



Diagnostic performance of MRI- versus MDCT-categorized T3cd/T4 for identifying high-risk stage II or stage III colon cancers: a pilot study

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Abstract

Purpose The aim of this study was to determine the diagnostic performance of magnetic resonance imaging (MRI)-categorized T3cd/T4 tumors for identifying high-risk stage II or stage III cancer in patients with curatively resectable colon cancer in comparison to that of multidetector computed tomography (MDCT).

Materials and Methods Thirty-eight patients with histopathologically indicated adenocarcinomas prospectively underwent MRI of the colon. Two radiologists independently and retrospectively assessed for T-category, including T3 substage (\leq T3ab vs. \geq T3cd). The diagnostic accuracies and interreader agreements between assessments using each modality were compared using a pairwise comparison of receiver-operating characteristic curves and a weighted κ statistic, respectively.

Results Twenty-nine patients (76.3%) were histopathologically diagnosed with high-risk stage II or stage III colon cancer. The false-positive rate with MRI was lower than that with MDCT (0% vs. 7.9% for reader 1, 2.6% vs. 10.6% for reader 2). The diagnostic performance of MRI was better than that of MDCT across both readers (AUC: 0.707 vs. 0.506 [$P = 0.032$] for reader 1, 0.651 vs. 0.485 [$P = 0.055$] for reader 2). Moreover, MRI interreader agreement for the assessment of T3cd/T4 was significantly better than that of MDCT ($\kappa = 0.821$ vs. 0.391 [$P = 0.017$]).

Conclusion The diagnostic performance of MR imaging of the colon may be better than that of MDCT for identifying high-risk stage II or stage III cases. Particularly, colon MRI reduced the false-positive rate and improved the interreader agreement, although further studies with a larger sample size are required.

Keywords Colon cancer · Magnetic resonance imaging (MRI) · Multidetector computed tomography (MDCT) · Staging · Neoadjuvant chemotherapy

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Introduction

In patients with high-risk stage II or stage III colon cancer, curative surgery followed by adjuvant chemotherapy has become the standard treatment of care over a decade [1–4]. Although use of a monoclonal antibody, such as cetuximab or panitumumab depending on the KRAS mutation present, can improve disease control, approximately 20–30% patients develop metachronous metastasis after curative treatment [5]. If only the existing standard treatments are provided to patients with advanced colon cancer, the current plateau in survival rate may remain. Given its benefits to survival rates, improved compliance, and a higher rate of R0 resections with neoadjuvant treatment in rectal, gastric,

and esophageal cancers, neoadjuvant chemotherapy might be an alternative solution [6–9].

Neoadjuvant chemotherapy is based on the hypothesis that reducing tumor burden and downstaging prior to resection surgery decrease the spread of tumor cells during the operation and thus offers better control of micrometastasis [10]. Although previous studies have shown promising results, the main indication for neoadjuvant chemotherapy remains a source of debate [10–15]. Prior to clinical trials of neoadjuvant chemotherapies, establishing appropriate radiological indications for its use will be essential to maximize treatment gains in high-risk patients and to prevent overtreatment in low-risk patients.

Recently, studies have demonstrated the diagnostic value of magnetic resonance imaging (MRI) for local staging of colon cancer [16–18]. However, while MR imaging of the colon offers some diagnostic performance advantages in terms of a higher spatial resolution, multi-detector computed tomography (MDCT) is used in daily clinical practice due to better controlling over motion artifacts as well as its superior temporal resolution. In the pilot phase of the Fluoropyrimidine Oxaliplatin and Targeted Receptor Preoperative Therapy (FOXROT) trial, the author group suggested that T3cd/T4 colon cancers might be an indication for neoadjuvant chemotherapy use [10]. However, no modality-based T3cd/T4 studies have demonstrated superior identification of high-risk stage II or stage III colon cancers. Therefore, the purpose of the present study is to determine the diagnostic performance of MRI-categorized T3cd/T4 tumors for identifying high-risk stage II or stage III cancer in patients with curatively resectable colon cancer in comparison to that of MDCT.

Materials and methods

The local research ethics committee approved this prospectively registered, retrospectively reviewed study and written informed consent was obtained from all participants.

Patients

Between September 2016 and August 2017, 322 patients, who had elective, curative surgery for colon cancer scheduled at our institution, were assessed for study eligibility. Inclusion criteria for recruitment were as follows: (a) biopsy-proven adenocarcinoma of the colon; (b) no history of endoscopic resection; and (c) tolerance for contrast-enhanced colon MR imaging at our institution within 2 weeks of undergoing a CT scan. Forty-four patients who satisfied these inclusion criteria gave their

consent to participate in this study and underwent contrast-enhanced colon MRI (Fig. 1).

