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FULL PAPER

Rectal cancer confined to the bowel wall: the role of 3 Tesla phased-array MR imaging in T categorization

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Objective: To determine the diagnostic value of 3 Tesla MR imaging in detection of mucosal (T_{is}), submucosal (T_1) and muscularis propria (T_2) invasion in patients with early rectal cancer.

Methods: A total of 50 consecutive patients who underwent 3 Tesla MR imaging and curative-intent intervention for MRI-staged $T_{is}/T_1/T_2$ rectal cancer from March 2012 to December 2016 were included. The radiological T category of each rectal tumour was compared retrospectively with histopathological results assessed according to the tumor, node, metastasis (TNM) classification. The sensitivities, specificities, and overall accuracy rates of 3 Tesla MR imaging for T_{is} , T_1 , and T_2 cases were calculated using MedCalc statistical software v. 16.

Results: The sensitivity, specificity, PPV, NPV of 3 Tesla MR imaging in T categorization for T_2 were: 93.7% [95% CI (0.79–0.99)], 77.7% [95% CI (0.52–0.93)], 88.2% [95% CI (0.75–0.94)] and 87.5%

[95% CI (0.64–0.96)]; for T_1 were 92% [95% CI (0.63–0.99)], 91.8% [95% CI (0.78–0.98)], 80% [95% CI (0.57–0.92)] and 97.1% [95% CI (0.83–0.99)]; for T_{is} were: 20% [95% CI (0.51–0.71)], 100% [95% CI (0.92–1)], 100%, 91.8% [95% CI (0.87–0.94)], respectively. MR categorization accuracy rates for T_2 , T_1 and T_{is} were calculated as 88, 92 and 92%, respectively.

Conclusion: 3 Tesla MR imaging seems to be useful for accurate categorization of T-stage in early rectal cancer, especially for T_1 cancers. The method is not a reliable tool to detect T_{is} cases. The potential for overstaging and understaging of the technique should be realized and taken into consideration when tailoring the treatment protocol for each patient.

Advances in knowledge: High-resolution MR with phased-array coil is being increasingly used in the pre-operative assessment of rectal cancer. 3 Tesla high-resolution MR imaging allows improved definition of bowel wall and tumour infiltration.

INTRODUCTION

Increased signal-to-noise ratio in 3 Tesla MR imaging allows the acquisition of high-resolution (HR) images. On the basis of imaging, the ability to discern anatomical detail and distinguish layers of bowel wall is an important contribution of technology to the interpretation of pathologies that involve the rectal wall. In rectal cancer, according to the TNM system, T category demonstrates the invasion depth of cancer in the bowel wall. Tumours that are limited to the mucosal layer are known as tumour *in situ* (T_{is}). The T_1 category is used to describe primary adenocarcinomas of the rectum, in which the invasive component is limited to the submucosa. Tumours that invade to muscularis propria but do not go beyond it are categorized as T_2 .^{1,2} These tumours are at an early stage and constitute approximately 10% of newly diagnosed rectal cancers. Of

these, 45% are in T_1 and 55% in T_2 categories.³ Prognosis is good in early cancers confined to the rectal wall. The overall 5-year survival rates for T_{is} , T_1 , and T_2 cases are 100, 98 and 97%, respectively.⁴ Assessment according to the depth of invasion is useful in the formulation of appropriate guidelines for the treatment of early invasive cancer.⁵

Recent guidelines in oncology (National Institute for Health and Care Excellence, 2014; National Comprehensive Cancer Network, 2015) do not recommend local resection and transanal resection approaches instead of a radical resection for patients with early rectal cancer. However, the topic is controversial.⁶ Studies show patients with T_1 rectal cancers had fewer postoperative complications after a transanal excision or endoscopic surgery when compared with the transabdominal resection. Local excision is also

associated with lower perioperative mortality and need for a permanent stoma, but with higher local recurrence.⁷⁻⁹ Total mesorectal excision, especially for T_2 tumours, gives more favorable results in terms of local recurrence and survival.^{10,11}

