



Evidence Summary PET 15

The Utility of PET/CT in Colorectal Cancer Metastasis: An Evidence Summary

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QUESTIONS

In patients with colorectal cancer, what is the role of fluorodeoxyglucose (FDG) PET/CT in determining suitability for surgical removal for isolated lung and abdominal (nodal) metastasis?

Target Population

Patients with new or recurrent colorectal cancer who are potentially eligible for surgical resection of extrahepatic metastasis.

Target Users

This evidence summary is intended to guide the Ontario PET Steering Committee in their decision making concerning indications for the use of PET imaging.

This evidence summary may also be useful in informing clinical decision making regarding the appropriate role of PET imaging and in guiding priorities for future PET imaging research.

INTRODUCTION

At the request of the Ontario PET Steering Committee, literature pertaining to the utility of PET/CT in the clinical management of patients with extrahepatic colorectal cancer metastasis was summarized.

METHODS

This evidence-based report was developed by the Ontario PET Steering Committee in collaboration with the PEBC. For this project, the core methodology used to develop the evidentiary base was the systematic review. Evidence was selected and reviewed independently by one methodologist (SK).

Search Strategy

A literature search was performed using MEDLINE (1946 to present) and EMBASE (1988 to 2013 Week 10) through OVID. The search strategies are reported in Appendices 1 and 2, respectively.

Study Selection Criteria

Inclusion Criteria

Articles were eligible for inclusion in this systematic review if they met all the following criteria:

1. Were published in full text from Jan 1, 2000 to April 4, 2013.
2. Study type was any of the following:
 - a. randomized controlled trials,
 - b. meta-analyses of RCTs,
 - c. prospective studies (patient population >12), or
 - d. retrospective studies (patient population >50).
3. Specifically evaluated new or recurrent colorectal cancer.
4. Outcomes of interest were:
 - a. Detection of unsuspected extrahepatic metastasis.
 - b. Impact on initial staging.
 - c. Impact on clinical management.

Exclusion Criteria

Articles were excluded if they met any of the following criteria:

1. Did not report patient outcome.
2. PET-only (no co-registered CT component).
3. Published in a language other than English.
4. Were non-systematic reviews, letters, editorials, case studies, historical articles, or commentaries.

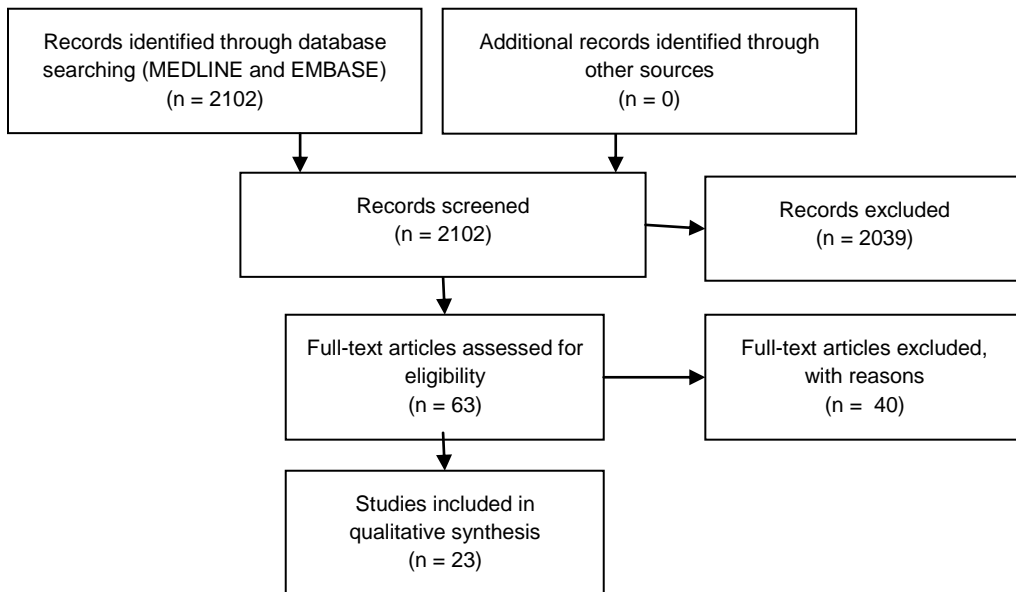
Data Extraction

One reviewer went through the retrieved citation titles and abstracts from MEDLINE and EMBASE to identify potentially relevant articles, which were obtained for full texts, and then checked all the related references from these full texts. For each eligible study, one reviewer would extract all study data (such as design features, patient population, PET/CT modality, comparison tests, reference standards and clinical management impact data).

