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ORIGINAL ARTICLE

Clinical impact of PET/MR in treated colorectal cancer patients

Barbara J. Amorim[1,2,3] · Theodore S. Hong[4] · Lawrence S. Blaszkowsky[5] · Cristina R. Ferrone[6] · David L. Berger[6] · Liliana G. Bordeianou[6] · Rocco Ricciardi[6] · Jeffrey W. Clark[5] · David P. Ryan[5] · Jennifer Y. Wo[4] · Motaz Qadan[6] · Mark Vangel[1,2,7] · Lale Umutlu[8] · David Groshar[9] · Lina G. Cañamaques[10] · Debra A. Gervais[1] · Umar Mahmood[1,2] · Bruce R. Rosen[2] · Onofrio A. Catalano[1,2,11]

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Abstract

Purpose The primary aim of the present study was to evaluate if PET/MR induced management changes versus standard of care imaging (SCI) in treated colorectal cancer patients. The secondary aim was to assess the staging performance of PET/MR and of SCI versus the final oncologic stage.

Methods Treated CRC patients who underwent PET/MR with ^{18}F-FDG and SCI between January 2016 and October 2018 were enrolled in this retrospective study. Their medical records were evaluated to ascertain if PET/MR had impacted on their clinical management versus SCI. The final oncologic stage, as reported in the electronic medical record, was considered the true stage of disease.

Results A total of 39 patients who underwent 42 PET/MR studies were included, mean age 56.7 years (range 39–75 years), 26 males, and 13 females. PET/MR changed clinical management 15/42 times (35.7%, standard error ± 7.4%); these 15 changes in management were due to upstaging in 9/42 (21.5%) and downstaging in 6/42 (14.2%). The differences in management prompted by SCI versus PET/MR were statistically significant, and PET/MR outperformed SCI (P value < 0.001; odds ratio = 2.8). In relation to the secondary outcome, PET/MR outperformed the SCI in accuracy of oncologic staging (P value = 0.016; odds ratio = 4.6).

Conclusions PET/MR is a promising imaging tool in the evaluation of treated CRC and might change the management in these patients. However, multicenter prospective studies with larger patient samples are required in order to confirm these preliminary results.

Keywords Colorectal cancer · PET/MR · FDG · Management changes

This article is part of the Topical Collection on Oncology – Digestive tract

✉ Onofrio A. Catalano
ocatalano@mgh.harvard.edu; onofriocatalano@yahoo.it

[1] Department of Radiology, Massachusetts General Hospital, Harvard Medical School, 55 Fruit Street, White 270, Boston, MA 02114, USA

[2] Martinos Center for Biomedical Imaging, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA

[3] Division of Nuclear Medicine, State University of Campinas (UNICAMP), Campinas, Brazil

[4] Department of Radiation Oncology, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA

[5] Department of Hematology/Oncology, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA

[6] Department of Surgery, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA

[7] Biostatistics Center, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA

[8] Department of Diagnostic and Interventional Radiology and Neuroradiology, University Hospital Essen, Essen, Germany

[9] Department of Nuclear Medicine, Assuta Medical Centers, Tel Aviv, Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel

[10] Hospital Universitario Madrid Sanchinarro, Madrid, Spain

[11] Department of Radiology, University of Naples "Parthenope", Naples, Italy

Introduction

Colorectal cancer (CRC) is the third most common cancer worldwide and the second in number of deaths per year [1]. In the USA, CRC ranks third both for incidence and mortality, with an estimated 51,020 deaths in 2019 [2]. The incidence and mortality rates are decreasing among patients older than 50 years and increasing among adults younger than 50 years [3].

Advancements in medical and surgical oncology have increased attempts for curative resection in up to 80% of CRC patients while decreasing recurrence rates. However, one-third of the patients with locally advanced rectal cancer are expected to die within 5 years from completion of treatment [4], and even in those treated with curative intents, recurrences occur in up to 30–45% of cases, especially in cases more advanced at initial diagnosis [5, 6].

Diagnostic imaging is a pivotal part of surveillance in treated CRC. The National Comprehensive Cancer Network (NCCN) guidelines recommend a contrast-enhanced CT of the chest, abdomen, and pelvis in the surveillance of treated CRC. ^{18}F-fluorodeoxiglucose (^{18}F-FDG) PET/CT is indicated only in the case of serial CEA elevation despite negative physical examination, colonoscopy and chest and abdominopelvic contrast-enhanced CT, and in patients with presumably resectable metastatic disease, in order to rule out other occult metastases (www.nccn.org/professionals/physician_gls/pdf/colon.pdf; www.nccn.org/professionals/physician_gls/pdf/rectal.pdf). Although the accuracy of MR is considered higher than that of CT, CT is still the most frequently used modality since it is readily available. Moreover, MR, despite the promising results of the very few published studies, has not been extensively investigated in this setting [7, 8].

