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DIAGNOSTIC AND INTERVENTIONAL RADIOLOGY INNOVATIONS IN COLORECTAL CANCER (S GOURTSOYIANNI, SECTION EDITOR)

The Role of Contrast-Enhanced Imaging for Colorectal Cancer Management

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Abstract

Purpose of Review Imaging is fundamental in the management of colorectal cancer (CRC). Contrast-enhanced computed tomography (CECT) and contrast-enhanced magnetic resonance (CEMR) are the imaging modalities recommended to stage and restage CRC. The aim of this review is to summarize the most relevant studies published on the role of contrast-enhanced imaging for the management of CRC.

Recent Findings There are published data demonstrating the accuracy of CECT and CEMR for local staging of both colon and rectal cancer, as well as for the evaluation of distant metastases. Moreover, different aspects of these methods, in particular perfusion techniques, are emerging as prognostic biomarkers. The optimization of contrast media injection protocols is essential to ensure reproducibility and high image quality.

Summary Contrast-enhanced imaging is mandatory in the management of CRC both for the evaluation of the primary tumor and of distant metastases.

Keywords Contrast-enhanced computed tomography · Perfusion magnetic resonance imaging · Colorectal cancer · Cancer staging · Biomarkers · Multimodal imaging

Abbreviations

CRC	Colorectal cancer
CT	Computed tomography
MR	Magnetic resonance
CECT	Contrast-enhanced computed tomography
CTC	Computed tomography colonography

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CTP	Computed tomography perfusion
CEMR	Contrast-enhanced magnetic resonance
DCE-MR	Dynamic contrast-enhanced magnetic resonance
EMVI	Extramural venous invasion
CRT	Chemoradiotherapy
CHT	Chemotherapy

Introduction

Colorectal cancer (CRC) represents the second most common cause of death in Europe for men and the third for women [1•]. Imaging plays a fundamental role in all the phases of the management of CRC, namely, in the screening, staging and assessment of response to treatment [2•].

The World Health Organization (WHO) refers to CRC as a single entity. However, colon cancer and rectal cancer should be considered as separate diseases/entities since the diagnostic workup, treatment strategies and prognosis are different [3].

Patients affected by colon cancer are treated with surgery or with chemotherapy according to the resectability of the primary tumor and the presence of distant metastases [4], thus the role of imaging is to determine the operability and for this purpose contrast-enhanced computed tomography (CECT) is the imaging modality of choice. Moreover, the surveillance of treated colon cancers is based on the identification of local recurrence as well as the onset of distant metastases. In this setting, CECT is routinely performed and contrast-enhanced magnetic resonance (CEMR) is used as problem solving technique especially for liver metastasis [5].

Recently, the role of neoadjuvant chemotherapy (CHT) in high-risk colon cancer patients has been investigated in a large trial, using CECT as the imaging modality to identify advanced colon tumors [6]. This experience stimulated many researchers to investigate the role of different imaging modalities for the risk stratification as well as for the evaluation of the response to neoadjuvant treatment [2•].

Differently from colon cancer, the treatment of rectal cancer is determined by the local staging since advanced cancers are treated with neoadjuvant CRT while early/superficial tumors are treated with surgery [7]. Both staging and restaging after CRT are usually performed with MRI which is the imaging modality of choice also for the surveillance in case of the watch and wait approach [8, 9].

In this last setting, the use of contrast-enhanced imaging is not always required but it is essential in specific clinical scenario.

In this review we will discuss the role of CECT and CEMR for the management of CRC analyzing the latest research published. More in detail, we will discuss the specific role of contrast-enhanced imaging for the clinical management of colon cancer, rectal cancer, liver metastasis, and carcinomatosis.

Colon Cancer

Local Staging with CECT

Once a colon cancer is detected, usually with endoscopy, a CECT of the thorax, abdomen, and pelvis is performed to stage the primary tumor and to exclude the presence of distant metastases [4]. For the identification of small lesions, CECT can be supplemented with a CT colonography (CTC). CTC, using dedicated reduced bowel preparations based on oral administration of cathartic agents and iodinated contrast medium (CM) for fecal tagging and bowel distension with room air or CO_2, allows a better identification of small tumors and depiction of synchronous lesions, especially if the initial colonoscopy was incomplete. This technique is also required for the screening of CRC as recommended by international guidelines [10, 11].

The accuracy of CECT for the local staging of colon cancer is influenced by tumor's dimensions and bowel wall infiltration. CECT does not allow discrimination between T1 (submucosa invasion) and T2 (muscularis propria invasion) tumors while it is accurate for the identification of T3 (subserosa invasion) and T4 (extracolonic organ invasion) tumors [12].

A recent meta-analysis reports a pooled sensitivity and specificity, for the differentiation between T1-T2 and T3-T4 tumors, of 90% and 69% respectively [13••] using CECT (Table 1). These results indicate that CECT has a risk of overstaging in almost one-third of the patients.

Evidence suggests that advanced cancers (T3cd-T4) should be treated with neoadjuvant CRT even if the debate on the impact on survival is still open [6]. CECT showed a low accuracy in the differentiation of T1-T3ab from T3cd-T4 colon tumors providing a sensitivity of 77% and a specificity of 70%, confirming the trend to overstage. These results may be explained by the tendency of Radiologists to interpret the presence of desmoplastic reaction as a tumor growth 5 mm or more beyond the bowel wall to reduce the risk of understaging.