RESULTS

No existing systematic reviews or practice guidelines specifically addressed how PET/CT affected the clinical management of patients with extrahepatic metastasis eligible for surgical resection. Of the 2102 studies identified from the electronic searches, 2039 primary studies were excluded after reviewing the titles and abstracts and removing duplicates. These 63 articles were potentially relevant, but upon full-text review, 40 did not meet the inclusion criteria. Twenty-three primary studies were subsequently included in this systematic review. Details of the individual studies can be found in Appendix 3. All studies used a prospective or retrospective cross-sectional design with the exception of two randomized controlled trials.

FIGURE 1. Literature Flow Diagram



Using a comprehensive search strategy and efforts to avoid publication and selection bias, this review aimed to identify any available evidence pertaining to the utility of FDG PET/CT as compared to conventional imaging specific to patients with pulmonary or extrahepatic colorectal cancer metastasis who are eligible for surgical resection. The

Evidence Summary PET 15

literature review did not uncover any primary studies that were specific to the research question of this evidence summary. The studies included in this review (1-23) were observational studies of patients who are eligible for liver resection who underwent FDG PET/CT with the objective of providing additional information about possible distant disease. In most cases, FDG PET/CT was more sensitive than conventional imaging and was able to detect extrahepatic metastasis in 1% to 88% (median, 15%) of cases (1-6,8-21,23). The sites of distant disease varied but were commonly in abdominal lymph nodes with some areas of pulmonary metastasis. The majority of staging changes were in patients being upstaged as a result of finding occult disease in both intrahepatic and extrahepatic sites. As with staging, changes to the clinical management of patients were also variable and occurred in approximately 3% to 65% (median, 24%) of cases (1,4,9,20-21). In about one third of treatment changes, the FDG PET/CT scan identified occult metastasis that precluded the patient from receiving planned liver resection, thus resulting in fewer laparotomies (1,3-6,9,11,13,15-18,20-23). Other changes to therapy included extending the liver resection or adjusting the chemoradiotherapy regimen based on the new findings by PET/CT (1,14,21). In several studies, the addition of PET/CT was observed to have a potential negative impact on some patients (range across studies: 3%-9%) (2,5,7,11,13,15,16,19,22). In most cases, the potential negative impact was due to false upstaging. False upstaging was due to FDG uptake due to benign inflammatory causes (7). These false-positive results may lead to further investigation and a resultant delay in treatment.

DISCUSSION

It should be noted that a limited number of the observational studies included in this review had a sufficient follow-up protocol to determine if the changes in therapeutic or surgical management were detrimental or beneficial to patient outcomes. In several studies, most commonly the retrospective studies, results for extrahepatic metastasis on PET/CT were unable to be verified by the gold standard (biopsy, histopathology or follow-up scans) as to its true or false nature. In these studies, true-positive findings were straightforward to confirm; however, true-negative findings only meant that it was not possible to acquire positive findings during the follow-up period, making it uncertain whether the findings were truly negative. Overall, the addition of FDG PET/CT to the pre-surgical protocol of metastatic colorectal patients suggests that FDG PET/CT may be useful in patients scheduled for aggressive treatment (i.e., surgical resection) where conventional imaging shows potential extrahepatic metastasis that may impact the surgical treatment plan.

A current randomized controlled trial in the United Kingdom (PulMiCC Trial: <http://www.rbht.nhs.uk/research/cteu/projects/respiratory-disease/pulmicc/>) is being conducted to determine if there is any survival and/or quality-of-life advantage attributable to pulmonary metastasectomy for colorectal cancer. FDG PET/CT is included in the pre-planning protocol. In correspondence with the chief investigator, Dr. Thomas Treasure, he indicated that the evidence for the inclusion of FDG PET/CT in the pre-planning protocol was

Evidence Summary PET 15

weak; however, it was used to disclose unsuspected disease in sites other than the lungs that may exclude the patient from the study.

