per patient analysis
Unable to extract 2x2 table from descriptive statistics of the per patient analysis.

Per lesion analysis

	Liver mets +	Liver mets -	total
CT+	78	3	81
CT -	21	1	22
total	99	4	103

Sensitivity	79%
Specificity	25%
PPV	96%
NPV	5%
Accuracy	77%

	Liver mets +	Liver mets -	total
PET+	78	1	79
PET-	21	4	25
total	99	5	104

Sensitivity	79%
Specificity	80%
PPV	99%
NPV	16%
Accuracy	79%

General comments
Comparable results between PET and CT with regard to liver mets. Any additional lesions identified are extra hepatic

Citation: Vidiri A, Carpanese L, D'Annibale M, Caterino M, Cosimelli M, Zeuli M, David V, Crecco M. Evaluation of hepatic metastases from colorectal carcinoma with MR-superparamagnetic iron oxide. Journal of Experimental & Clinical Cancer Research 2004; 23:53-60

Design: prospective
Country: Italy

Aim: To compare the results obtained with SPIO-MRI, unenhanced MRI to that of spiral CT (does not say triple phase but I think it is) in order to select those patients suitable for liver resection.

Really difficult to make sense of their despcriptive statistics to get 2x2 table.

Inclusion criteria
Patients with known colorectal neoplasm who were candidates for liver resection

Exclusion criteria
age <18
pregnancy and or lactation
hypersensitivity to Destran's administration
stage C liver cirrhosis (Child-Pugh classification)
serious kidney insufficiency
haematological disease with splenomegaly
administration of a different contrast within 24 hours.

Population
35 patients , mean age 65, 20 men, 15 women, all potentially suitable for hepatic resection of metastatic lesions

Interventions
All patients had all the investigations.
spiral CT
SPIO-MRI (with body coil)
unenhanced MRI

All imaging was performed within 7 days
Pre and post op evaluation time period max 30 days

Gold standard:IOUS combined with palpation and surgical inspection together with histopathologic reliefs on resected specimens.

Outcomes
Sensitivity per lesion basis
Change in overall decision per patient basis

Results
Of the 35 patients included 26 went to surgery and 9 did not (unresectable). Of the 9 unresectable cases 8 had chemo and 1 had radiofrequency ablation.

Of patients submitted to surgery

dimensions	No of lesions	CT	MRI	SPIO-MRI	IOUS
	48	34	32	41	48
<1cm	13	4	2	9	13
1-2cm	14	10	10	12	14
>2cm	21	20	20	20	21

3 FP on CT
2 FP on MRI
2 FP on SPIO-MRI (same as above)
5 patients were found to have unresectable disease at operation (missed by both CT and MRIs)
2 lesions considered by CT to be mets were correctly identified by MRIs to be non-metastatic.
1 lesion identified by MRI as a met and not picked up by CT at all was not a met (angioma)

Of patients not operated

dimensions	CT	MRI	SPIO-MRI
	8	8	15
<1cm			4
1-2cm	2	2	5
>2cm	6	6	6

Per patient

In 5 cases SPIO-MRI concluded that surgery was contraindicated – the opposite to the CT conclusion (in 4 cases SPIO-MRI showed greater number of lesions per segment, in 1 case it identified the lesion as benign not metastatic).

Statistics

Kappa CT v MRI 0.9 good agreement
Kappa CT v SPIO-MRI 0.59 mild agreement
Kappa MRI v SPIO-MRI 0.51 mild agreement

Per patient analysis

	Liver mets +	Liver mets -	total
CT+	9+	3	
CT -	5		
total			35

	Liver mets +	Liver mets -	total
MRI+	9+	2	
MRI -	5		
total			35

	Liver mets +	Liver mets -	total
SPIO MRI+	9+	2	
SPIO MRI -	5		
total			35

Per lesion analysis

	Liver mets +	Liver mets -	total
CT+	34	3	37
CT -	14		
total	48		

Sensitivity	71%
Specificity	%
PPV	%
NPV	%
Accuracy	%

	Liver mets +	Liver mets -	total
MRI+	32	2	34
MRI -	16		
total	48		

Sensitivity	66.6%
Specificity	%
PPV	%
NPV	%
Accuracy	%

	Liver mets +	Liver mets -	total
SPIO MRI+	41	2	43
SPIO MRI -	7		
total	48		

Sensitivity	85.4%

Specificity	%
PPV	%
NPV	%
Accuracy	%

McNemar test: significantly greater number lesions identified with SPIRO-MRI v MRI (p=0.008

Citation: Wiering B, Ruers TJM, Krabbe PFM, Dekker HM, Oyen WJG. Comparison of multiphase CT, FDG-PET and intra-operative ultrasound in patients with colorectal liver metastases selected for surgery. Ann.Surg.Oncol. 2007; 14:818-826

Design: prospective
Country: The Netherlands

Aim: to evaluate the predictive value of CT and FDG PET of the liver and extra hepatic findings compared to findings at laparotomy and 6 months follow up.

Inclusion criteria
Consecutive patients between Jan 1999 and Nov 2004.
Suitable for liver resection of hepatic metastases from colorectal cancer on CT imaging

Exclusion criteria
Presence of local recurrence on colonoscopy or colonography
No previous liver surgery
Poorly regulated diabetes

Population
131 consecutive patients thought suitable for liver resection of hepatic metastases on CT imaging

Interventions
CT dual phase helical with IV contrast – iodine
PET

Outcomes
Diagnostic 2x2 tables for each modality for liver metastases, extra hepatic intra abdominal and other sites.
Only liver-related results presented.

Results

Per patient analysis

	Liver mets +	Liver mets -	total
CT+	127	3	130
CT -	1	0	1
total	128	3	131

Sensitivity	99.2%
Specificity	NA%
PPV	97%
NPV	NA%
Accuracy	97%

	Liver mets +	Liver mets -	total
PET+	126	0	126
PET-	2	3	5
total	128	3	131

Sensitivity	98.4%
Specificity	100%
PPV	100%
NPV	60%
Accuracy	98.5%

Per lesion analysis

	Liver mets +	Liver mets -	total
CT+	257	3	260
CT -	106	0	106
total	363	3	366

Sensitivity	70.8%
Specificity	NA%

PPV	98.8%
NPV	NA%
Accuracy	70.2%

	Liver mets +	Liver mets -	total
PET+	260	0	260
PET-	103	3	106
total	363	3	366

Sensitivity	71.6%
Specificity	100%
PPV	100%
NPV	2.8%
Accuracy	71.8%

PET and CT both missed the majority of lesions that were smaller than 10mm. Many were only a few mm.

Detection rate of histologically proven liver metastases

Lesion size	IOUS	CT	PET	CT and/or PET
<10mm	63	10 (16%)	10 (16%)	12 (19%)
10-20mm	172	123 (72%)	129 (75%)	142 (83%)
>20mm	128	124 (97%)	121 (95%)	125 (98%)
All	363	257 (71%)	260 (72%)	279 (77%)

CT and PET may be discongruent and complementary for detection of metastases.

After 6 months follow up 42 new lesions developed in 15 patients. CT and PET had previously detected all the lesions though it had not been possible to identify them at laparotomy with palpation and IOUS.

General comments

CT and PET have similar diagnostic yield for the detection of liver metastases; both modalitiesare adequate on a patient basis but inadequate to detect the smallest of liver lesions. The significance of the latter is limited clinically.