On the other hand CTC, with intravenous CM, is highly accurate for the identification of any colon cancer providing an overall sensitivity and specificity of 97% and 81%, respectively [15]. CTC is as accurate as CECT to discriminate between T1-T2 and T3-T4 tumors (Se 90%, SP 60%) but is more accurate for the differentiation of T1-T3ab and T3cd-T4 (Se 83%, Sp 88%) reducing the tendency of overstaging with CECT [16••].

Extramural venous invasion (EMVI) represents the invasion of peritumoral veins and is a morphologic feature, identifiable on imaging, which has been demonstrated to correlate with survival as an independent prognostic factor [14••, 19•, 20, 21•]. CECT has showed a sensitivity of 71% and a specificity of 75% for the identification of EMVI while CTC has showed a slightly lower sensitivity of 67% but a higher specificity of 92% [16••].

Table 1 Sensitivity (Se) and specificity (Sp) values of CECT, CTC, and CEMR for detecting colon cancer

Modality	Overall	T1-T3 ab	T3 cd-T4	EMVI
CECT	Se: 90%; Sp: 69% [13••]	Se: 77%; Sp: 70% [13••]	Se: 64%; Sp: 83% [14••]	Se: 71%; Sp:75% [14••]
CTC	Se: 97%; Sp: 81% [15]	Se: 46%; Sp: 95% [16••]	Se: 83%; Sp: 88% [16••]	Se: 67%; Sp: 92% [16••]
CEMR	Se: 67%; Sp: 79% [17]	Se: 40%; Sp: 92% [18]	Se: 75%; Sp: 100% [14••]	Se: 63%; Sp: 91% [18]

Local Staging with CEMR

Few studies investigated the role of CEMR for the local staging of colon cancer [14••, 17, 18, 22, 23•, 24•] (Table 1). The sensitivity and specificity of CEMR for the discrimination between T1-T2 and T3-T4 tumors ranges between 42% and 91% and 58% and 89%, respectively. Similar results have been demonstrated for the differentiation of T1–T3ab from T3cd–T4 with a sensitivity and specificity ranging between 40% and 92% and 75% and 100%, respectively.

CEMR showed better results for the identification of EMVI demonstrating a sensitivity and a specificity ranging between 63% and 100% and 62% and 91%, respectively.

Rectal Cancer

Role of DCE-MRI

Differently from colon cancer, the role of imaging in the management of rectal cancer is mainly based on MR imaging [25–27]. MR has demonstrated to be the imaging modality of choice for the staging and for the evaluation of the response to neoadjuvant combined CRT in rectal cancer [9]. In both settings, unenhanced MR based on T2 weighted and diffusion-weighted imaging, has demonstrated high accuracy [28••]. Recently, numerous researches have investigated the role of contrast-enhanced MR as dynamic contrast-enhanced (DCE-MRI) for the evaluation and prediction of the response to neoadjuvant CRT as well as in the risk stratification [29•]. This technique is based on multiple acquisitions during the intravenous injection of paramagnetic contrast media which allows the in vivo evaluation of tumor microcirculation. From these datasets, many quantitative parameters can be extracted like washout (velocity of enhancement loss), Ktrans (the volume transfer constant), Kep (extravascular-to-plasma volume transfer constant), Ve (extravascular extracellular volume fraction per unit of tissue volume), Vp (plasma volume), Wash-in (velocity of enhancement), Curve-washout (washout slope), Peak enhancement, Peak (maximal concentration of contrast agent), and TME (time-to-maximal enhancement) [30, 31].

Among these parameters Ktrans showed a greater correlation with tumor angiogenetic factors like microvessel density (MVD), vascular endothelial growth factor (VEGF), and epidermal growth factor receptor (EGFR) suggesting a role for DCE-MRI in the identification of more aggressive tumors as well as prediction of the response to target therapies [31–33]. In particular, a higher Ktrans at pretreatment DCE-MRI was found in complete and good responders to CRT [34–37].

The impact of DCE-MRI for the primary staging has been also investigated. A higher Ktrans is associated with greater T and N stage and higher grading. A lower Kep was associated with lower T stage while higher Kep was associated with distant metastases. Finally, a lower time to peak (TPP) was associated with distant metastases and lymph node metastases [31, 32, 38–41].

Finally, the role of DCE-MRI as biomarker for the assessment of the response to CRT was investigated. In most of the studies a reduction of Ktrans in the post-treatment DCE-MRI was associated to a better response to CRT [31, 32, 38–44].

Role of CECT

The role of CECT in the management of rectal cancer is the overall staging of the disease in particular for the evaluation of distant metastases [45]. The role of CECT in the T staging has been evaluated reporting an accuracy of 86%; however, the technique is less accurate for the evaluation of circumferential margin (CRM) showing a sensitivity lower than 50% [46, 47]. Better results have been obtained for the identification of EMVI suggesting a role for CECT in the stratification of patient's prognosis [6, 48, 49] (Table 2).

CT can be acquired also using the perfusion technique (CTP). Similarly to DCE-MRI, this method, based on the continuous image acquisition during the intravenous contrast media injection, allows the extraction of several perfusion parameters like mean transit time (MTT), blood flow (BF), blood volume (BV), and permeability surface (PS) [50–53].