Imaging techniques

MR imaging

Contrast-enhanced colon MRIs were performed on a 3.0T system (Discovery 750; GE Healthcare, Milwaukee, Wis, USA) with a torso phased-array body coil. Each patient received an intramuscular injection of spasmolytic (5 mg of cimetropium bromide; Algiron; Boehringer Ingelheim GmbH, Ingelheim, Germany) prior to scanning. Although it is not known whether the use of contrast agent on MRI is beneficial to local staging of colon cancer, we used an intravenous bolus injection of gadobutrol (Gadovist; Bayer Schering Pharma, Berlin, Germany) at the recommended dose (0.1 mL/kg of body weight) [16, 17]. The colon MR imaging protocol used here is summarized in Table 1.

CT imaging

All patients underwent preoperative colon CTs on an MDCT scanner (Discovery 750, GE Healthcare, Milwaukee, Wis, USA; LightSpeed VCT, GE Healthcare, Milwaukee, Wis, USA; Somatom Definition AS+, Siemens Healthcare, Erlangen, Germany). Three planned colon CT images were acquired from a single phase obtained from the portal venous phase. Scan parameters were as follows: detector collimation of 0.6–0.625 mm, pitch 0.8–0.984, a gantry rotation time 0.5 s, 100 kVp, 130–300 effective mAs, reconstruction slice thickness 2–2.5 mm. Each patient received a 90–95 mL intravenous injection of

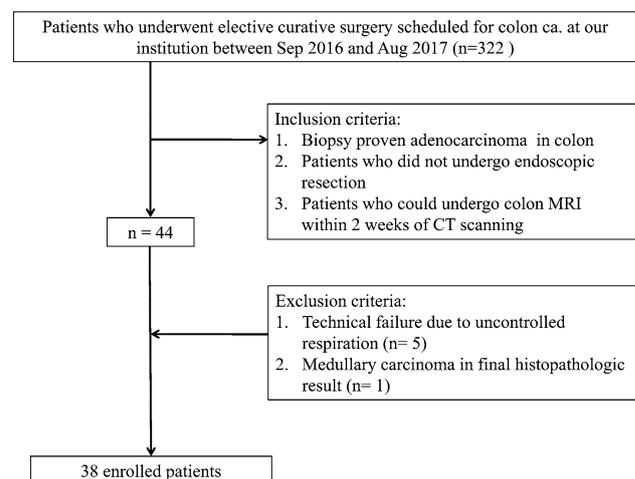


Fig. 1 Flow diagram of patient enrollment. *Ca* cancer, *MRI* magnetic resonance imaging, *CT* computed tomography

Table 1 Sequences and parameters for conventional colon MRI

Parameters	Sagittal T2WI	Coronal T2WI	Axial T2WI	Axial DWI	Axial T1WI	CE axial T1WI	CE coronal T1WI	CE sagittal T1WI
FOV (cm)	30	30	30	32	30	30	30	30
Matrix size	512 × 320	512 × 320	512 × 512–320	160 × 160	320 × 224	156 × 288	284 × 288	284 × 288
Slice thickness (mm)	3	3	3	3	2	2	2	2
TR	10,000–14,000	10,000–12,000	11,000–14,000		5000–12,000	3.6–3.7	4.4–4.5	4.4–4.5
TE	89–93	89–93	89–93	77–83	8	2	2	2
NEX	2	2	2	6	2	1	1	1
<i>b</i> factor (s/mm ²)				600, 1000				

T2WI T2-weighted image, DWI diffusion-weighted image, T1WI T1-weighted image, CE contrast enhanced, FOV field of view, NEX number of excitation, *mini* minimum

nonionic contrast media (Iomeron[®] 300; Bracco Diagnostics, Milan, Italy) at a rate of 1.2–1.5 mL/s.

Image analysis

Two experienced radiologists (with 4 and 17 years of clinical experience in local staging of colon cancer), blinded to patient information, independently reviewed MDCT and MR images. Using these images, the two readers assessed T- and N-categories, including the T3 substages (T3ab vs. T3cd), in accordance with the American Joint Committee on Cancer's Staging Manual (5th ed.), as well as extramural venous invasion (EMVI) status [19].

T-category

Intraluminal polypoid mass or semiannular wall thickening confined to the colon wall with clear adjacent pericolic fat were considered to indicate T1- or T2-category tumors. If the primary tumor had thickened spicules or nodular extensions into pericolic fat beyond the muscularis propria layer, it was classified as T3 or T4a. In the evaluation of T4a tumors, the readers considered the anatomic coverage of the colon by visceral peritoneum. For T3 colon cancers, the readers selected an image slice including the deepest point of tumor penetration and magnified that image using image-processing software (G3; Infinitt Co. Ltd., Seoul, Republic of Korea) on a picture-archiving communication system workstation monitor to measure the extramural depth of invasion (EMD) in millimeters [20]. Then, the readers classified the T3 cancer as either T3ab (EMD ≤ 5 mm) or T3cd (EMD > 5 mm) [21]. A T4b classification was made if the primary tumor invaded an adjacent organ. Finally, we categorized all patients with T1–T3ab or T3cd–T4 tumors according to the reader's independent interpretation.