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Contact Information

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Evidence Summary PET 15

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Evidence Summary PET 15

Appendix 1: Searching Strategies from Medline OVID (April 4, 2013) (N=603)

#	Searches	Results
1	Tomography, Emission-Computed/ or (positron adj emission adj tomography).ti,ab. or PET.ti,ab. or PET-FDG.ti,ab. or Fluorodeoxyglucose F18/ or 18f fluorodeoxyglucose.ti,ab. or 18f fluorodeoxyglucose.ti,ab. or 18fdg.ti,ab. or 2-fluoro-2-deoxy-d-glucose.ti,ab. or 2-fluoro-2-deoxyglucose.ti,ab. or 18f-fdg.ti,ab. or fluorine-18-fluorodeoxyglucose.ti,ab. or fluorine-18-fluorodeoxyglucose.ti,ab. or flourine-18-fluorodeoxyglucose.ti,ab. or flourine-18-fluorodeoxyglucose.ti,ab. or fluorine-18-fluorodeoxyglucose.ti,ab. or positron emission tomography/ or PET-CT.ti,ab. or PET\$CT.ti,ab.	73385
2	deoxyglucose/ or deoxyglucose.ti,ab. or desoxyglucose.ti,ab. or desoxy-glucose.ti,ab. or desoxy-d-glucose.ti,ab. or deoxy-d-glucose.ti,ab. or 2deoxyglucose.ti,ab. or 2deoxy-d-glucose.ti,ab. or fluorodeoxyglucose.ti,ab. or fluorodesoxyglucose.ti,ab. or fludeoxyglucose.ti,ab. or fluordeoxyglucose.ti,ab. or fluordesoxyglucose.ti,ab. or fluordesoxyglucose.ti,ab. or 18fluorodeoxyglucose.ti,ab. or 18fluorodesoxyglucose.ti,ab. or fdg\$.ti,ab. or 18fdg\$.ti,ab. or 18f-dg\$.ti,ab.	32952
3	(fluor or 2fluor\$ or fluoro or flouro or fluorodeoxy or fludeoxy or flourodeoxy or fluorine or 18f or 18flu\$ or 18fluo\$).ti,ab.	33109
4	glucose.ti,ab.	308398
5	(pet or petscan\$ or pet ct).ti,ab.	48866
6	Tomography, Emission-Computed/	24239
7	emission.ti,ab.	104849
8	(tomograph or tomographs or tomographic\$ or tomogrpahy or tomographies).ti,ab.	34421
9	7 and 8	3318
10	5 or 6 or 9	62133
11	3 and 4	5655
12	2 or 11	33513
13	10 and 12	17905
14	exp neoplasm/ or neoplasm staging/ or cancer\$.ti,ab. or tumor\$.ti,ab. or tumour\$.ti,ab. or carcinoma\$.ti,ab. or neoplasm\$.ti,ab. or staging.ti,ab. or metastas\$.ti,ab. or metastatic.ti,ab. or exp neoplasm metastasis/ or exp neoplastic processes/ or neoplastic process\$.ti,ab. or adenocarcinoma\$.ti,ab.	2868799
15	1 and 14	27244
16	13 and 14	11574
17	15 or 16	27248
18	limit 17 to english language	24279
19	(comment or editorial or letter or case reports).pt.	2682443
20	18 not 19	18269
21	(conference or conference proceeding or conference proceeding\$ or conference paper or conference paper\$ or discussion or discussion\$ or in brief or invited comment or invited comment\$).ti,ab.	214508
22	20 not 21	18058
23	(colorectal or colon or colonic or rectal or rectum or rectosigmoid or adenomat\$).ti,ab.	267600
24	(recur\$ or metastas:).ti,ab.	533919
25	22 and 23 and 24	677
26	limit 25 to yr="2000 -Current"	603

Evidence Summary PET 15

Appendix 2: Searching Strategies from EMBASE OVID (April 4, 2013) (N=1499)