The role of CTP as method for monitoring or predicting the response to CRT has been investigated [52, 54, 55]. Neoadjuvant CRT induces the development of fibrosis within the tumor; therefore, it impairs the accuracy of the evaluation with unenhanced MR. It has been demonstrated that the development of fibrosis after treatment can be identified with CTP thanks to the decrease of BF and BV and the increase of MTT [56, 57].

The evaluation of pretreatment CTP to predict the response to CRT has been investigated; however, in this setting, results are controversial and data are limited [54, 55]. However, CTP showed good results in the prediction of recurrence and a good

Table 2 Sensitivity (Se) and specificity (Sp) values of CECT and CEMR for detecting rectal cancer

Modality	Overall	T1-T3 ab	T3 cd-T4	EMVI
CECT	Se:70%; Sp: 88% [46]	Se: 43%; Sp: 97% [47]	Se: 50%; Sp:98% [46]	Se:86%; Sp:61% [49]
CEMR	Se: 97%; Sp: 97% [26]	Se:92%; Sp: 92% [26]	Se:100%; Sp: 100% [25]	Se:77%; Sp:86% [27]

correlation with prognosis [53, 56]. In this setting, pretreatment BF has shown to be significantly lower in patients who developed distant metastases.

Liver Metastases

The liver is the most common site of CRC metastases with an incidence of 32% for metachronous metastases and 24% for synchronous metastases [58–60].

The main imaging modalities recommended to investigate CRC liver metastasis by the European and American guidelines are CECT and CEMR with a reported sensitivity/specificity of 73%/76% and of 85%/96%, respectively [60, 61••, 62••, 63, 64].

Between them, the first one is CECT, even though CEMR has now proved a better diagnostic accuracy and the gadolinium chelates contrast agent has shown a lower percentage of collateral effects. The reason behind the choice of CECT, as primary imaging modality, is its higher availability, shorter acquisition time, lower cost, and the possibility to detect extra-hepatic disease. CEMR becomes the recommended primary modality when CECT is contraindicated, e.g., allergy to iodine contrast media, and the recommended complementary modality when CECT is controversial or in the preoperative assessment of the liver [62••, 65].

Regarding the CECT acquisition protocol, the administration of contrast media of high or low iodine concentration (400 mg I/mL and 300 mg I/mL or less, respectively) is still debated [66], while it is well established that the dose of contrast media should be adjusted in consideration of patient's weight and not fixed [67]. The weight-adapted measure should be made on the base of lean body weight instead of total body weight, which can be estimated or calculated [68]. The recommended dose of contrast media used is 0.7 g of iodine [gI] per kg of lean body weight, which is estimated according to Boer formula [69] and the flux of contrast media is adapted to the available CM concentration in order to achieve an iodine delivery rate of 1.6 gI/s. These parameters should ensure a hepatic enhancement higher than 50 HU in portal venous phase which ensures a good conspicuity of hypovascular lesions. This approach has been demonstrated to increase reproducibility despite patient's dimensions.

In CECT, the universally accepted phase after contrast administration is the portal venous phase while the use of unenhanced phase and arterial phase are controversial for radiation dose-related reasons [70].

The use of unenhanced phase in CECT is controversial because liver metastases may have a variable density. However, unenhanced phase is useful to find internal calcifications (occurring in 1/10 of metastases) [71]. However, in the clinical routine of most centers, the unenhanced phase is traditionally acquired during the primary exam to detect eventual other liver lesions and to help in differential diagnosis, even if this is also frequently debated. That is not the case with the new dual-energy technique, still not widely used but increasingly studied, in which the acquisition of the unenhanced phase can be avoided, thanks to the possibility to subtract the iodine contribute on the enhanced images to obtain a virtual unenhanced phase [72].

Unenhanced MR examination is also poorly specific for the characterization of liver metastases since they can appear hypo or iso-intense on T1-weighted images and iso or hyperintense on T2-weighted images compared with the healthy liver [73].

The low specificity of unenhanced imaging demands the use of CM in both modalities for an accurate characterization. The reason why the acquisition of a portal venous phase is recommended is that, during this phase, the conspicuity of CRC liver metastases is maximized since they appear hypovascular while liver parenchyma shows its greater enhancement [74, 75].

During the arterial phase, most of metastases show a peripheral enhancement or "ring" enhancement, with a washout in the portal venous phase, which could be due to different reasons, namely, the peripheral vascular proliferation and/or inflammatory reaction and/or desmoplastic reaction [75, 76].

The incidence of hypervascular CRC hepatic metastases, which receive strong arterial supply, is about 1/10 of all metastases [77•]. These metastases show an enhancement at the arterial phase stronger than the rest of the liver, followed by washout during the portal venous phase. That is one of the reasons, as well as the detection of "ring enhancement" when it occurs, in favor of the use of arterial phase during CECT acquisition protocol, which is still debated as the unenhanced phase.

At the delayed phase, all metastases appear hypovascular compared with the rest of the liver.

While the number of acquisitions is limited for CECT, because of radiation exposure concerns, for CEMR, the acquisition of multiple enhanced phases is routinely performed.