Endorectal ultrasonography (EUS) with high frequency probe is the best method for imaging early and superficial cancers in the rectum.⁴ By showing the layers of the rectum wall, it allows the assessment of the invasion depth of tumour into the mucosa, submucosa or muscularis propria. MR imaging with endorectal coil also allows highly accurate differentiation of the layers of the intestinal wall. However, both endorectal coil and EUS share the same disadvantages, namely a field of view that is small, causing inadequate evaluation of perirectal tissues, circumferential resection margin, and lateral pelvic lymph nodes. Additionally, insertion and bypass of an endoluminal coil or probe through stenotic lesions is not always possible.^{12,13}

MR solutions to overcome the above-mentioned limitations of endorectal coil have been searched. The development of the phased-array coil systems, which combine high spatial resolution imaging, eliminates the need for an invasive endorectal techniques. Today, HR phased-array MR imaging is being increasingly used in the pre-operative assessment of rectal cancer. In this context, this technique can be considered as an opportunity which has the potential to display the tumoral tissue in the bowel wall. With a large field of view, it has the additional benefit of improved visualization of mesorectum and , mesorectal, superior rectal and iliac lymph nodes, and the tumour's relationship to the anal sphincter complex and levator ani muscle.^{2,14,15}

The accuracy of MR imaging for staging rectal cancer has been reported between 44 and 100% for T stage.^{14,16-20} The studies showed the role of MR imaging with phased-array coil in staging of early rectal cancer is limited. This technique is widely accepted the modality of choice for staging T_2 and more advanced tumours.^{3,12,13,20} To the best of our knowledge, no other study has been described in the literature that has investigated the role of 3 Tesla phased-array MR imaging in only early T-stage rectal cancer. In this study, using histopathological results as the reference standard, we aimed to determine the diagnostic value of HR 3 Tesla MR imaging in Tis, T_1 and T_2 rectal tumours.

METHODS AND MATERIALS

The institutional review board approved this retrospective study protocol and waived informed consent.

Study population

Medical records (original radiology and histopathology reports, discharge summaries and operative reports) of 215 consecutive patients who underwent prospective 3 Tesla HR rectal MR imaging from 1 March 2012 to 31 December 2016 were reanalysed by one author (AE). 61 patients in whom rectal cancer was reported to be confined to the bowel wall in MR imaging were identified. These patients proceeded to local excision or radical surgery without pre-operative long course chemoradiotherapy. 11 patients were excluded for the following reasons: absence of histopathological results ($n = 8$) and histopathological findings that indicated tubular

adenoma ($n = 3$). The final study population consisted of 50 patients (mean age $\pm$ SD, 61.7 years $\pm$ 10.6; range, 36–91 years). 27 of these patients were males and 23 were females.

MR image acquisition

MR images were obtained by using a 3 Tesla imaging system (MAGNETOM Verio, Siemens Medical Solutions, Erlangen, Germany). Signal reception was performed by using a standard body matrix coil. The patient cohort was subjected to a pre-examination food fast (5 to 6 h) to reduce bowel peristalsis. An antiperistaltic agent, rectal cleansing, rectal distention and/or an enema was not administered prior to MR imaging.

The sequences and planes used in this study were as follows: T_2 weighted TSE sagittal and axial images, HR T_2 weighted TSE oblique axial and oblique coronal images, and HR contrast-enhanced fat suppressed T_1 weighted TSE oblique axial and oblique coronal images. The sagittal images were used to plan then oblique axial and oblique coronal images which were perpendicular and parallel to the long axis of the rectal tumour, respectively. Diffusion-weighted axial images were also obtained. The pulse sequence parameters utilized in our study are listed in detail in Table 1.