N-category and extramural venous invasion

The readers assessed the statuses of regional lymph node (LN) metastasis and EMVI. A diameter ≥ 10 mm or three or more clustered nodes smaller than 10 mm in CT images were taken to indicate node metastasis [22]. LNs with irregular borders or mixed internal heterogeneous signal intensity was considered to indicate the presence of metastasis on MRI [23, 24].

The readers additionally evaluated images for the absence or presence of EMVI. If either an intermediate signal intensity within a vessel or a definite tumor signal intensity and nodular expansion of irregularly contoured vessel were noted, EMVI was diagnosed [25]. Finally, the readers recorded the statuses of node metastasis and EMVI as absent or present node metastasis (LN–ve vs. LN+ve) and absent vs. present EMVI (EMVI–ve vs. EMVI+ve).

Assessment of T/N-categorization depending on MR sequences

To assess which MR imaging set provides the best result for the T- and N-categorization, we reevaluated T- (T1–T3ab vs. T3cd–T4) and N-categories (LN–ve vs. LN+ve) in all cases of MR images by consensus review. We divided reassessment into three phases. The first phase is based on only three planned T2-weighted images (T2WI), the second on three planned T2WIs combined with axial diffusion-weighted image (DWI), and the third phase is based on three planned T2WIs combined with precontrast T1-weighted images (T1WI) and gadolinium-enhanced-T1WIs.

Histopathologic analyses

Histopathologic analyses of all resected specimen were performed by one of two experienced pathologists (with 9

and 26 years of clinical experience in the assessment of colorectal cancer specimens) who were blinded to patient information. We recorded T- and N-category, histologic grade, status of lymphovascular invasion (LVI), perineural invasion (PNI), and EMVI. In particular, elastin staining was used for the evaluation of EMVI in histopathologic specimens at our institution [26]. In patients with T3-category tumors, a pathologist measured the EMD in millimeters and then categorized it as either T3ab or T3cd, per the above-mentioned criteria. High-risk stage II cancer was diagnosed in patients with any one of the following histopathologic features: a T4 tumor, poor differentiation, LVI, PNI, positive resection margins, obstruction, and perforation. In the present study, unfavorable histopathology was defined as high-risk stage II or stage III colon cancer, which is currently treated with adjuvant chemotherapy worldwide [3].

Statistical analyses

The diagnostic performance of colon MRI and MDCT were evaluated with receiver-operating characteristic analyses that included sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV). To compare the diagnostic accuracies, a pairwise comparison was performed. The interreader agreement for MRI- and MDCT-categorized T3cd/T4 tumors was evaluated with the weighted κ statistic. Weighted κ statistics categorized agreement as poor ($\kappa = 0-0.2$), fair ($\kappa = 0.21-0.40$), moderate ($\kappa = 0.41-0.60$), substantial ($\kappa = 0.61-0.80$), or almost perfect ($\kappa = 0.81-1.0$). A two-tailed Z-test was also used to assess interreader agreement between MRI and MDCT assessments. Statistical analyses were performed using commercial software programs (MedCalc, version 18.5, MedCalc Software, Ostend, Belgium). A P value < 0.05 was considered to be statistically significant.

Results

Study population

Of the 44 patients recruited for the present study, 6 were excluded for the following reasons: (a) technical failure due to uncontrolled respiration (11.4% [5 of 44]; cecum, $n = 1$; ascending colon, $n = 1$; rectosigmoid colon, $n = 2$; sigmoid colon, $n = 1$); (b) medullary carcinoma per histopathology (2.3% [1 of 44]). Finally, 38 patients (18 women, 20 men; mean age 59.5 ± 12.6 years; age range 25–78 years) were included in the study.

Patient characteristics

The characteristics of the 38 enrolled patients are briefly summarized in Table 2. All patients underwent curative surgical resections of the following regions: right hemicolectomy (39.4% [15 of 38]), left hemicolectomy (15.8% [6 of 38]), anterior resection (42.1% [16 of 38]), and low anterior resection (2.6% [1 of 38]). No patients had surgically perforated or obstructed colon cancer.

Histopathologic characteristics

Patient histopathologic characteristics are explicated in Table 3 as follows: well-differentiated (5.3% [2 of 38]), moderately differentiated (78.9% [30 of 38]), and poorly differentiated (15.8% [6 of 38]); T1 (5.3% [2 of 38]), T2 (10.5% [4 of 38]), T3ab (47.4% [18 of 38]), T3cd (26.3% [10 of 38]), and T4 (10.5% [4 of 38]); N0 (60.5% [23 of 38]), N1 (26.3% [10 of 38]), and N2 (13.2% [5 of 38]); absent EMVI (63.2% [24 of 38]), and present EMVI (36.8% [14 of 38]).