PET/MR has been recently approved for clinical usage. It allows the synchronous acquisition of PET and MR data from the same body region. Some preliminary studies suggest that the combination of the high sensitivity of PET with the superior anatomic layout and functional information of MR can improve assessment of soft tissues, facilitate characterization of small hepatic lesions, and provide better anatomic layout of the pelvis and abdomen than other imaging modalities, including PET/CT [9]. This could lead to a superior performance in staging and restaging of a number of solid organ neoplasms [10]. Preliminary studies have shown that ^{18}F-FDG PET/MR (PET/MR) can outperform ^{18}F-FDG PET/CT and contrast-enhanced CT in local and distant staging of CRC [11, 12].

The objective of the present study was to determine whether PET/MR might influence clinical management of patients with treated colorectal cancer versus standard of care imaging (SCI).

Methods

Patient selection

In this retrospective observational diagnostic study, we assessed the electronic medical records of adult patients with treated CRC who underwent PET/MR between January 2016 and October 2018. This study was approved by the institutional review board and informed written consent was waived due to its retrospective nature.

Inclusion criteria were history of treated CRC and acquisition of SCI as well as PET/MR. Exclusion criteria were absence of confirmatory tests of the PET/MR findings (pathology or follow-up imaging) undertaken by the caring physicians.

^{18}F-FDG PET/MR acquisition

Patients fasted for at least 6 h before the study and peripheral blood glucose levels were measured immediately before ^{18}F-FDG injection to ensure blood glucose levels were less than 200 mg/dl. Images were collected about 1.5 h following intravenous injection of ^{18}F-FDG, mean activity 4.44 MBq/kg (0.12 mCi/kg). All patients were scanned utilizing a Biograph mMR scanner (Siemens Healthcare, Erlangen, Germany). At first, a whole-body non-contrast-enhanced PET/MR was acquired from the mid-thighs to the base of the neck, to be followed by a focused upper abdominal protocol. A dedicated pelvic protocol was acquired if the referring clinicians had a high suspicion for pelvic recurrence. Table 1 summarizes the technical details of the PET/MR protocol.

Standard of care imaging

All patients underwent a combination of standard of care imaging (SCI): chest, abdominal and pelvic contrast-enhanced CT (CE-CT), and/or contrast-enhanced ^{18}F-FDG PET/CT (CE-PET/CT), and/or non-contrast-enhanced ^{18}F-FDG PET/CT (NCE-PET/CT), and/or abdominal or pelvic enhanced MR (CE-MR).

The maximal temporal interval between PET/MR and the SCI was 3 months (mean = 20.9 days; from 0 to 99 days).

Imaging and medical records analysis

All images and electronic medical records were evaluated by a dedicated multidisciplinary team, including one or more radiologists, oncologic surgeons, medical oncologists, and radiation oncologists. All electronic medical records were evaluated to ascertain if PET/MR had inspired any change in management versus SCI. This constituted the primary aim of the study.

Table 1 PET/MR technical protocol

MR sequence	Plane	Area scanned	iPat	TR (ms)	TE (ms)	Matrix	NEX	FOV (mm)	Thickness (mm)	Gap (mm)	FA (degrees)	Voxel size (mm)	TI (ms)	Fat saturation
						Whole body before contrast								
T1w 2-Point Dixon VIBE	Coronal	Whole body	2	3.6	1st TE 1.225 2nd TE 2.45	79 × 192	1	500	3.1	0	10^0	4.1 × 2.6 × 3.1		
DWI (b-values 50–400-800)	Axial	Whole body	2	9100–18800	66–83	112 × 156	2	420	6.0	0.6		2.7 × 2.7 × 6.0	220	
T2w HASTE	Axial	Whole body	2	1400	86–97	288 × 384	1	380	6.0	0.6		1.3 × 1.0 × 6.0		
						Upper abdomen								
T1w Dual GE	Axial	Upper abdomen	0	90	1st TE 1.2 2nd TE 2.46	192 × 256	1	380	5.0	6.0	32^o	1.05 × 1.5 × 5.0		
T2w FSE FS	Axial	Upper abdomen	2	3740	100	206 × 448	2	400	5.0	6.5		1.3 × 0.9 × 5.0		SPAIR
T2w HASTE	Coronal	Upper abdomen	3	1400	66–96	253 × 256	1	380	5.0	6.0		1.5 × 1.5 × 5.0		
T1w VIBE Contrast enhanced	Axial	Upper abdomen	2	4.06–4.1	1.81–1.91	180 × 230	1	380	3.0	0	9^o	1.6 × 1.2 × 3.0		Quick spectral fat saturation
						Pelvis								
T2w FSE	Sagittal	Pelvis	2	4000–7480	101–103	310 × 320	3	200	3.0	3.6		0.6 × 0.6 × 3.0		
T2w FSE	Axial	Pelvis	2	4960–9611	103–112	358 × 448	2	380	3.0	3.6		0.6 × 0.6 × 3.0		
T2w FSE	Coronal	Pelvis	2	4000–6150	103–112	336–448	2	380	3.0	3.6		0.6 × 0.6 × 3.0		
						Whole body after contrast								
T1w VIBE	Axial	Whole body	2	4.06–4.1	1.81–1.91	180 × 230	1	380	3.0	0	9^o	1.6 × 1.2 × 3.0		Quick spectral fat saturation
PET	BP	Acquisition time/BP (min)			Iterative reconstruction algorithm	Iterations		Subsets		FOV axial (mm)		Voxel size (mm^3)	Image grid	
	5–6	4			AW OSEM 3D	3		21		258		2.0 × 2.0 × 2.0	172 × 172	