Image analysis

MR images of the 50 consecutive patients retrieved from a Picture Archiving and Communication System (PACS; Centricity, v. 5.0 RIS-i, GE Healthcare) were reviewed by two radiologists (EP and HÇE, with 7 and 5 years of experience in rectal MR imaging, respectively) in consensus. The reviewers were aware that the MR images were from patients with early rectal cancer who later underwent elective resection but were blinded to histopathological results. Predefined morphologic criteria were used to assess T category. Lesions classified as mrTis showed involvement of inner hypointense mucosal layer and intact hyperintense submucosal layer. In T_1 category, tumour signal intensity was confined to submucosal layer and signal intensity of tumour was low compared with high signal intensity of the adjacent submucosa. In T_2 category, the tumour signal intensity extended to the muscularis propria, causing loss of interface between submucosa and circular muscle layer, irregularity and/or thinning of the outer hypointense muscle layer. In this category, the tumoral lesion was estimated to be confined to the rectal wall and no evidence of perirectal infiltration was detected.^{17,21} The radiological T category of each rectal tumour were compared retrospectively with histopathological results (pTis to pT₂), assessed according to the TNM classification.

Statistical analysis

Histopathological findings were used as the gold standard. All statistical analysis was carried out using MedCalc statistical software v. 16. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and diagnostic accuracy were calculated for 3 Tesla rectal MR imaging.

RESULTS

The rectal cancer location was categorized according to the distance from the anal verge to the lower edge of the tumour measured by MR imaging as within 6 cm in 36 patients, between

Table 1. 3.0 Tesla MR imaging pulse sequence parameters used in our study

	T2W TSE	T2W TSE	T2W TSE (HR)	T2W TSE (HR)	T1W FS CE TSE	T1W FS CE TSE	DWI ^a EPI
Parameter							
Matrix size	384 × 307	320 × 256	320 × 256	320 × 256	320 × 256	320 × 256	320 × 288
Slice thickness (mm)	3.5	5.0	3.0	3.0	3.5	3.5	5.0
Distance factor	15%	20%	16%	16%	14%	14%	%30
Repetition time (ms)	4500	5450	5460	5180	495	495	646
Echo time (ms)	104	93	58	58	12	12	11
Echo trains per slice	13	8	12	15	39	39	47
Flip angle (degrees)	120	150	145	135	140	140	140
Reduction factor	2	2	2	2	2	2	2
Average	2	3	4	4	3	2	2
FoV (mm)	220 × 220	220 × 220	180 × 180	180 × 180	200 × 200	200 × 200	300 × 300
Orientation	Sagittal	Axial	Oblique axial	Oblique coronal	Oblique axial	Oblique coronal	Axial
Bandwidth (Hz/Px)	250	260	260	260	260	260	260
Acquisition Time (min:s)	4:05	2:18	4:54	6:00	4:31	3:35	3:06

CE, contrast enhanced; DWI, diffusion-weighted imaging; EPI, echo planar imaging; FoV, field of view; FS, fat suppressed; HR, high resolution; T1W, T₁ weighted; T2W, T₂ weighted; TSE, turbo spin echo.

^ab values for DWI: 50, 400 and 1000 s mm⁻².

6.1 and 12 cm in 12 patients, and between 12.1 and 18 cm in 2 patients. The size in tumours exhibiting vegetating morphology ($n = 6$) measured from pre-operative rectal MR imaging ranged from 2 to 5 cm. The wall thickness in flat or infiltrating tumours ranged from 0.7 to 1.6 cm.

Among the 50 rectal adenocarcinoma patients, the final histopathological T category was classified as Tis in 5 patients, T₁ in 13 patients, and T₂ in 32 patients. T categories that were based on MR imaging were as follows: one patient staged as mrTis, 15 as mrT₁ and 34 as mrT₂.

Only one patient with histopathologically *in situ* rectal tumour (pTis) was evaluated correctly at MR imaging (mr Tis). MR evaluation of the other four patients that were pathologically diagnosed as Tis were evaluated as T₂ in three patients (Figure 1) and T₁ in one patient (Figure 2).

Out of 15 cases evaluated as mrT₁ (Figure 3), 12 were also categorized as T₁ at histopathology. Two of the patients were in T₂, and one was in Tis category according to pathological staging.