#	Searches	Results
1	Tomography, Emission-Computed/ or (positron adj emission adj tomography).ti,ab. or PET.ti,ab. or PET-FDG.ti,ab. or Fluorodeoxyglucose F18/ or 18f fluorodeoxyglucose.ti,ab. or 18f fluorodeoxyglucose.ti,ab. or 18fdg.ti,ab. or 2-fluoro-2-deoxy-d-glucose.ti,ab. or 2-fluoro-2-deoxyglucose.ti,ab. or 18f-fdg.ti,ab. or fluorine-18-fluorodeoxyglucose.ti,ab. or fluorine-18-fluorodeoxyglucose.ti,ab. or fluorine-18-fluorodeoxyglucose.ti,ab. or fluorine-18-fluorodeoxyglucose.ti,ab. or positron emission tomography/ or PET-CT.ti,ab. or PET\$CT.ti,ab.	118166
2	deoxyglucose/ or deoxyglucose.ti,ab. or desoxyglucose.ti,ab. or desoxy-glucose.ti,ab. or desoxy-d-glucose.ti,ab. or deoxy-d-glucose.ti,ab. or 2deoxyglucose.ti,ab. or 2deoxy-d-glucose.ti,ab. or fluorodeoxyglucose.ti,ab. or fluorodesoxyglucose.ti,ab. or fludeoxyglucose.ti,ab. or fluoroxyglucose.ti,ab. or fluoroxyglucose.ti,ab. or fluoroxyglucose.ti,ab. or 18fluorodeoxyglucose.ti,ab. or 18fluorodesoxyglucose.ti,ab. or fdg\$.ti,ab. or 18fdg\$.ti,ab. or 18f-dg\$.ti,ab.	42907
3	(fluor or 2fluor\$ or fluoro or fluoro or fluorodeoxy or fludeoxy or flurodeoxy or fluorine or 18f or 18flu\$ or 18flu\$).ti,ab.	47689
4	glucose.ti,ab.	363388
5	(pet or petscan\$ or pet ct).ti,ab.	73627
6	Tomography, Emission-Computed/	14651
7	emission.ti,ab.	119147
8	(tomograph or tomographs or tomographic\$ or tomogrpahy or tomographies).ti,ab.	38237
9	7 and 8	3794
10	5 or 6 or 9	82895
11	3 and 4	8125
12	2 or 11	43704
13	10 and 12	27102
14	exp neoplasm/ or neoplasm staging/ or cancer\$.ti,ab. or tumor\$.ti,ab. or tumour\$.ti,ab. or carcinoma\$.ti,ab. or neoplasm\$.ti,ab. or staging.ti,ab. or metastas\$.ti,ab. or metastatic.ti,ab. or exp neoplasm metastasis/ or exp neoplastic processes/ or neoplastic process\$.ti,ab. or adenocarcinoma\$.ti,ab.	3495003
15	1 and 14	51894
16	13 and 14	18844
17	15 or 16	51898
18	limit 17 to english language	46499
19	(comment or editorial or letter or case reports).pt.	1238445
20	18 not 19	43921
21	(conference or conference proceeding or conference proceeding\$ or conference paper or conference paper\$ or discussion or discussion\$ or in brief or invited comment or invited comment\$).ti,ab.	295355
22	20 not 21	42815
23	(colorectal or colon or colonic or rectal or rectum or rectosigmoid or adenomat\$).ti,ab.	333613
24	(recur\$ or metastas:).ti,ab.	675792
25	22 and 23 and 24	1584
26	limit 25 to yr="2000 -Current"	1499