VIBE, volume-interpolated breath hold T1 weighted; *DWI*, diffusion-weighted imaging; *HASTE*, half Fourier single shot fast spin echo T2 weighted; *FSE*, fast spin echo; *FS*, fat saturated; *GE*, gradient echo; *iPat*, integrated parallel acquisition technique; *TR*, time of repetition; *TE*, time of echo; *FOV*, field of view; *FA*, flip angle; *TI*, time of inversion; *SPAIR*, spectral adiabatic inversion recovery; *BP*, bed position; *AW OSEM 3D*, 3-dimensional attenuation weighted ordered subsets expectation maximization iterative reconstruction algorithm

Differences between PET/MR and SCI were classified as *no change* or as *change in management* when PET/MR, compared with standard of care imaging, led to the same or different management, respectively. Changes in management were further classified as follows: (1) *upstaging prompting surgery*, when detection of metastatic lesions or local recurrence prompted surgical resection; (2) *upstaging aborting surgery in favor of chemotherapy or palliation or radiation therapy*, when detection of an increased number of metastatic lesions or a locally more extensive disease prohibited a potential resection; (3) *downstaging making patients resectable*, when the detection of a decreased number of metastatic lesions allowed surgical resection; (4) *downstaging avoiding unnecessary surgery*, when PET/MR ruled out recurrence or metastases leading to cancelation of surgery. It was also assessed if PET/MR falsely upstaged or downstaged leading to an erroneous conduct.

The secondary aim was analyzing the staging performance of PET/MR and of SCI versus the final oncologic stage. The final oncologic stage, attributed by the multidisciplinary team, was part of the patients' electronic medical records and was considered the true stage of disease. Our clinicians, as part of standard of care, did establish the final TNM recurrence clinical stage following the classification of the American Joint Committee on Cancer (AJCC) and relying on pathology and/or imaging follow-up.

Statistical analysis

Changes in management and staging performance were assessed using McNemar's test with continuity correction. The percentage of cases for which PET/MR resulted in a change in management was estimated using the normal approximation to the binomial distribution. A P value of 0.05 was chosen for statistical significance.

Results

Patient

A total of 42 treated CRC patients underwent PET/MR. Three patients were scanned twice by PET/MR, from 5 to 16 months apart. Three patients were excluded due to lack of SCI in one and lack of pathology confirmation and of follow-up scans in two.

Therefore, 39 patients who underwent 42 studies were included in the analysis. Clinical management was retrospectively assessed at the 42 time points of the PET/MR acquisitions. At all 42 time points, the whole body plus the upper abdomen PET/MR were acquired. On top of that, in 14/42 scans (33%), a dedicated pelvic PET/MR protocol was also obtained.

Table 2 summarizes patients' characteristics. Mean age was 56.7 years, range 39–75 years. Twenty-six patients were males and 13 females. Mean CEA level was 9.5 ng/mL, range 0.7–75.7 ng/mL; 24 patients had colon cancer and 15 patients rectal cancer.

All patients had been previously treated: neoadjuvant chemoradiation and primary cancer resection in 3; neoadjuvant chemoradiation, primary cancer resection, and adjuvant chemotherapy in 10 (7 also with metastasectomy); neoadjuvant chemoradiation without primary resection in 6 (2 also with metastasectomy); primary resection only in 6 (1 also with metastasectomy); and primary resection and adjuvant chemotherapy in 17 (7 also with metastasectomy and 1 also with immunotherapy).

According to pathology evaluation, 31 patients presented with invasive adenocarcinoma, 4 mucinous adenocarcinoma, 2 invasive adenocarcinoma with mucinous features, 1 adenocarcinoma with signet ring cells, and 1 adenosquamous carcinoma.