The use of hepatospecific contrast agents in MR is now considered necessary. In the hepatobiliary phase, excretion of contrast into the biliary system takes place which allows both hypovascular and hypervascular metastases to show a strong low signal intensity compared with the rest of the liver. This aspect is absolutely useful, along with diffusion-weighted imaging (DWI) with apparent diffusion coefficient (ADC) map review, in differentiating malignant and benign lesions [78]. The only case in which the extracellular contrast agent is suggested is for the differential diagnosis with small hemangiomas [62]. To date, two hepatobiliary agents are commercially available, gadobenate dimeglumine (Gd-BOPTA) and gadoxetate disodium (Gd-EOB-DTPA) [78]. The main difference between the two agents is the timing for hepatobiliary phase, with a delay after contrast administration of 120 min for Gd-BOPTA and 20 min for Gd-EOB-DTPA. Also, for these two CM, the amount of contrast administered should be tailored according to patient's body weight. A dose of 0.05 mmol/kg is recommended for Gd-BOPTA and 0.025 mmol/kg for Gd-EOB-DTPA [79]. The concentration of the two CM is different, Gd-BOPTA is 0.5 M while Gd-EOB-DTPA is 0.25 M; however, for both, 0.1 ml/Kg should be injected. Therefore, as an example, for a 70 kg patient, the dose of hepatobiliary contrast agent will be 7 mL.

Carcinomatosis

Carcinomatosis is defined as a condition of neoplastic involvement of the peritoneal cavity representing the advanced stage of abdominal and pelvic organs' tumors, with an association to a poor prognosis,with a mean survival of 6 months (range 1–9 months) after initial diagnosis [80].

CRC is the third most common cause of carcinomatosis after ovarian and stomach tumor with an incidence of about 10%, 70%, and 15%, respectively [81].

In most cases, PC is diagnosed late in very advanced stage due to not specific symptoms and is associated with a poor survival. Surgical procedures as peritonectomy, associated with perioperative chemotherapy, combined with hyperthermia, hyperthermic intraperitoneal chemotherapy (HIPEC) can guarantee an improvement of patient's quality of life. For this reason, the extent of peritoneal metastases with a correct staging is essential for evaluating patients' outcome after treatment [82].

CECT and CEMR are considered as diagnostic tools for a correct staging of peritoneal involvement that can give accurate information about location, size, and morphology.

CECT is the preferred imaging modality that can give accurate preoperative or pretreatment information on morphology, size, location of peritoneal implants, lymphadenopathy, and presence of ascites with several advantages. It allows to evaluate the entire abdomen, it can be performed rapidly and relatively easily, it is free from misregistration artifacts, and thin sections allow the detection of subcentimetric implants [83]. The use of iodinated CM is essential for the assessment of PC: arterial phase is mandatory in case of hypervascular primary tumors and to assess vascular infiltration; delayed phase, acquired from 8 to 10 min after intravenous CM injection is fundamental in case of pelvic implants or retroperitoneal metastases in which a delayed enhancement is observed [83].

A recent meta-analysis reported the high diagnostic accuracy of CECT for the diagnosis of PC showing a sensitivity of 83% and a specificity of 86% on a per patient analysis, a sensitivity of 78% and 76% for epigastrium, and pelvis respectively and a high specificity of 95% in right upper abdomen and small bowel [84••].

CEMR is considered a second-choice imaging modality in selected patients when CECT findings are equivocal; as for CECT, the role of CM in CEMR is mandatory due to the higher conspicuity of peritoneal lesions on delayed phase. MR has the incremental advantage of the use of diffusion-weighted images (DWI) providing signal suppression from surrounding ascites, bowel contents, and fat, increasing the contrast-to-noise-ratio of peritoneal implants [83]. Although few studies are present in literature, a recent meta-analysis reported a good accuracy for CEMR in detecting PC showing a cumulative sensitivity of 83% and a specificity of 86% [84••].

Conclusions

Imaging plays a fundamental role in the management of CRC (Table 3). The use of contrast-enhanced imaging is required for most of the clinical indications. CECT is the main imaging modality for staging of both colon and rectal cancers. In this setting, CM injection protocol should be tailored according to patients' characteristics and acquisition timings need to be adapted to the clinical indication. The role of CTP has been investigated in limited studies, but its role seems to be promising for the evaluation of the response after neoadjuvant therapy especially in patients with contraindications for MR.

For the T staging of colon and rectal cancer, MRI is routinely performed without the administration of CM; however, the emerging role of DCE-MR has been widely demonstrated and it can be considered as a prognostic biomarker for the risk stratification or for the prediction of response to CRT.

The role of contrast-enhanced imaging for the evaluation of distant metastases has been widely demonstrated in literature. In this scenario, CECT should be considered the primary imaging modality while CEMR should be reserved as a problem solving imaging method.