Evidence Summary PET 15

Appendix 3: Details of Primary Studies

Study									Impact of PET/CT (%)				
Reference	Year	Type	Setting	# of pts	PET/CT Modality	CI Performed	Reference Standard	Patients Eligible for Surgery (Y/N)	Detection of Extrahepatic Metastasis	Location of Extrahepatic Metastasis, if Specified	Modification of Disease Stage	Modification of Treatment Plan	Modification Details
Cipe et al (1)	2013	Prospective	Stage II and III	64	WB PET/CT	abdomino-pelvic MDCT and MRI	Histopathology	Y	1.6 (1/64)	1: Supraclavicular LN <i>NOTE: PET/CT detected mets in the mediastinum for 4 ptns – all FP</i>	21.9 (14/64)	3.2 (2/64)	1: Liver mets: changed chemo regimen 2: Supraclavicular LN changed surgical treatment strategy
Yu et al (2)	2012	Prospective	Not specified	68	PET/CT	CT, MRI	Pathology	Y	8.8 (6/68) sensitivity, specificity, PPV, and NPV were 85.71%, 70.00%, 66.67%, and 62.5%, respectively.	Abdominal Nonjuxtaintestinal LN's <i>NOTE: PET/CT detected a total of 9 LN's; however, 3 were FP. 1 LN at the root of the mesentery was missed.</i>	NA	NA	NA
McLeish et al (3)	2012	Retrospective	Not specified	54	PET/CT	CT	NA	Y	14.8 (8/54)	Sites not specified	NA	20.3 (11/54)	8 ptns: Surgery cancelled 3 ptns: deemed suitable for surgery (no extrahepatic mets as thought on CT)
Engledow et al (4)	2012	Prospective	Not specified	64	PET/CT	Clinical examination, CT	Histology	Y	31 (20/64)	6: peritoneal disease 6: multiple lung metastases 4: retroperitoneal LN 2: mediastinal LN 1: porta hepatitis nodes 1: previously undiagnosed thyroid cancer with bone mets	43 (28/64)	34 (22/34)	upstaging in 20 patients (31%) and downstaging in two patients (3%). patient with thyroid cancer underwent resection to remove the thyroid lesion; however, primary treatment in upstaged ptns was changed from surgical resection to chemotherapy
Amin et al (5)	2012	Retrospective	Recurrent or metastatic CRC	60	PET/CT	CT, MRI	Pathology, histopathology, follow-up scans	Y	6	4: inoperable metastasis 1: nodal metastasis at porta hepatitis	NA	37 (22/60)	14: Surgery appropriately avoided 3: Inappropriately avoided surgery

Evidence Summary PET 15

Study									Impact of PET/CT (%)				
Reference	Year	Type	Setting	# of pts	PET/CT Modality	CI Performed	Reference Standard	Patients Eligible for Surgery (Y/N)	Detection of Extrahepatic Metastasis	Location of Extrahepatic Metastasis, if Specified	Modification of Disease Stage	Modification of Treatment Plan	Modification Details
										1: sacral recurrence			
Briggs et al (6)	2011	Retrospective	Metastatic CRC	102	PET/CT	CECT	Histology	Y	8.8 (9/108)	3: bone 3: abdominal and mediastinal LN 2: peritoneum 1: lung lesion (turned out to be a secondary primary)	NA	30 (31/108)	16: inoperable metastatic disease, detecting 9: previously unsuspected metastatic disease 3: second primary tumours, 3: down-staging Potential negative impact group: 6 FP patients, 4 FN ptns.
Wiering et al (7)	2010	RCT	Not specified	Control: 75 Intervention: 70	PET/CT	CT, MRI, US, chest x-ray	Histology, follow-up	Y	NA	NA	NA	7.1 (5/70) (diagnostic performance increased and futile laparotomies were reduced by 38% (relative risk reduction).)	Cancellation of planned resection. Futile laparotomies performed with PET: 28% Futile laparotomies performed without PET: 45%
Metser et al (8)	2010	Retrospective	Recurrent CRC	50	PET/CT	MDCT	Clinical follow-up	N	34 (17/50)	recurrence in the presacral space ($n = 5$), metastatic subcentimeter lymph nodes ($n = 4$), peritoneal deposits ($n = 3$), and recurrences at the periphery of radiofrequency ablated metastatic lesions of the liver ($n = 2$) and in the abdominal wall ($n = 1$), liver ($n = 1$), and uterine cervix ($n = 1$).	NA	NA	NA
Kochhar et al (9)	2010	Retrospective	CRC	157	PET/CT	CECT and/or MRI	Histology and follow-up	Y	33.2 (52.157)	Locations not specified (extra-	Total: 58 (91/157)	33.8 (53/157)	Surgery averted