30 of the 34 patients who were reported as T₂ in the MR staging (Figures 4 and 5) were evaluated pathologically as T₂, one as T₁ and three as Tis.

The sensitivity, specificity, PPV, NPV of 3 Tesla MR imaging in T categorization for T₂ were: 93.7 [95% confidence interval (CI): (0.79–0.99)], 77.7% [95% CI (0.52–0.93)], 88.2% [95% CI (0.75–0.94)], 87.5% [95% CI (0.64–0.96)]; for T₁ were 92% [95% CI (0.63–0.99)], 91.8% [95% CI (0.78–0.98)], 80% [95% CI

(0.57–0.92), 97.1% (0.83–0.99)]; for Tis were: 20% [95% CI (0.51–0.71), 100% (0.92–1), 100%, 91.8% (0.87–0.94)], respectively. MR categorization accuracy rates for T₂, T₁ and Tis were calculated as 88, 92 and 92% respectively.

DISCUSSION

In our study, we found that 3 Tesla MR imaging was highly sensitive in staging T₁ and T₂ tumours (92 and 93%, respectively).

Figure 1. A 57-year-old male with Tis NO rectal adenocarcinoma. Sagittal (a) and axial (b) T₂ weighted TSE MR images show a lobulated 4.7 × 3.5 cm mass predominantly located in the distal rectum. It has slightly lobulated surface facing the lumen. It was overstaged by MRI as T₂ because of the interruptions of muscularis propria (arrows). The patient was treated with abdominoperineal resection. Histopathological examination of the surgical specimen revealed that the tumour developed from adenomatous polyp and showed only intramucosal invasion. TSE, turbo spin echo.

Figure 2. Histopathological T_{is} NO rectal cancer in 75-year-old male, overstaged by MRI as T_1 tumour. Axial T_2 weighted TSE MR images show a midrectal mass located predominantly at the left wall. Note fine high signal submucosal layer (thin arrows) which is thought to be partially replaced by intermediate intensity of tumour (large arrow) and staged as T_1 on the basis of MRI. Biopsy showed well differentiated adenocarcinoma with invasion restricted to lamina propria (*intramucosal carcinoma*). Muscular layer is identified as hypointense outer circular layer surrounding the rectum.

However, its sensitivity was very low (20%) in T_{is} stage and it had limited ability to correctly determine the patients who had T_{is} tumours. The specificity was found to be higher in T_1 than that in T_2 tumours (91 vs 77%). Also, NPV value of the method was slightly better for T_1 category than that in T_2 category (97 vs 87%, respectively). These results are interesting, since the perceivability of muscularis propria is relatively better than the other layers, due to its relative low signal intensity and high thickness. Thus, if the tumour invades the muscularis propria, the changes in this layer such as thinning, interruption or disappearance, was expected to be evaluated more readily. It is hard to

Figure 3. A 36-year-old female with T_1 NO rectal adenocarcinoma. Oblique axial T_2 weighted TSE MR images (a and b) show eccentric thickening of right anterolateral wall in midrectum. It reached a thickness of 15 mm. The tumour has grown into the submucosa and abuts to the inner surface of the muscle layer. It had higher signal intensity than the muscle layer and lower signal intensity than the surrounding sub mucosa on the T_2 weighted images. The patient was treated with low anterior resection. Histopathological examination of the surgical specimen revealed a tubulovillous adenoma found to have *cancer* developing in it. Tumour showed deep submucosal invasion (sm3; extending to the inner surface of the muscularis propria).

Figure 4. A 63-year-old male with T_2 NO rectal adenocarcinoma. Oblique axial T_2 weighted TSE MR image shows tumour signal intensity extended into muscle layer. Note loss of interface between submucosa and circular muscle layer of left posterolateral aspect of rectal wall. Large arrow indicates thinning of hypointense muscular layer. The outer layer has an irregular, pseudospiculated appearance with interruptions due to hypertrophied longitudinal muscle fibers and vessels entering the rectal wall (thin arrows). TSE, turbo spin echo.

explain why there is difficulty to exclude invasion of muscularis propria with MR imaging and also, the accuracy of the method in T_2 cases was less than that in more superficial tumours. This result, however, may be due to the fact that the contrast difference between the intermediate signal intensity of the tumour and the hypointensity of the muscle layer is lower compared with the hyperintensity of the submucosa.