Diagnostic performance of MRI depending on sequences for T/N-category

Diagnostic performance of MRI depending on sequences for the assessment of T3cd/T4 and node metastasis is provided in Table 4. In the evaluation of T3cd/T4, T2WI combined with contrast-enhanced T1WI showed the best result, while T2WI combined with DWI revealed the best diagnostic yield in the prediction of node metastasis.

Table 2 Patient characteristics

Characteristics	Number of patients (%)
Age, years (mean \pm SD ^a)	59.5 \pm 12.6
Sex	
Men	20 (52.6)
Women	18 (47.4)
Tumor location	
Cecum	3 (7.9)
Ascending	9 (23.7)
Transverse	4 (10.5)
Descending	2 (5.3)
Sigmoid	18 (52.6)
Pathologic tumor stage	
I	6 (15.8)
II	17 (44.7)
III	15 (39.5)

^aStandard deviation

Table 3 Histopathologic tumor characteristics

Characteristics	Number of patients (%)
Differentiation	
Grade 1/2	32 (84.2)
Grade 3	6 (15.8)
T-category	
pT1-3	34 (89.5)
pT4	4 (10.5)
LN ^a metastasis	
Negative	23 (60.5)
Positive	15 (39.5)
PNI ^b	
Negative	15 (39.5)
Positive	23 (60.5)
LVI ^c	
Negative	16 (42.1)
Positive	22 (57.9)

“p” prefix refers to pathologic staging

^aLymph node

^bPerineural invasion

^cLymphovascular invasion

However, no significant difference was observed in the diagnostic performance of MRI depending on sequences for T/N-categorization.

Diagnostic performance of MRI and MDCT for pT3cd/T4 diagnoses

The diagnostic performance of MRI and MDCT for identifying differences between \leq T3ab and \geq T3cd tumors is summarized in Table 5. MRI appeared superior to MDCT based on the performance of both readers (MRI: AUC 0.872 [95% CI 0.724–0.958] for reader 1 and AUC 0.908 [95% CI 0.769–0.977] for reader 2) (MDCT: AUC 0.738 [95% CI 0.570–0.867] for reader 1 and AUC 0.789 [95% CI 0.626–0.904] for reader 2). However, a significant difference between the classifications made while using the

two modalities was observed in only one reader ($P = 0.159$ for reader 1, $P = 0.024$ for reader 2.)

The diagnostic performances of MRI and MDCT in the detection of node metastasis and EMVI are described in Supplementary Tables 1 and 2.

Interreader agreement

The interreader agreement for MRI-categorized T3cd/T4 tumors was almost perfect ($\kappa = 0.821$ [95% CI 0.628–1.000]), whereas, that for MDCT was fair ($\kappa = 0.391$ [95% CI 0.095–0.686]). Interreader agreement for MRI-based assessment of T3cd/T4 tumors was significantly better than that for MDCT ($P = 0.017$).

The interreader agreements for MRI-predicted node metastasis and EMVI were substantial ($\kappa = 0.617$ [95% CI 0.371–0.863]) and almost perfect ($\kappa = 0.839$ [95% CI 0.665–1.000]), respectively. However, those for MDCT were moderate ($\kappa = 0.579$ [95% CI 0.326–0.832]) and fair ($\kappa = 0.339$ [95% CI 0.051–0.628]), respectively. Finally, while interreader agreement for MRI-predicted EMVI was significantly better than that for MDCT ($P = 0.004$), there was no significant difference in predicting node metastasis between two modalities ($P = 0.834$).

Diagnostic performance of MRI- and MDCT-categorized T3cd/T4

The diagnostic performance of MRI- and MDCT-categorized T3cd/T4 for identifying high-risk stage II or stage III colon cancer cases are summarized in Tables 6 and 7. Overall, both modalities had relatively high false-negative rates across both readers, indicating a tendency toward underestimating disease incidence. Both readers had a lower false-positive rate using MR images than MDCT (MRI, 0% [0 of 38] vs. MDCT, 7.9% [3 of 38] for reader 1 and MRI, 2.6% [1 of 38] vs. MDCT, 10.6% [4 of 38] for reader 2). In terms of diagnostic accuracy, MRI-based assessments were more accurate than MDCT-based ones across both readers (AUC: MRI, 0.707 [95% CI 0.537–0.843; $P < 0.001$] vs. MDCT, 0.506 [95% CI 0.339–0.671; $P = 0.952$], $P = 0.032$ for reader 1 and AUC: MRI, 0.651 [95% CI 0.480–0.798; $P = 0.037$] vs. MDCT,

Table 4 Diagnostic performance of MRI for T3cd/T4 and positive node depending on sequences

	T3cd/T4			Positive node		
	T2WI	T2WI + DWI	T2WI + CE T1WI	T2WI	T2WI + DWI	T2WI + CE T1WI
Consensus	0.896 (0.753–0.971)	0.902 (0.761–0.974)	0.923 (0.788–0.984)	0.762 (0.596–0.885)	0.777 (0.613–0.895)	0.753 (0.586–0.878)