Table 2 Characteristics of 39 patients who underwent 42 time points PET/MR

Characteristic	Value
Age (years)	
Mean	56.7
Range	39–75
Sex	
Male	26/39 (67%)
Female	13/39 (33%)
Primary site of colorectal cancer	
Colon	24/39 (62%)
Rectal	15/39 (38%)
CEA (ng/mL)	
Mean	9.5
Range	0.7–75.7
Previous treatment for 42 time points PET/MR studies	
Neoadjuvant CR + primary resection	3/42 (7%)
Neoadjuvant CR + primary resection + adjuvant CTh*	10/42 (24%)
Neoadjuvant CR**	6/42 (14%)
Primary resection***	6/42 (14%)
Primary resection + adjuvant CTh****	17/42 (41%)
Pathology	
Invasive adenocarcinoma	31/39 (79%)
Mucinous adenocarcinoma	4/39 (10%)
Invasive adenocarcinoma with mucinous features	2/39 (5%)
Adenocarcinoma with signet ring cells	1/39 (3%)
Adenosquamous carcinoma	1/39 (3%)

CR, chemoradiation; *CTh*, chemotherapy; *7 also underwent metastasectomy; **2 also underwent metastasectomy, ***1 also underwent metastasectomy; ****7 also underwent metastasectomy and 1 also underwent immunotherapy

The SCI tests performed at the 42 time points were as follows: 12/42 CECT and CE-PET/CT; 7/42 CECT; 6/42 CECT and NCE-PET/CT; 5/42 CE-PET/CT; 3/42 CE-PET/CT and CE-MR; 3/42 CE-PET/CT and CECT and CE-MR; 3/42 CECT and CE-MR; 2/42 CE-MR; and 1/42 NCE-PET/CT.

For confirmation of the PET/MR findings, the referring physician had used histopathology in 24 cases, imaging follow-up plus clinical findings in 13, correlation with prior imaging studies along with clinical findings in 5. Mean follow-up was 10.25 months (range 1–33 months).

Change in management

PET/MR did not change clinical management, in comparison to SCI, in 27/42 (64.3%) time points. PET/MR prompted changes in management in 15/42 cases (35.7%, standard error ± 7.4%). Changes in management were distributed as follows: *upstaging prompting surgery* in 5/42 (11.9%); *upstaging aborting surgery in favor of chemotherapy or palliation* in 2/42 (4.8%), *upstaging aborting surgery in favor of chemoradiotherapy combined with immunotherapy* in 2/42 (4.8%); *downstaging making patients resectable* in 5/42 (11.9%); *downstaging avoiding unnecessary surgery* in 1/42 (2.3%).

The differences in management prompted by SCI versus PET/MR were statistically significant, and PET/MR outperformed SCI (P value < 0.001; odds ratio = 2.8). Table 3 summarizes the results of change in management. Figure 1 displays a case whose management was changed from surgical resection of one lesion in a single organ to surgical resection of two lesions in two different organs due to PET/MR upstaging. Figure 2 shows a case of PET/MR downstaging that rendered the patient amenable to surgical resection.

In a subgroup of 30 patients who underwent same day PET/CT and PET/MR, PET/MR prompted management changes in 8/30 (26.7%, standard error 8.1%). The differences in management prompted by SCI versus PET/MR in this subgroup were also statistically significant (P value = 0.027; odds ratio = 3.81).

Additionally, the same analysis was performed in the subgroup of patients with mucinous pathology (n = 4) and mucinous features (n = 2) encompassing 7 PET/MR studies (1 patient underwent 2 PET/MR). PET/MR changed management in 2/7 cases (28%, standard error 17%). However, the differences in management prompted by PET/MR versus SCI in this subgroup were not statistically significant (P value = 0.48; odds ratio = 1.5). In one case, a same day PET/CT showed pelvic lesions suspicious for infection. PET/MR confirmed some lesions as infection and, additionally, showed a focal tumor recurrence, which was confirmed by biopsy. In the other case, PET/MR detected more abdominal lesions than CE-CT and one additional lesion in the thorax, changing the clinical conduct to chemotherapy.

Performance of oncologic staging

Most patients presented a very advanced final oncologic stage in the 42 time points: stage 0 = 6/42 (14%); stage I (local recurrence) = 4/42 (10%); stage IVA = 15/42 (36%); stage IVB = 5/42 (12%); stage IVC = 12/42 (28%).

Compared with the final oncologic stage, PET/MR and SCI were both in agreement and correct in 28/42 time points (67%), and both in agreement and incorrect in 3/42 (7%). In the remaining 11/42 time points (26%), PET/MR and CSI were discordant, with PET/MR being correct in 10/42 (24%). In most of these cases, 6/42 (14%), PET/MR resulted in upstaging, showing lesions which were not detected by the SCI: 2 cases with peritoneal lesions; 1 case with abdominal lymphadenopathy; 2 with local recurrence; and 1 with liver metastases. Table 4 summarizes the staging performances of SCI and PET/MR.