Figure 5. A 58-year-old male with T_2 NO rectal adenocarcinoma. Oblique axial T_2 weighted TSE MR images (a and b) and high b-value diffusion-weighted image (c) show ulcerated semiannular lesion in distal rectum. Note thinning of muscle layer from the 11 o'clock to 12 o'clock position (arrow in a). Tumour abuts to muscle layer from the 11 o'clock to 2 o'clock position (arrows in b and c). Asterisk in b shows high signal submucosal layer seen beneath the tumour which seems intact between 2 to 5 o'clock position. The patient was treated with abdominoperineal resection. Lesion was staged as T_2 NO at histopathological examination of the surgical specimen.

A meta-analysis published in 2004 by Bipat et al demonstrated that EUS and MR imaging had similar sensitivities and EUS had better specificity (86%) for evaluating muscularis propria invasion, than MRI in rectal cancer patients.²² However, this study may not fully reflect present conditions since it includes publications prior to 2002, when experience with rectal cancer is insufficient and spatial resolution MRI is low due to outdated technology. Al-Sukhni et al²³ reported that T category assessment is improved with the use of higher field strength MRI machines and review of images by consensus of two or more radiologists. This study demonstrated a sensitivity of 87% [95% CI (81–92%)] of MRI for T category, and specificity of 75 [95% CI (68–80%)].²³ In a recent meta-analysis published in 2016 by Zhang and colleagues evaluated the diagnostic performance of MRI in tumour staging in rectal cancer and revealed the sensitivity of 97% [95% CI (0.96–0.98)] and specificity of 97% [95% CI (0.96–0.98)] for muscularis propria invasion.²⁴ Li et al²⁵, in another recent meta-analysis, recommended that high-resolution MRI should be used routinely together with 3 T MRI, if conditions allow. The authors concluded that, this combination of techniques provides excellent discrimination between T_2 and borderline T_3 cancers. They also reported that EUS is not suitable for rectal tumour staging for its significantly decreased accuracy; nevertheless, those with MRI-defined T_1/T_2 disease may be candidates for subsequent EUS examination.²⁵

Early cancers can be seen as malignant polyps, villous tumours, polypoid or sessile cancers. Although the ESGAR meeting index recommends EUS-based evaluation for differentiation of T_1 and T_2 tumours,²⁶ the size and luminal extension of an intramucosal or villous tumour may be so large that its stalk and the depth of invasion may not be adequately assessed by EUS. Konishi et al²⁷ found that it is difficult to determine the depth of invasion in villous lesions, especially large (≥ 20 mm wide, ≥ 5 mm high) or rectal lesions, using only EUS. The overall accuracy of EUS for tumour invasion depth is 60% in villous lesions and 91% in nonvillous lesions. The villous lesions are more commonly overstaged with EUS compared with the nonvillous lesions (37 vs 6%). In both types, understaging rates are same (3%). It is concluded that EUS-based evaluation alone cannot determine the appropriate treatment for colorectal villous lesions.²⁷ In this context, the base of the tumour can be better identified with MR imaging. The employment of MR imaging in early rectal cancer is suggested to be limited to uncertain T_2 patients.¹⁰ If extramural component of tumour is not adequately evaluated with EUS, and if it is required to determine the status of local lymph nodes, MR imaging is also useful. The technical parameters used in MR imaging is very important in early rectal cancer. It is shown that if the imaging parameters are appropriately adjusted, the 1.5 Tesla and 3 Tesla machines can be used with comparable accuracies for staging rectal cancer.^{28,29} In the study of Kim et al the diagnostic accuracy 3 Tesla MR imaging is 97% for T_1 , and 89% for T_2 tumours, respectively.³⁰ In the study of Abreu et al³¹ the sensitivity, specificity, PPV, and NPV values are 33.3, 94.7, 33.3 and 94.7% for T_1 ; and 62.5, 32, 37.0 and 57.1% for T_2 tumours. The values, other than T_1 specificity and NPV, are rather low compared to our study. T_{is} tumours are not included to the above-mentioned studies.^{28–31} In a study reported by De