The utility of PET/CT in colorectal cancer metastasis: an evidence summary

Evidence Summary PET 15

Study									Impact of PET/CT (%)				
Reference	Year	Type	Setting	# of pts	PET/CT Modality	CI Performed	Reference Standard	Patients Eligible for Surgery (Y/N)	Detection of Extrahepatic Metastasis	Location of Extrahepatic Metastasis, if Specified	Modification of Disease Stage	Modification of Treatment Plan	Modification Details
										pulmonary and extrahepatic sites)	33.2 (52/157) - Upstaged 24.8 (39/157) - downstaged		
Schmidt et al (10)	2009	Retrospective	Recurrent CRC	24	PET/CT	WB MRI	Histology	N	14 (versus MRI=8)	12 – lung 2 – peritoneal spread	NA	NA	NA
Ruers et al (11)	2009	Phase III RCT	CRC treated by R0 Surgical resection	150 (75 PET and 75 no PET)	PET/CT	CT	Histology and follow-up	Y	9.3 (7/75)	5: lung or mediastinal 2: extensive abdominal LN	NA	6.7 (5/75)	2: benign disease 3: unresectable extrahepatic At laparotomy 17 ptns (23%) in non-PET/CT arm and 7 ptns (9%) in the PET/CT arm were found to have significant met disease or benign disease which led to futile laparotomies.
Liu et al (12)	2009	Prospective	Not Specified	15	PET/CT	CECT	Pathology and follow-up	N	80 (12/15) (32 lesions) (1 patient FP due to uptake in chronic inflammation)	Extrahepatic mets. Location not specified.	NA	40 (6/15)	NA
Kitajima et al (13)	2009	Prospective	Suspected recurrence or metastatic CRC	170	WB PET/CT	CT	Histopathology	Y	Lesions: 88 (97/110 lesions)	Compared to CT PET/CT detected more recurrence and/or mets except for lung (CT detected 1 additional site)	NA	38 (64/170)	41: Initiating unplanned treatment 14: changing the treatment strategy 9: obviating the need for treatment 1 ptns underwent unnecessary surgery, 3 ptns had unnecessary biopsy, 5 ptns had lost proper therapy.
Akiyoshi et al (14)	2009	Retrospective	Primary CRC	65	PET/CT	MDCT	Histology, follow-up	Y	15 (10/65)	3: supraclavicular LN 1: cervical	NA	15 (10/65)	1: best supportive care because of widespread bone

Evidence Summary PET 15

Study									Impact of PET/CT (%)				
Reference	Year	Type	Setting	# of pts	PET/CT Modality	CI Performed	Reference Standard	Patients Eligible for Surgery (Y/N)	Detection of Extrahepatic Metastasis	Location of Extrahepatic Metastasis, if Specified	Modification of Disease Stage	Modification of Treatment Plan	Modification Details
										vertebral bone mets 1: iliac bone mets 3: multiple bone mets 1: anterior mediastinal LN 1: synchronous lung cancer			metastases 3: systemic chemotherapy without surgery, 5: systemic chemotherapy after surgery to release intestinal obstruction (palliative resection, n = 3; stoma construction, n = 2) 1:secondlook right lower lobectomy for synchronous lung cancer.
Scott et al (15)	2008	Prospective	Recurrent CRC	191 <i>Group A:</i> CI appearances equivocal for recurrent tumour (n=93) <i>Group B:</i> pulmonary or hepatic metastases that were potentially resectable as determined by CI (n=98)	PET/CT	CT	Follow-up	Y	Group A: 48.4 (45/93) Group B: 43.9 (43/98)	Liver, Pelvis, Lung, Retroperitoneum, Mesentery , Bone, Bowel, Adrenal, Other	NA	Group A: 65.6 (61/93) Group B: 49 (48/98)	Group A: change from curative to palliative: 14% Palliative to curative: 15% Group B: change from curative to palliative: 21.5% change from palliative to curative: 2% 1FP result and 4FN result based on PET findings
Kong et al (16)	2008	Retrospective	CRC, not specified	65	PET/CT	CECT	Histopathology or clinical follow-up	Y	17 (11/65) and 3 FP	** See below table	NA	17 (11/65)	6: upstaged and received palliative therapy; 5: required surgical intervention for extrahepatic disease as well
Davey et al (17)	2008	Prospective	Primary rectal cancer	83	PET/CT	MRI, CT or endoanal US	Histology	Y	13.9 (12/86)	4: mesorectal LN 3: iliac LN 4: systemic metastatic disease 1; both systemic	31 (26/83)	8 (7/86)	8 Percent: (curative to palliative 6 patients; palliative to curative 1 patient