Table 3 The table summarizes the role of each imaging modality in the different steps in management of colon and rectal cancer respectively

COLON CANCER	RECTAL CANCER
CECT Staging ↑ T1-T2 Vs T3-T4 ↓ T1-T3ad Vs T3cd-T4 ↑ EMVI ↑ Carcinomatosis ↑ Distant metastases Restaging ↑ Local recurrence ↑ Carcinomatosis ↑ Distant metastases **CTC (with IV CM)** Staging ↑ T1-T3 and Vs T3cd-T4 ↑ Small lesions Restaging ↑ Local recurrence ↑ New polypoid lesions **CEMR** Staging	**CECT** Staging ↓ T staging ↓ CRM ↑ EMVI ↑ Distant metastases ↑ Carcinomatosis Restaging ↓ Local recurrence ↑ Carcinomatosis ↑ Distant metastases Prognosis with CTP ↓ Prediction of response to CRT ↑ Response to CRT **CEMR** Staging ↑ T staging ↑ EMVI ↑ CRM ↑ Liver metastases ↑ Carcinomatosis
CM injection protocol for CT	**CM injection protocol for MR**

LBW
• Measure body fat percentage
• Estimate LBW
  • James formula
  • Boer formula
CM volume
• 0.7 gr of iodine per Kg of LBW
Injection flow rate
	TBW
	• Measure with scale
	CM volume
	• Gd-BOPTA
	  • 0.05 mmol per Kg of TBW
	• Gd-EOB-DTPA
	  • 0.025 mmol per Kg of TBW
	Injection flow rate
	• Gd-BOPTA: 2 ml per second

For each application, the up-arrow signal (↑) indicates good accuracy while the down arrow signal (↓) represents poor accuracy
In the bottom, a list summarizing the contrast medium injection protocol for CT and MR respectively is included

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflicts of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

References

Papers of particular interest, published recently, have been highlighted as:
- • Of importance
- •• Of major importance

1.• Ferlay J, et al. Cancer incidence and mortality patterns in Europe: estimates for 40 countries and 25 major cancers in 2018. Eur J Cancer. 2018;103:356–87 **Updated data on incidence and mortality of CRC in Europe.**
2.• Ganeshan, D., et al., Locally recurrent rectal cancer: what the radiologist should know. Abdom Radiol (NY), 2019. **Interesting review focused on the role of the radiologist for the evaluation of recurrent rectal cancer.**
3. Binefa G, Rodríguez-Moranta F, Teule A, Medina-Hayas M. Colorectal cancer: from prevention to personalized medicine. World J Gastroenterol. 2014;20(22):6786–808.
4. van de Velde CJ, et al. EURECCA colorectal: multidisciplinary management: European consensus conference colon & rectum. Eur J Cancer. 2014;50(1):1.e1–1.e34.
5. Cho JY, Lee YJ, Han HS, Yoon YS, Kim J, Choi Y, et al. Role of gadoxetic acid-enhanced magnetic resonance imaging in the preoperative evaluation of small hepatic lesions in patients with colorectal cancer. World J Surg. 2015;39(5):1161–6.
6. Foxtrot Collaborative G. Feasibility of preoperative chemotherapy for locally advanced, operable colon cancer: the pilot phase of a randomised controlled trial. Lancet Oncol. 2012;13(11):1152–60.
7. Balyasnikova S, Brown G. Optimal imaging strategies for rectal cancer staging and ongoing management. Curr Treat Options in Oncol. 2016;17(6):32.
8. Rengo M, et al. Magnetic resonance tumor regression grade (MR-TRG) to assess pathological complete response following neoadjuvant radiochemotherapy in locally advanced rectal cancer. Oncotarget. 2017;8(70):114746–55.
9. Beets-Tan RGH, Lambregts DMJ, Maas M, Bipat S, Barbaro B, Curvo-Semedo L, et al. Correction to: Magnetic resonance imaging for clinical management of rectal cancer: Updated recommendations from the 2016 European Society of Gastrointestinal and Abdominal Radiology (ESGAR) consensus meeting. Eur Radiol. 2018;28(6):2711.
10. Laghi A, Iafrate F, Rengo M, Hassan C. Colorectal cancer screening: the role of CT colonography. World J Gastroenterol. 2010;16(32):3987–94.
11. Iafrate F, Hassan C, Ciolina M, Lamazza A, Baldassari P, Pichi A, et al. High positive predictive value of CT colonography in a referral centre. Eur J Radiol. 2011;80(3):e289–92.