Vargas Macciucca, which includes 23 rectal villous tumours (22 of them confined to bowel wall), 1.5 Tesla MR and EUS are found to be in accordance in 86.9% of cases.³²

It appears that, although larger T_3 tumours are easy to distinguish with MR imaging, considerable experience and high-quality images are required to assess the subtle findings that help distinction small T_3 tumours from stage T_1 – T_2 tumours.³³ One of the suggested approaches to assess early tumours is rectal distention. The role of administration of rectal contrast material for the distinction of T stage of primary rectal cancer is controversial.³⁴ Luminal distention with rectally administered ultrasound gel (or sometimes water) can result in better depiction of polypoid tumours (e.g. villous adenomas) and small rectal tumours (< 3 cm).³³ In polypoid masses, the gel delineates the margins of the tumour and allows definition of the site of tumour attachment to the rectal wall. In smaller tumours, it may not be easy to identify the primary tumour. This problem is partially related to size but also exists because the signal intensity characteristics of tumours are frequently similar to those of the adjacent rectal wall. Endoluminal filling with gel might help to better delineate the tumour in such cases and might prevent problems with staging.^{33,34} Expanding the rectum with air, however, can have disadvantages. Artefacts due to the movement of insufflated air can cause staging errors. Its use may be associated with compression of the tumours growing within the rectum, and thinning of the deeper layers, in particular of the muscularis propria, which may be therefore unidentifiable.³² Also, opponents mention the problems of moving the rectal wall and its tumour falsely closer to the mesorectal fascia and may reduce the perceived distance between them.^{33,34}

Our study has several limitations, such as the low number of T_{is} cases and the retrospective, single-centre design. In addition, a correlation with EUS was not performed in regards to the invasion depth of the tumour. In several cases who had local excision, we used proctoscopic biopsy results to correlate with MR results. Proctoscopy with biopsy may not determine the precise intramural extension of cancer and may not accurately distinguish submucosal and intramural tumours from extramural tumours. We also did not evaluate local lymph nodes. The prognosis of patients with rectal cancer is known to be influenced by the number of involved lymph nodes.^{2,35} The risk of lymph node metastasis is 14.3% in T_1 and 18.4% in T_2 colorectal cancer.³⁶ Since lymphatic metastasis plays an important role in determining the surgical method to be applied,^{4,35} we need to point out that this is also an important limitation. Another limitation of our study was the readers' awareness of the fact that the cancer cases are in the early stages and this may have increased the accuracy of T staging in our study.

In conclusion, using 3 Tesla MR system provides us an advantage in achieving HR images and enables detailed evaluation of tumours confined to the rectal wall, as well as the relevant pelvic anatomy. The overall accuracy rates for detection of the submucosal invasion (T_1), and muscularis propria invasion (T_2) are high in 3 Tesla MR imaging. The method is not a reliable tool to detect T_{is} cases, although the false positive rate is quite

low. Also, 3 Tesla MR imaging is able to exclude the tumour in the submucosal layer, however, it has difficulty in ruling out the tumour in the muscularis propria. The potential for overstaging and understaging of patients should be realized and taken into account when making treatment decisions. We believe larger and executed prospective studies are needed to better understand the role of MR imaging on this topic.

CONCLUSION

3 Tesla MR imaging seems to be useful for accurate categorization of T-stage in early rectal cancer, especially for T1 cancers. The method is not a reliable tool to detect Tis cases. The potential for overstaging and understaging of the technique should be realized and taken into consideration when tailoring the treatment protocol for each patient.

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