Evidence Summary PET 15

Study									Impact of PET/CT (%)				
Reference	Year	Type	Setting	# of pts	PET/CT Modality	CI Performed	Reference Standard	Patients Eligible for Surgery (Y/N)	Detection of Extrahepatic Metastasis	Location of Extrahepatic Metastasis, if Specified	Modification of Disease Stage	Modification of Treatment Plan	Modification Details
										and iliac LN spread			
Sorensen et al (18)	2007	Prospective	CRC, not specified	54	PET/CT	CT	Histology	Y	5.5 (3/54)	2: LN 1: local recurrence of the CRC	NA	19 (10/54)	6: liver resection cancelled 2: Liver resection extended 1: Resection and per-operative RFA of 3 malignant liver Tumours 1: SRT cancelled, patient down-staged with chemotherapy and then RFA of liver lesions
Lubezky et al (19)	2007	Prospective	CRC, not specified	27 Group 1 (patients assigned to immediate liver resection)	PET/CT	CT	Histopathology	Y	1 FP suspected recurrence in colonic anastomosis, abdominal wall 1TP: recurrence in mesocolic LN 1FN: peritoneal metastases	1: colonic anastomosis, abdominal wall 1: recurrence in mesocolic LN 1: peritoneal metastases	NA	NA	NA
Chen et al (20)	2007	Retrospective	Postoperative CRC	68	PET/CT	CT	Pathology	Y	14.2 (8/56)	Not specified	14.2 (8/56)	16.2 (11/68)	Identified unresectable disease
Gearhart et al (21)	2006	Retrospective	Adenocarcinoma of the rectum	37	PET/CT	CT	Pathology or follow-up	Y	18.9 (7/37)	Distant LN mets	27 (10/37) upstaging of 7 patients and downstaging of 3 patients	27 (10/37)	6/10: Alteration in surgical plan 7/10 (3 overlap): alteration in neoadjuvant/adjuvant therapy
Park et al (22)	2006	Prospective	Primary CRC	100	PET/CT	Chest x-ray, CT	Follow-up	Y	NA	NA	NA	27 (27/100)	9: intermodality change (TP:8; FN:1) 10: increase in operative extent (TP:8;

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													FP:2) 8: prevention of unnecessary procedure (all TP)
Selzner et al (23)	2004	Prospective	CRC patients eligible for liver resection	76	PET/CT	CT	Histopathology	Y	88.8 % (32/36) Sensitivity: 89% Sensitivity of CT: 64%	Not specified	NA	21 (16/76)	10: surgery cancelled 6: surgical strategy changed

CRC = colorectal cancer; PET/CT = positron-emission tomography/computed tomography; CT = computed tomography; WB = whole body; MRI = magnetic resonance imaging; MDCT = Multidetector computed tomography; NA = not applicable/not stated; TP = true positive; TN = true negative; FP = false positive; FN = false negative; LN = lymph node; sens = sensitivity; spec = specificity; US = ultrasonography; mets = metastasis; CECT = contrast-enhanced computer tomography

****location of extrahepatic metastasis from Kong et al (16).**

- Anastomotic recurrence, malignant mesenteric nodules
- Malignant peritoneal deposits
- Retroperitoneal and bone metastases
- Possible second primary in rectum
- Malignant mesenteric deposit and rib metastasis
- Malignant mesenteric nodules
- Pancreatic malignant involvement – EUS biopsy-confirmed metastases
- Local recurrence left peri-rectal soft tissue
- Malignant peritoneal nodule. No liver metastasis (confirmed granuloma)
- Active bowel polyp (histology-confirmed tubulovillous adenoma with variable dysplasia with a focus of high-grade dysplasia). No liver metastases (confirmed hemangioma). Confirmed lung metastasis, equivocal on CT
- Two bowel lesions—metachronous primary, and anastomotic recurrence