12. Dighe S, Blake H, Koh MD, Swift I, Arnaout A, Temple L, et al. Accuracy of multidetector computed tomography in identifying poor prognostic factors in colonic cancer. Br J Surg. 2010;97(9):1407–15.
13.•• Nerad E, et al. Diagnostic accuracy of CT for local staging of colon cancer: a systematic review and meta-analysis. AJR Am J Roentgenol. 2016;207(5):984–95 **Rigorouse meta-analysis dimostrating the accuracy of CT in the local staging of colon cancer.**
14.•• Park SY, et al. Diagnostic performance of MRI- versus MDCT-categorized T3cd/T4 for identifying high-risk stage II or stage III colon cancers: a pilot study. Abdom Radiol (NY). 2019;44(5):1675–85 **Small but very insteresting paper comparing CT and MRI for the risk assessment of colon cancer.**
15. Laghi A, Rengo M, Graser A, Iafrate F. Current status on performance of CT colonography and clinical indications. Eur J Radiol. 2013;82(8):1192–200.
16.•• Horvat N, et al. CT colonography in preoperative staging of colon cancer: evaluation of FOxTROT inclusion criteria for neoadjuvant therapy. AJR Am J Roentgenol. 2019;212(1):94–102 **Well-designed study demostrating the role of CTC in the management of colon cancer.**
17. Hunter C, et al. Local staging and assessment of colon cancer with 1.5-T magnetic resonance imaging. Br J Radiol. 2016;89(1064):20160257.
18. Rollvén E, Holm T, Glimelius B, Lörinc E, Blomqvist L. Potentials of high resolution magnetic resonance imaging versus computed tomography for preoperative local staging of colon cancer. Acta Radiol. 2013;54(7):722–30.
19. Hospers GA, Punt CJ, Tesselaar ME, Cats A, Havenga K, Leer JW, et al. Preoperative chemoradiotherapy with capecitabine and oxaliplatin in locally advanced rectal cancer. A phase I-II multicenter study of the Dutch Colorectal Cancer Group. Ann Surg Oncol. 2007;14(10):2773–9.
20. Dighe S, Swift I, Brown G. CT staging of colon cancer. Clin Radiol. 2008;63(12):1372–9.
21.• Yao X, et al. Prognostic significance of computed tomography-detected extramural vascular invasion in colon cancer. World J Gastroenterol. 2016;22(31):7157–65 **One of the few studies investgatig the role of CT for the detection of EMVI in colon cancer.**
22. Dam C, Lindebjerg J, Jakobsen A, Jensen LH, Rahr H, Rafaelsen SR. Local staging of sigmoid colon cancer using MRI. Acta Radiol Open. 2017;6(7):2058460117720957.
23. Nerad E, Lambregts DM, Kersten EL, Maas M, Bakers FC, van den Bosch H, et al. MRI for local staging of colon cancer: can MRI become the optimal staging modality for patients with colon cancer? Dis Colon Rectum. 2017;60(4):385–92.
24.• Hunter C, et al. CT and 3-T MRI accurately identify T3c disease in colon cancer, which strongly predicts disease-free survival. Clin Radiol. 2017;72(4):307–15 **Interesting data demostrating the role of CT and MRI for the identification high-risk colon cancer.**
25. Giusti S, et al. Preoperative rectal cancer staging with phased-array MR. Radiat Oncol. 2012;7:29.
26. Colakoglu Er H, et al. Rectal cancer confined to the bowel wall: the role of 3 Tesla phased-array MR imaging in T categorization. Br J Radiol. 2018;91(1082):20170581.
27. Bae JS, Kim SH, Hur BY, Chang W, Park J, Park HE, et al. Prognostic value of MRI in assessing extramural venous invasion in rectal cancer: multi-readers' diagnostic performance. Eur Radiol. 2019;29(8):4379–88.
28.•• Gourtsoyianni S, Papanikolaou N. Role of magnetic resonance imaging in primary rectal cancer-standard protocol and beyond. Semin Ultrasound CT MR. 2016;37(4):323–30 **Reference paper focused on the practical issues related to MRI for the management of rectal cancer.**
29.• Dijkhoff RAP, et al. Value of DCE-MRI for staging and response evaluation in rectal cancer: a systematic review. Eur J Radiol.