The differences between the performance in oncologic staging of SCI and of PET/MR were statically significant and in favor of PET/MR (P value = 0.016; odds ratio = 4.6).

There were 3 cases in which both SCI and PET/MR were incorrect and falsely downstaged the diseases extent. One

Table 3 Management changes at 42 time points PET/MR

Change management	Cases (%)	Upstaging or downstaging	Cases (%)	Reason of change in management	Cases (%)	P value odds ratio
No change	27/42 (64.3%)	–	–	–	–	P < 0.001
Change in management	15/42 (35.7%)	Upstaging	9/42 (21.5%)	Prompting surgery	5/42 (11.9%)	OR = 2.8
				Aborting surgery in favor of CTh	2/42 (4.8%)	
				Aborting surgery in favor of CTh + immunotherapy	2/42 (4.8%)	
		Downstaging	6/42 (14.2%)	Making patients resectable	5/42 (11.9%)	
				Avoiding unnecessary surgery	1/42 (2.3%)	
				Total	42 studies	

OR, odds ratio; *CTh*, chemotherapy

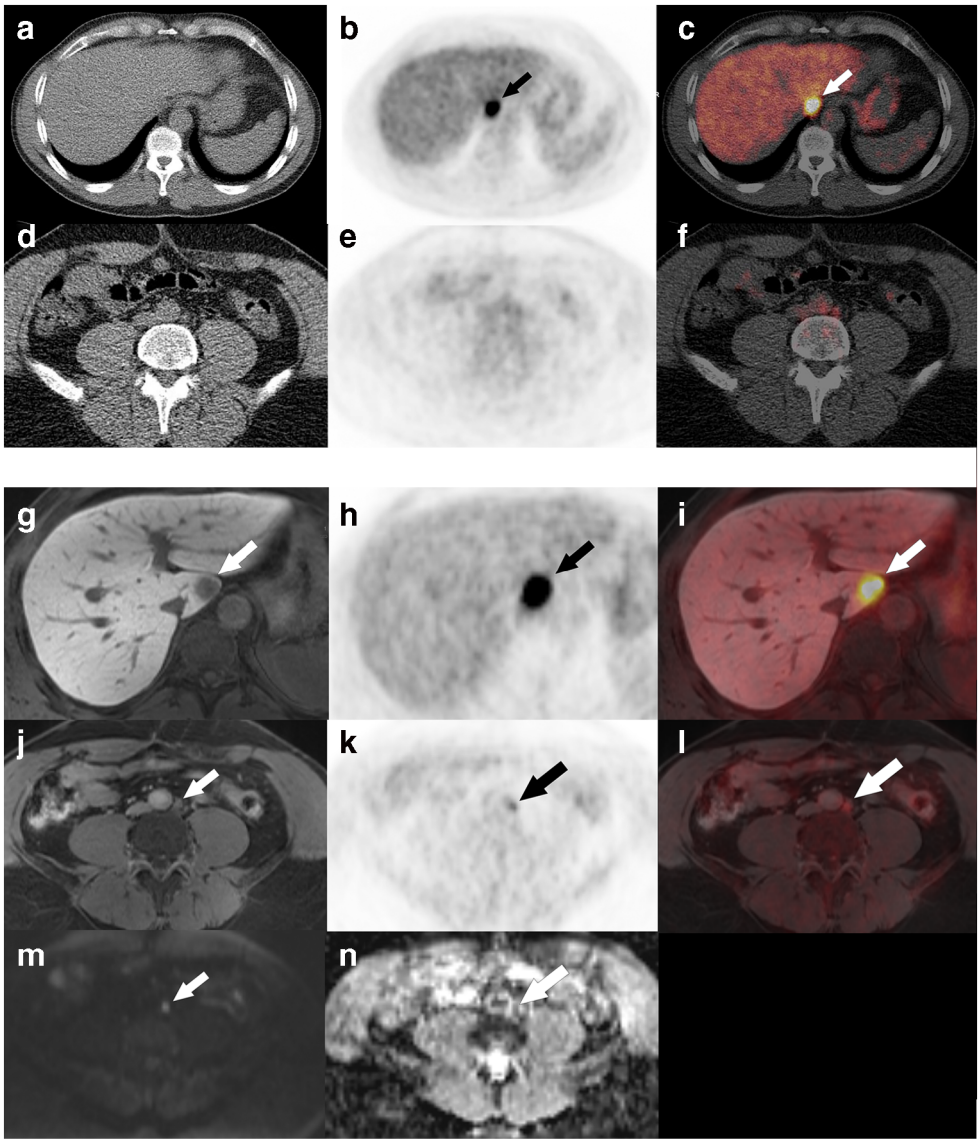

Fig. 1 Upstaging based on PET/MR leading to changes in surgical plans. 51-year-old male, with rectal cancer, increasing CEA (CEA = 12.0 ng/mL; normal values < 3.4 ng/mL). Contrast-enhancing CT showed one liver lesion suspected for metastasis in segment I. Patient underwent a PET/CT and PET/MR on same day to exclude other lesions in preparation for the caudate lobe resection. Axial NCE-CT (**a**), PET (**b**), and fused PET/CT (**c**) from NCE-PET/CT show a single metastasis (arrow). No other metastases were detected by PET/CT in any other locations, including in the left paraaortic region, as on axial NCE-CT (**d**), PET (**e**), and fused PET/CT (**f**). PET/MR confirmed the liver metastasis as on axial T1 weighted (**g**), PET (**h**), and fused PET/MR (**i**). However, PET/MR, axial T1 weighted (**j**), PET (**k**), fused PET/MR (**l**), DWI (**m**), and ADC map (**n**), demonstrated a left paraaortic metastatic lymphadenopathy (arrow). Therefore, 20 days after PET/MR, in addition to the already planned caudate lobe resection, a left paraaortic lymphadenectomy was also performed. PET/MR findings were confirmed by surgical pathology