T2WI T2-weighted image, DWI diffusion-weighted image, CE contrast enhanced, T1WI T1-weighted image

Table 5 Reader-wise diagnostic performances of MDCT and MRI for the assessment of T3cd/T4

	Az ^a	Sensitivity	Specificity	PPV ^b	NPV ^c
Reader 1					
MDCT ^d	0.738 (0.570–0.867)	64.3% (35.1–87.2)	83.3% (62.6–95.3)	69.2% (45.9–85.7)	80.0% (66.0–89.2)
MRI ^e	0.872 (0.724–0.958)	78.6% (49.2–95.3)	95.8% (78.9–99.9)	91.7% (61.3–98.7)	88.5% (73.7–95.5)
Reader 2					
MDCT ^d	0.789 (0.626–0.904)	78.6% (49.2–95.3)	79.2% (57.8–99.9)	79.2% (57.8–92.9)	86.4% (69.5–94.6)
MRI ^e	0.908 (0.769–0.977)	85.7% (57.2–98.2)	95.8% (78.9–99.9)	92.3% (63.5–98.8)	92.0% (76.1–97.7)

^aArea under the curve by receiver-operating characteristic analysis

^bPositive predictive value

^cNegative predictive value

^dMultidetector computed tomography

^eMagnetic resonance imaging

0.485 [95% CI 0.320–0.652; $P = 0.891$], $P = 0.055$ for reader 2). In particular, the use of MRI resulted in higher specificity and PPV than MDCT (Figs. 2, 3, 4).

Discussion

Our study demonstrated that neither using DWI nor gadolinium-enhanced T1WI combined with T2WI did not significantly improve their accuracy for the diagnosis of T3cd/T4 and nodal metastasis when compared with T2WI alone. Although using gadolinium-enhanced T1WI and DWI combined with T2WI showed the best diagnostic yield for T- and N-categorization, respectively, this result is in line with those of prior studies showing no benefit of DWI or contrast agent for local staging in rectal cancer [27, 28]. If enough quality of T2WI is guaranteed, using DWI or gadolinium-enhanced T1WI may not be necessary [29]. However, in current daily practice, there may sometimes be problematic in achieving qualified T2WI using existing technique for colon cancer MRI. Therefore, despite our result, we believe that gadolinium-enhanced

study may be alternative solution in case of obtaining poorly qualified T2WI. Further studies with respect to the optimization of colon MRI protocol are essential.

In this study, we demonstrated that the diagnostic performance of MRI was better than that of MDCT in predicting histopathologic T3cd/T4 cancers. Although we observed a significant difference between the two modalities in only one of two readers, type II error may have resulted from our use of a small study population. The overall accuracy of colon MRI was approximately 89%, but only 76% for MDCT. The sensitivity and specificity of MRI were 82% and 95%, respectively. This result is comparable to that of a previous study by Erik Rollvén and colleagues, which reported 91% accuracy, 85% sensitivity, and 97% specificity using the similar technique [16]. Furthermore, given that a meta-analysis found 77% sensitivity and 70% specificity of CT to detect T3cd/T4, colon MRI may be the preferable imaging modality for predicting T3cd/T4 cancers [30]. Critically, however, two studies have reported relatively low sensitivity and specificity levels with MRI. Hunter et al. and Elias et al. reported that MRI has a 40–67% sensitivity and 75–94% specificity to detect T3cd/T4 cancers [17, 18]. Sensitivity differences between reports cannot be explained by a single factor. One difference between the studies which might have reflected disagreement in sensitivity and specificity values is that those which reported higher sensitivity, including the present study, used relatively higher-resolution MRI with a small FOV. Differences in MRI protocol may influence the accuracy of local staging of colon cancer [17]. In addition, differences in the ways the results are interpreted may also drive discrepant interpretations of the results. Although our study demonstrated acceptable performance of colon MRI, technical failure of the modality in five patients with uncontrolled respiration was

Table 6 Accuracy of MDCT- and MRI-categorized T3cd/T4 based on histopathology

	Reader 1		Reader 2	
	MDCT ^a	MRI ^b	MDCT ^a	MRI ^b
Correct	16 (42.1)	21 (55.3)	17 (44.7)	20 (52.7)
False negative	19 (50.0)	17 (44.7)	17 (44.7)	17 (44.7)
False positive	3 (7.9)	0 (0)	4 (10.6)	1 (2.6)

^aMultidetector computed tomography

^bMagnetic resonance imaging

Table 7 Diagnostic performance of MDCT- and MRI-categorized T3cd/T4 for the assessment of unfavorable^a histopathology