2017;**95**:155–68 **Very rationale sistematic review highlithing the role of DCE-MRI for the management of rectal cancer.**

30. Jackson A, O'Connor JP, Parker GJ, Jayson GC. Imaging tumor vascular heterogeneity and angiogenesis using dynamic contrast-enhanced magnetic resonance imaging. Clin Cancer Res. 2007;13(12):3449–59.
31. Yeo DM, Oh SN, Jung CK, Lee MA, Oh ST, Rha SE, et al. Correlation of dynamic contrast-enhanced MRI perfusion parameters with angiogenesis and biologic aggressiveness of rectal cancer: preliminary results. J Magn Reson Imaging. 2015;41(2):474–80.
32. Kim YE, Lim JS, Choi J, Kim D, Myoung S, Kim MJ, et al. Perfusion parameters of dynamic contrast-enhanced magnetic resonance imaging in patients with rectal cancer: correlation with microvascular density and vascular endothelial growth factor expression. Korean J Radiol. 2013;14(6):878–85.
33. Ciolina M, et al. Dynamic contrast-enhanced magnetic resonance imaging in locally advanced rectal cancer: role of perfusion parameters in the assessment of response to treatment. Radiol Med. 2018.
34. Tong T, Sun Y, Gollub MJ, Peng W, Cai S, Zhang Z, et al. Dynamic contrast-enhanced MRI: use in predicting pathological complete response to neoadjuvant chemoradiation in locally advanced rectal cancer. J Magn Reson Imaging. 2015;42(3):673–80.
35. Intven M, Reerink O, Philippens ME. Dynamic contrast enhanced MR imaging for rectal cancer response assessment after neo-adjuvant chemoradiation. J Magn Reson Imaging. 2015;41(6):1646–53.
36. George ML, Dzik-Jurasz AS, Padhani AR, Brown G, Tait DM, Eccles SA, et al. Non-invasive methods of assessing angiogenesis and their value in predicting response to treatment in colorectal cancer. Br J Surg. 2001;88(12):1628–36.
37. Lim JS, Kim D, Baek SE, Myoung S, Choi J, Shin SJ, et al. Perfusion MRI for the prediction of treatment response after preoperative chemoradiotherapy in locally advanced rectal cancer. Eur Radiol. 2012;22(8):1693–700.
38. Lollert A, et al. Rectal cancer: dynamic contrast-enhanced MRI correlates with lymph node status and epidermal growth factor receptor expression. J Magn Reson Imaging. 2014;39(6):1436–42.
39. Yao WW, Zhang H, Ding B, Fu T, Jia H, Pang L, et al. Rectal cancer: 3D dynamic contrast-enhanced MRI; correlation with microvascular density and clinicopathological features. Radiol Med. 2011;116(3):366–74.
40. Zhang XM, Yu D, Zhang HL, Dai Y, Bi D, Liu Z, et al. 3D dynamic contrast-enhanced MRI of rectal carcinoma at 3T: correlation with microvascular density and vascular endothelial growth factor markers of tumor angiogenesis. J Magn Reson Imaging. 2008;27(6):1309–16.
41. Shen FU, Lu J, Chen L, Wang Z, Chen Y. Diagnostic value of dynamic contrast-enhanced magnetic resonance imaging in rectal cancer and its correlation with tumor differentiation. Mol Clin Oncol. 2016;4(4):500–6.
42. Intven M, Monninkhof EM, Reerink O, Philippens ME. Combined T2w volumetry, DW-MRI and DCE-MRI for response assessment after neo-adjuvant chemoradiation in locally advanced rectal cancer. Acta Oncol. 2015;54(10):1729–36.
43. Kim SH, Lee JM, Gupta SN, Han JK, Choi BI. Dynamic contrast-enhanced MRI to evaluate the therapeutic response to neoadjuvant chemoradiation therapy in locally advanced rectal cancer. J Magn Reson Imaging. 2014;40(3):730–7.
44. Gollub MJ, Tong T, Weiser M, Zheng J, Gonen M, Zakian KL. Limited accuracy of DCE-MRI in identification of pathological complete responders after chemoradiotherapy treatment for rectal cancer. Eur Radiol. 2017;27(4):1605–12.
45. Poston GJ, et al. Diagnosis and management of colorectal cancer: summary of NICE guidance. BMJ. 2011;343:d6751.
46. Sinha R, et al. Diagnostic value of multidetector row CT in rectal cancer staging: comparison of multiplanar and axial images with histopathology. Clin Radiol. 2006;61(11):924–31.
47. Wolberink SV, Beets-Tan RG, de Haas-Kock DF, Span MM, van de Jagt E, van de Velde C, et al. Conventional CT for the prediction of an involved circumferential resection margin in primary rectal cancer. Dig Dis. 2007;25(1):80–5.
48. Burton S, Brown G, Bees N, Norman A, Biedrzycki O, Arnaout A, et al. Accuracy of CT prediction of poor prognostic features in colonic cancer. Br J Radiol. 2008;81(961):10–9.
49. Smith NJ, Bees N, Barbachano Y, Norman AR, Swift RI, Brown G. Preoperative computed tomography staging of nonmetastatic colon cancer predicts outcome: implications for clinical trials. Br J Cancer. 2007;96(7):1030–6.
50. Hayano K, Fujishiro T, Sahani DV, Satoh A, Aoyagi T, Ohira G, et al. Computed tomography perfusion imaging as a potential imaging biomarker of colorectal cancer. World J Gastroenterol. 2014;20(46):17345–51.
51. Goh V, Halligan S, Daley F, Wellsted DM, Guenther T, Bartram CI. Colorectal tumor vascularity: quantitative assessment with multidetector CT–do tumor perfusion measurements reflect angiogenesis? Radiology. 2008;249(2):510–7.
52. Sahani DV, Kalva SP, Hamberg LM, Hahn PF, Willett CG, Saini S, et al. Assessing tumor perfusion and treatment response in rectal cancer with multisection CT: initial observations. Radiology. 2005;234(3):785–92.
53. Goh V, Halligan S, Wellsted DM, Bartram CI. Can perfusion CT assessment of primary colorectal adenocarcinoma blood flow at staging predict for subsequent metastatic disease? A pilot study. Eur Radiol. 2009;19(1):79–89.
54. Curvo-Semedo L, et al. Usefulness of perfusion CT to assess response to neoadjuvant combined chemoradiotherapy in patients with locally advanced rectal cancer. Acad Radiol. 2012;19(2):203–13.
55. Bellomi M, Petralia G, Sonzogni A, Zampino MG, Rocca A. CT perfusion for the monitoring of neoadjuvant chemotherapy and radiation therapy in rectal carcinoma: initial experience. Radiology. 2007;244(2):486–93.
56. Hayano K, Shuto K, Koda K, Yanagawa N, Okazumi S, Matsubara H. Quantitative measurement of blood flow using perfusion CT for assessing clinicopathologic features and prognosis in patients with rectal cancer. Dis Colon Rectum. 2009;52(9):1624–9.
57. Satoh A, et al. Role of perfusion CT in assessing tumor blood flow and malignancy level of gastric cancer. Dig Surg. 2010;27(4):253–60.
58. Manfredi S, et al. Epidemiology and management of liver metastases from colorectal cancer. Ann Surg. 2006;244(2):254–9.
59. Mekenkamp LJ, Koopman M, Teerenstra S, van Krieken J, Mol L, Nagtegaal ID, et al. Clinicopathological features and outcome in advanced colorectal cancer patients with synchronous vs metachronous metastases. Br J Cancer. 2010;103(2):159–64.
60. Fowler KJ, et al. ACR appropriateness criteria. J Am Coll Radiol. 2017;14(5S):S234–44.
61.•• Van Cutsem E, et al. ESMO consensus guidelines for the management of patients with metastatic colorectal cancer. Ann Oncol. 2016;**27**(8):1386–422 **Refence document containig guidelines for the management of metastatic colorectal cancer.**
62.•• Glynne-Jones R, et al. Rectal cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2018;29(Supplement_4):iv263 **Refence document containig guidelines for the management of rectal cancer.**
63. Benson AB, Venook AP, al-Hawary MM, Cederquist L, Chen YJ, Ciombor KK, et al. NCCN guidelines insights: colon cancer, version 2.2018. J Natl Compr Cancer Netw. 2018;16(4):359–69.
64. Benson AB, Venook AP, al-Hawary MM, Cederquist L, Chen YJ, Ciombor KK, et al. Rectal cancer, version 2.2018, NCCN clinical