patient had elevation of CEA and negative imaging findings. After 6 months, due to increasing bilirubin and alkaline phosphatase, a biliary brushing was performed yielding malignant cells, considered metastatic from colonic primary. In one patient, all studies failed to show peritoneal lesions found at laparoscopy 2 months later. In the last case, PET/MR and SCI demonstrated liver metastases which were confirmed by pathology at the time of resection but neither PET/MR nor SCI revealed three lymph node metastases in the periportal region which were found and resected at the time of surgery.

There was 1 discordant case where PET/MR was incorrect compared with the SCI. PET/MR falsely downstaged a patient in whom a same day PET/CT detected a markedly FDG avid lesion in the skull base, suspicious for metastasis. However, the skull base was not imaged by PET/MR, whose coverage encompasses from the mid-thighs to the neck base, and therefore, this area was not included in the PET/MR field of view.

In the subgroup of 30 patients who underwent same day PET/CT and PET/MR, PET/MR staged correctly and SCI incorrectly 6/30 (20%) times; however, this difference in staging was not statistically significant (P value = 0.13; odds ratio = 6.4). On the other hand, from a therapeutic perspective, the additional information by PET/MR changed management in three of these cases having the same TNM stage both by PET/MR and PET/CT.

In fact, in 6/42 cases (14%), PET/MR did not change the clinical stage but still prompted management changes. In one patient that was candidate to peritonectomy only, PET/MR demonstrated additional liver lesion; therefore, the surgical plan was modified with the addition of liver segmentectomy. In two patients who were candidate for peritonectomy, therefore, already stage IV, PET/MR disclosed multiple lesions in other organs leading to abortion of the operation. In a fourth patient, PET/MR demonstrated more liver lesions than SCI,