	Az ^b	Sensitivity	Specificity	PPV ^c	NPV ^d
Reader 1					
MDCT ^e	0.506 (0.339–0.671)	34.5% (17.9–54.3)	66.7% (29.9–92.5)	76.9% (53.8–90.5)	24.0% (15.6–35.0)
MRI ^f	0.707 (0.537–0.843)	41.4% (23.5–61.1)	100% (66.4–100)	100%	34.6% (28.1–41.8)
Reader 2					
MDCT ^e	0.485 (0.320–0.652)	41.4% (23.5–61.1)	55.6% (21.2–86.3)	75.0% (56.2–87.5)	22.7% (13.2–36.3)
MRI ^f	0.651 (0.480–0.798)	41.4% (23.5–61.1)	88.9% (51.8–99.7)	92.3% (64.3–98.8)	32.0% (24.3–40.8)

^a“Unfavorable” refers to stage III or high-risk stage II cancers, defined as the presence of any of the following: T4, G3, lymphovascular invasion, perineural invasion, positive resection margin(s), obstruction, or perforation

^bArea under the curve per receiver-operating characteristic analysis

^cPositive predictive value

^dNegative predictive value

^eMultidetector computed tomography

^fMagnetic resonance imaging

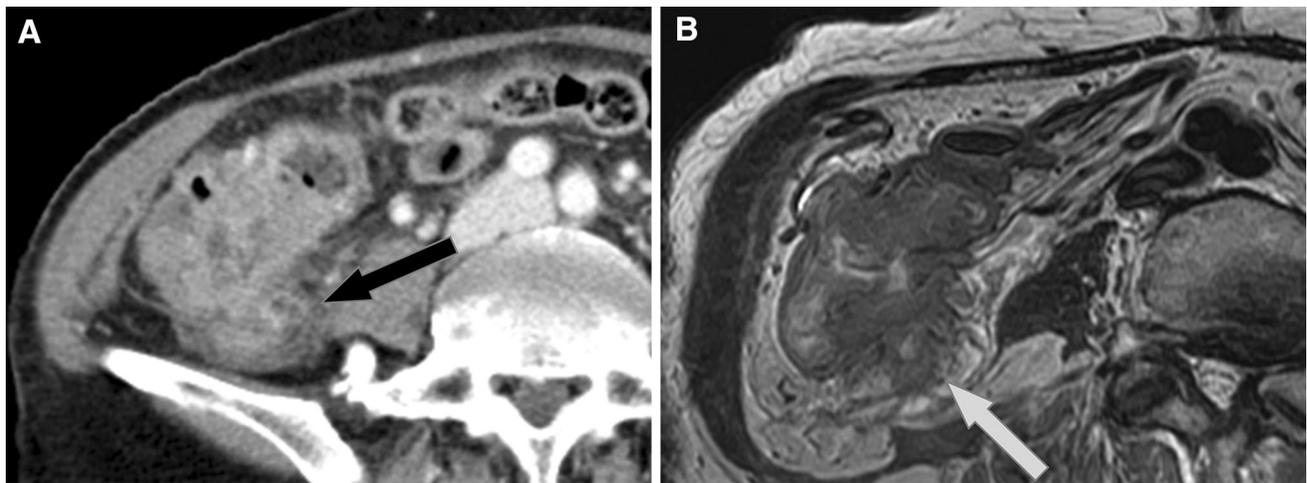


Fig. 2 Images of stage III (pT3cN2a) ascending colon cancer in 61-year-old woman. **a, b** A semiannular wall thickening with an irregular infiltrating border was noted in ascending colon. Multidetector CT (black arrow) and axial T2-weighted images (white arrow)

showed large nodular projection of tumor to posterior retroperitoneal fat. Readers interpreted this as T3cd cancer on both modalities, leading to correct category

unavoidable. Technical improvements, such as faster acquisition of T2W images of a higher resolution and small FOVs, as well as better control over motion artifacts, will be essential before the use of MRI for local staging of colon cancer is implemented in daily clinical practice.

This retrospective study also showed that the diagnostic performances of MRI for identifying node metastasis and EMVI were slightly higher than those of MDCT. In the prediction of node metastasis, MRI and MDCT showed approximately 82% and 74% accuracies, respectively. This can be attributed to the superior intrinsic soft-tissue contrast of MRI. In the MRI, we can analyze border and internal signal intensity of node. Whereas, it may be impossible for MDCT to perform the same analysis.

However, we need to be very cautious in terms of accepting the superiority of MRI. Although we believe that many radiologists can agree with the superiority of MRI in the evaluation of node metastasis, MRI's role can be also very limited. According to the recent consensus meetings of both the European Society of Gastrointestinal and Abdominal Radiology (ESGAR) and the Society of Abdominal Radiology (SAR) for making updated recommendations of rectal cancer MRI, approximately 70% participants gave the same opinion that although T2WI should be used for nodal staging, it could not reliably differentiate between N0 and N1 [29, 31]. Given the limited role of imaging in the prediction of node metastasis, it may be better to exclude nodal staging as an indication of