practice guidelines in oncology. J Natl Compr Cancer Netw. 2018;16(7):874–901.
65. Benson AB, et al. Colon cancer, version 1.2017, NCCN clinical practice guidelines in oncology. J Natl Compr Cancer Netw. 2017;15(3):370–98.
66. Rengo M, Caruso D, de Cecco CN, Lucchesi P, Bellini D, Maceroni MM, et al. High concentration (400 mgI/mL) versus low concentration (320 mgI/mL) iodinated contrast media in multi detector computed tomography of the liver: a randomized, single centre, non-inferiority study. Eur J Radiol. 2012;81(11):3096–101.
67. Rengo M, et al. The optimal contrast media policy in CT of the liver. *Part I: Technical notes*. Acta Radiol. 2011;52(5):467–72.
68. Rengo M, Bellini D, Businaro R, Caruso D, Azzara G, de Santis D, et al. MDCT of the liver in obese patients: evaluation of a different method to optimize iodine dose. Abdom Radiol (NY). 2017;42(10):2420–7.
69. Boer P. Estimated lean body mass as an index for normalization of body fluid volumes in humans. Am J Phys. 1984;247(4 Pt 2):F632–6.
70. Rengo M, Bellini D, de Cecco CN, Osimani M, Vecchietti F, Caruso D, et al. The optimal contrast media policy in CT of the liver. *Part II: Clinical protocols*. Acta Radiol. 2011;52(5):473–80.
71. Bonaldi VM, Bret PM, Reinhold C, Atri M. Helical CT of the liver: value of an early hepatic arterial phase. Radiology. 1995;197(2):357–63.
72. De Cecco CN, et al. Preliminary experience with abdominal dual-energy CT (DECT): true versus virtual nonenhanced images of the liver. Radiol Med. 2010;115(8):1258–66.
73. Khosa F, Khan AN, Eisenberg RL. Hypervascular liver lesions on MRI. AJR Am J Roentgenol. 2011;197(2):W204–20.
74. Tirumani SH, Kim KW, Nishino M, Howard SA, Krajewski KM, Jagannathan JP, et al. Update on the role of imaging in management of metastatic colorectal cancer. Radiographics. 2014;34(7):1908–28.
75. Kijima S, Sasaki T, Nagata K, Utano K, Lefor AT, Sugimoto H. Preoperative evaluation of colorectal cancer using CT colonography, MRI, and PET/CT. World J Gastroenterol. 2014;20(45):16964–75.
76. Coenegrachts K. Magnetic resonance imaging of the liver: new imaging strategies for evaluating focal liver lesions. World J Radiol. 2009;1(1):72–85.
77.• Beckers RCJ, et al. Advanced imaging to predict response to chemotherapy in colorectal liver metastases - a systematic review. HPB (Oxford). 2018;20(2):120–7 **Very interesting paper demotrating the role of advance imaging for the management of liver metastases in colorectal cancer.**
78. Thian YL, Riddell AM, Koh DM. Liver-specific agents for contrast-enhanced MRI: role in oncological imaging. Cancer Imaging. 2013;13(4):567–79.
79. Morana G, Cugini C, Scatto G, Zanato R, Fusaro M, Dorigo A. Use of contrast agents in oncological imaging: magnetic resonance imaging. Cancer Imaging. 2013;13(3):350–9.
80. Di Giorgio A, et al. Cytoreductive surgery (peritonectomy procedures) combined with hyperthermic intraperitoneal chemotherapy (HIPEC) in the treatment of diffuse peritoneal carcinomatosis from ovarian cancer. Cancer. 2008;113(2):315–25.
81. Koppe MJ, Boerman OC, Oyen WJ, Bleichrodt RP. Peritoneal carcinomatosis of colorectal origin: incidence and current treatment strategies. Ann Surg. 2006;243(2):212–22.
82. Sammartino P, Biacchi D, Cornali T, Accarpio F, Sibio S, Luraschi B, et al. Computerized system for staging peritoneal surface malignancies. Ann Surg Oncol. 2016;23(5):1454–60.
83. Iafrate F, Ciolina M, Sammartino P, Baldassari P, Rengo M, Lucchesi P, et al. Peritoneal carcinomatosis: imaging with 64-MDCT and 3T MRI with diffusion-weighted imaging. Abdom Imaging. 2012;37(4):616–27.
84.•• Laghi A, et al. Diagnostic performance of computed tomography and magnetic resonance imaging for detecting peritoneal metastases: systematic review and meta-analysis. Radiol Med. 2017;122(1):1–15 **Very interesting meta-analysis demostrating the role of CT and MRI for the evaluation of peritoneal carcinosis.**