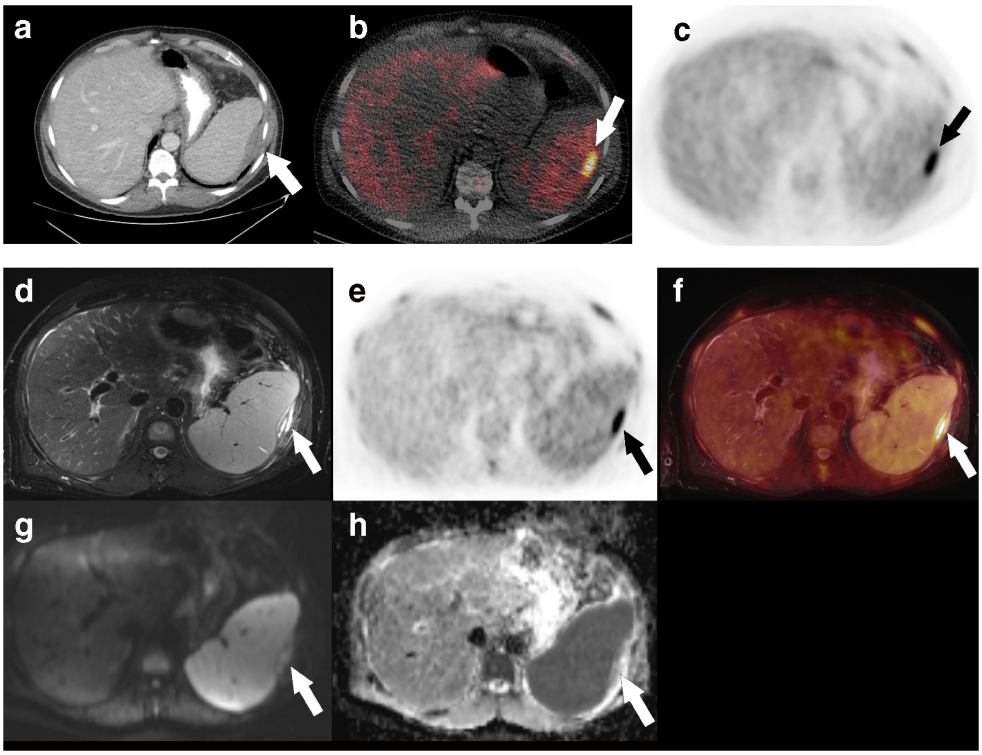

Fig. 2 Downstaging based on PET/MR making patient resectable. 53-year-old male, with treated rectosigmoid adenocarcinoma with suspicious recurrent disease in the liver and perisplenic peritoneum. CEA was not elevated (1.0 ng/mL; normal values < 3.4 ng/mL). Axial CE-CT (**a**) and NCE-PET/CT (**b** fused PET/CT; **c** PET) showed a lenticular-shaped metabolically avid lesion (arrow) indenting the spleen, consistent with peritoneal metastasis. In this case, surgeons considered that the peritoneal metastasis would preclude a curative surgery. Corresponding level PET/MR: axial T2-weighted fat-saturated (**d**), PET (**e**), fused PET/MR (**f**), DWI (**g**), and ADC map (**h**) images demonstrated the strand-like appearance of the perisplenic metabolically active lesion and the lack of restricted diffusion, favoring sequelae of prior surgery. After 1 week, patient underwent a hepatic segmentectomy. The peritoneum was biopsied and pathology revealed fibrosis with chronic inflammation

contraindicating the surgery. In the last two cases, PET/MR downstaged the metastatic burden to the liver altering the surgical plan from chemotherapy to surgery.

The same analysis was performed in the subgroup of patients with mucinous pathology ($n = 4$) and mucinous features ($n = 2$) encompassing 7 PET/MR studies (1 patient underwent 2 PET/MR). In this subgroup, PET/MR staged correctly and SCI incorrectly 1/7 patients (14%). However, this difference in staging was not statistically significant (P value = 1.0; odds ratio = 1.2).

Discussion

CRC recurrences might be amenable to potentially curative surgical resection if detected early, with resultant improved overall survival. However, in recurrences, survival has remained persistently poor especially in the case of positive resection margins. In one study, which evaluated locally recurrent rectal cancer treated by curative intent surgery, the 5-year survival rate dropped from 43%, in the case of negative

Table 4 Performances in oncologic staging at 42 time points PET/MR

Stage concordance	Cases (%)	Stage correct or incorrect	Cases (%)	Change in stage	Cases (%)	P value odds ratio
PET/MR and SCI agreement	31/42 (74%)	Both correct	28/42 (67%)			$P = 0.016$
		Both incorrect	3/42 (7%)			OR = 4.6
PET/MR and SCI disagreement	11/42 (26%)	PET/MR correct and SCI incorrect	10/42 (24%)	Upstaging	6/42 (14%)	
				Downstaging	4/42 (10%)	
		PET/MR incorrect and SCI correct	1/42 (2%)	False downstaging	1/42 (2%)	
		Total		42		

SCI, standard of care imaging; *OR*, odds ratio

resection margins, to 14%, in the case of positive resection margins [13].

The surgical approach to CRC metastases has changed in the last few years, from what is resected to what remains after resection. Currently, surgery of hepatic CRC metastases is contemplated when the disease can be completely resected and at least two adjacent liver segments or at least 20% of total estimated liver volume (in the case of non-steatotic, non-cirrhotic parenchyma) is spared [14]. Moreover, the presence of extra-hepatic metastases, including those to the peritoneum, is no longer an absolute contra-indication for liver metastasectomy. In fact, a multicentric study has shown that cytoreductive surgery combined with perioperative intraperitoneal chemotherapy can improve the overall survival. Achievement of a complete cytoreductive surgery was the most important favorable prognostic index [15]. This explains the need of an accurate pre-operative assessment of the extent of recurrent disease, so that the proper clinical and surgical procedures necessary to ensure a complete resection can be planned.

Routinely, CT is the most frequently used technology for re-staging and follow-up of treated CRC patients. However, CT has a lower diagnostic performance than PET/CT or MR. In a meta-analysis that explored the performance of different imaging technologies in evaluating for local and distant recurrent CRC, CT had a lower diagnostic performance than PET/CT, with an area under curve (AUC) of 0.83 and 0.94 respectively [7]. In this meta-analysis, only one study used MR and this study resulted in an AUC of 0.92 for MR [7]. A more recent study comparing PET/CT and MR in CRC recurrence found PET/CT accuracy higher than that of MR (88.6% vs 65.7%) [16]. This was in part explained by the superior capability of PET to differentiate scar tissue from cancer over CT and MR. Although MR has been shown to be capable of detecting local recurrences, it is not routinely used in the follow-up of CRC. PET/CT has demonstrated good results in detecting recurrent CRC (pooled sensitivity of 94.1% in a recent meta-analysis) [17], but its relatively low specificity (77.2% in the same study) made it unsuitable to be recommended in routine surveillance of CRC.