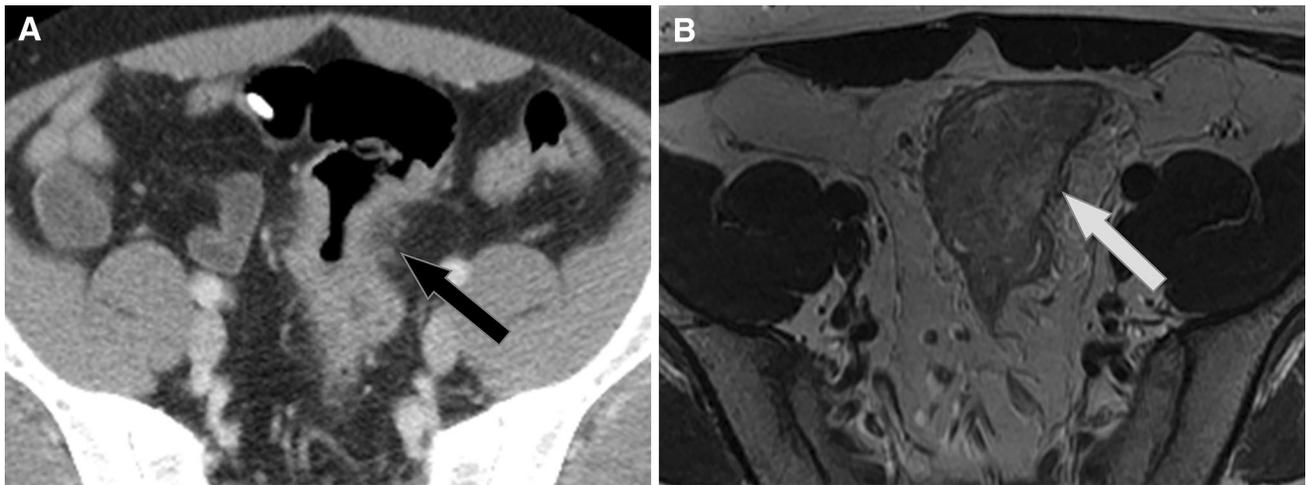


Fig. 3 Images of low-risk stage II (pT3bN0) sigmoid colon cancer in 26-year-old man. **a** Multidetector CT suspiciously showed fuzzy nodular extension of primary tumor to adjacent mesocolic fat (black arrow). Readers categorized this as T3cd cancer, leading to false positive on CT. **b** Axial T2-weighted MR image revealed focal

disruption of low signal intensity muscularis propria layer (white arrow), which appeared less than 5 mm in extramural depth of invasion. Readers classified this as T3ab cancer, leading to correct category on MRI

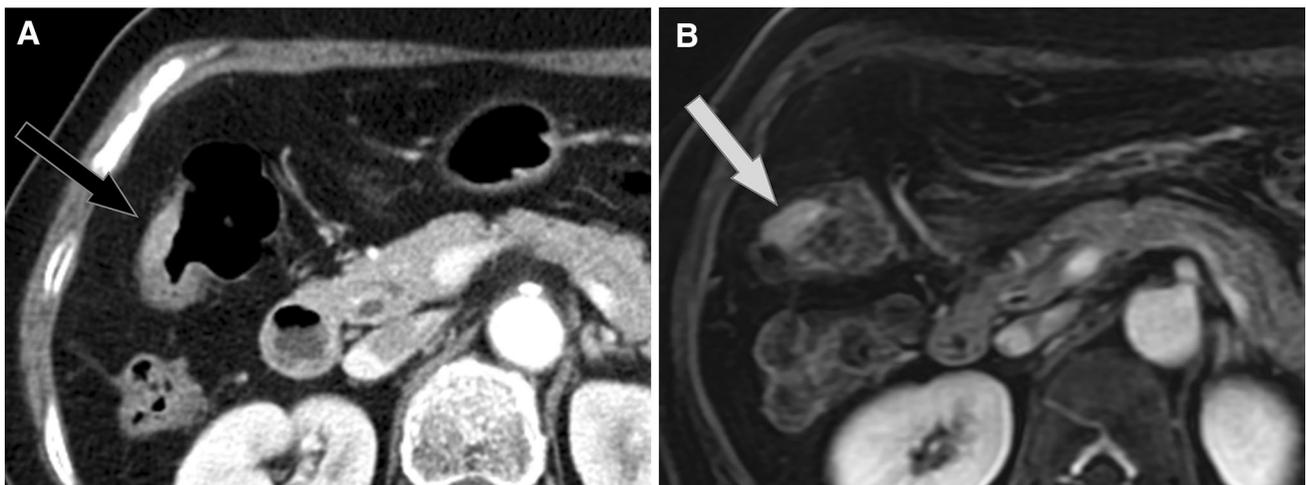


Fig. 4 Images of high-risk stage II (pT3bN0) transverse colon cancer in 75-year-old woman. **a, b** there was a semiannular wall thickening in proximal transverse colon, which appeared to be confined to the colon wall. Both readers interpreted this as full-thickness T2 on

multidetector CT (black arrow) as well as axial contrast-enhanced T1-weighted MR image (white arrow). However, the result of final histopathology was pT3b cancer with lymphovascular and perineural invasions, leading to false-negative rates on both modalities

neoadjuvant chemotherapy for colon cancer. In the prediction of EMVI, MRI and MDCT revealed approximately 75% and 63% accuracies, respectively, in this study. This result of MRI is similar to those of prior studies by E. Nerad et al. and C. Hunter et al., diagnostic accuracies of which were 77% and 75%, respectively [17, 18]. However, there seems to be relatively a wide range of variations of CT diagnostic performance in the evaluation of EMVI. Further studies regarding radiological prediction of EMVI in patients with colon cancer are necessary to be established as one of essential item to be reported.