In the present study on treated CRC patients, PET/MR prompted changes in oncologic management in 36% of patients. This figure was statistically significant. Of the 15 cases whose management was changed by PET/MR, 10/15 (67%) underwent an operation. In agreement with the literature, we observed a tendency in increasingly using surgery to treat recurrences, even when advanced.

Regarding the performance of oncologic staging, PET/MR proved superior to SCI. PET/MR outperformed SCI both in detecting metastatic lesions and in ruling out lesions that were erroneously interpreted as metastases or as local recurrences by SCI. This resulted from a combination of factors. In particular, the superior anatomic layout of MR as compared with CT, the synchronous acquisition of PET and MR with resultant-improved co-registration and fusion, translated into the possibility of:

1- taking advantage of the high sensibility of PET and of diffusion weighted images in detecting lesions;
2- employing the superior soft tissue signal noise and contrast to noise ratios of MR for allocating metabolic event;
3- performing a comprehensive multiparametric and multimodality assessment of "candidate" lesions.

PET/MR did not falsely upstage any case; however, it did falsely downstage two cases. In fact, although PET/MR outperformed SCI, it was incapable of detecting microscopic tumors that attained neither metabolic nor morphologic thresholds. In the subgroup of patients with mucinous neoplasms or mucinous features, PET/MR changed the management in 2/7 patients (28%). These tumors are reported to have less FDG uptake due to their relative hypocellularity [18]. In these two cases, PET/MR added information due to the higher capability of detecting and characterizing lesions/tissues from MR. However, in comparison with the SCI, the difference was not significant, probably due to the very small sample size of this sub-group that made analysis and interpretation very limited.

Our study is in line with others that have shown the superior performance of PET/MR versus SCI in staging solid organ neoplasms, some of which have reported treatment implications. However, limited literature has evaluated CRC with PET/MR. The few available studies have assessed smaller and more heterogeneous cohorts of patients, usually including both treatment-naïve and treatment-treated CRC, and they have rarely explored the clinical implications of PET/MR versus SCI. They have reported better staging performance of PET/MR versus PET/CT in smaller mixed populations of treated and un-treated CRC [11, 12]. One of these studies compared PET/MR with CECT in a mixed population of untreated and treated CRC and showed that PET/MR added value in 27.5% of patients leading to treatment changes in 21.6% patients [12]. However, in this study, patients underwent only abdomen and pelvis CETC, without imaging the chest. In a different study that did not analyze colon cancers but investigated a cohort composed only by rectal cancers that had undergone treatment, PET/MR demonstrated an excellent accuracy (94%) for detecting pelvic recurrences of the previously treated rectal cancer, with management changes in 8/47 cases [19]. Lastly, it has been reported that PET/MR with DWI might be superior to PET/CT in detecting liver lesions but not in the remaining body regions [20]; however, in this last study, PET/MR covered only the abdomen and pelvis.

Compared with previous literature, our study was performed on a larger cohort, recruited a homogenous population composed only of treated CRC patients, and compared a

whole-body PET/MR to whole-body SCI. More importantly, it was focused on exploring the clinical implications of PET/MR rather than only the staging performances.

Limitations

Our study has several limitations. First of all, its retrospective nature and the fact that PET/MR was often performed in the most challenging cases might have introduced a selection bias. Besides this, it is relatively a small sample; the origin from a single and specialized oncologic institution and the fact that management might differ at other institutions are important limitations of our study. The patients of this retrospective study were enrolled consecutively and had had heterogeneous preceding therapies; however, they represent the routine clinical scenario at our institution. Lastly, the various imaging techniques used as standard of imaging care and the interval up to 3 months between them and PET/MR make the results less robust. After an interval of 3 months, it is more likely that additional lesions can be detected. However, the analysis performed in the subgroup of patients undergoing same day PET/CT and PET/MR also showed statistically significant changes in management induced by PET/MR. Additionally, in 6/15 (40%) of studies, PET/MR prompted a downstaging instead of an upstaging, mainly due to the complementary information of simultaneously acquired MR and PET that helped better characterizing tissue and lesions.

Conclusions

PET/MR is a promising imaging tool in the evaluation of treated CRC and might change the management in these patients. However, multicenter prospective studies with larger patient samples are required in order to confirm these preliminary results.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures were in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This retrospective study had been conducted under IRB approval granted by Partners Healthcare Institutional Review Board (IRB), Protocol no. 2018P001334. Patient consent has been waived by IRB.

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