The primary objective of the present study was to determine the diagnostic performance of MRI-categorized T3cd/T4 tumors for identifying high-risk stage II or stage III cancer in patients with curatively resectable colon cancer in comparison with MDCT. Although the diagnostic performance of MRI was poorer than anticipated here, we saw statistically significant differences from a chance diagnosis by means of this modality (approximately 70% and 65% accuracy levels for readers 1 and 2, respectively). However, diagnoses resolved from MDCT images did not differ significantly from a chance diagnostic accuracy of

approximately 50% across both readers. The basic problem in terms of poor diagnostic performance is not derived from the imaging modality, but from the capacity of histopathologic T3cd/T4 to identify high-risk stage II or stage III colon cancers. According to the histopathologic results reported here, only 55% of patients with pT1–T3ab or T3cd/T4 were correctly categorized as favorable or unfavorable. This was because most patients with pT3ab had unfavorable histopathologic features. Of the 18 patients with pT3ab, 16 had high-risk stage II or stage III cancer. If this T3cd/T4-categorization method were to be used as an indication for neoadjuvant chemotherapy, approximately 40% of patients might needlessly fail to meet treatment criteria and thus be undertreated, regardless of the diagnostic performance of imaging modality. However, only 2.5% of patient would have the potential to be overtreated. In terms of the ethical issues implicated in the prevention of overtreatment, the suggested T3cd/T4 may be quite attractive, and on the contrary, this criterion may be disappointing to maximize treatment gain in high-risk patients. This may underlie the change to the FOxTROT trial wherein entry criteria were extended to include all radiologically diagnosed T3 patients after the pilot phase. While further consideration regarding this issue is beyond the scope of the present study, we look forward to the results of the FOxTROT trial (NIH NCT00647530), which will likely help to further clarify these issues.

Nevertheless, the present study was able to demonstrate that the identification of high-risk stage II or stage III cancers using colon MRI has a higher specificity and positive predictive value, which could reduce the false-positive rate by as much as 8%, than does MDCT. This means that the use of MRI-categorized T3cd/T4 tumors may prevent overtreatment that often results from MDCT-based diagnoses. This advantage is crucial to the use of imaging in determining indications of neoadjuvant chemotherapy. Moreover, the present study reports interreader agreement using MRI for the assessment of T3cd/T4, which was significantly better than that for MDCT. MR imaging revealed almost perfect agreement between the two readers included, whereas interreader agreement with MDCT was only fair. Given the diagnostic performance of MRI here, especially in reducing the false-positive rate, and its high level of associated interreader agreement, it may serve as the preferred imaging modality in the era of forthcoming neoadjuvant chemotherapy for colon cancer. However, further studies with a larger number of study sites and greater sample size, as well as further technological development of methods with higher spatial resolution and fewer artifacts, remain necessary to more definitively determine the value and relevance of colon MRI to the assessment of indicators for neoadjuvant chemotherapy.

Despite its advantages, our study has several limitations that warrant discussion. First, the present study was a single centre pilot trial, consisting of a small number of participants. We did not a priori perform a power analysis to calculate the sample size and statistical power. For these results to be more definitive, further study with a larger number of patients is required. Second, in the present study, overtreatment and undertreatment were assessed from the perspective of comparison with the existing adjuvant chemotherapies. Although we believe this approach to be reasonable, the use of clear clinical prognoses would have improved it. Finally, colon MRIs FOVs were derived from preexisting MDCT images, which allowed for small FOVs. After a radiologist checked the location of the primary tumor using MDCT images, the MRI scan site was determined. Future studies should examine these two imaging modalities independently.

Despite these limitations, the present study found that interreader agreement as well as the diagnostic accuracy of MRI to predict pT3cd/T4 cancers was better than that of MDCT. Moreover, the results of this study showed that in identifying high-risk stage II or stage III colon cancers, MRI-categorized T3cd/T4 was superior to MDCT. In particular, colon MRI had higher specificity and positive predictive value, which can decrease false positives, compared to those of MDCT. Further prospective trials with larger numbers of participants, as well as more expert discussion in the field of potential indications for neoadjuvant chemotherapy for colon cancer, remain necessary.

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Compliance with ethical standards

Conflict of interest All authors have no conflict of interest to declare.

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