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**Abbreviations:**
$A_z$ = area under the ROC curve
CI = confidence interval
NPV = negative predictive value
PPV = positive predictive value
ROC = receiver operating characteristic
SE = spin echo

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# Rectal Cancer: MR Imaging in Local Staging—Is Gadolinium-based Contrast Material Helpful?[1]

**PURPOSE:** To determine retrospectively whether addition of gadolinium-enhanced T1-weighted magnetic resonance (MR) sequence to T2-weighted turbo spin-echo (SE) MR imaging is valuable for preoperative assessment of T stage and circumferential resection margin in patients with primary rectal cancer.

**MATERIALS AND METHODS:** Local institutional review board approved study and waived informed patient consent. Eighty-three patients with operable primary rectal cancer underwent preoperative MR imaging. Retrospectively, two observers independently scored T2-weighted turbo SE MR images and, in a second reading, T2-weighted images combined with gadolinium-enhanced T1-weighted turbo SE MR images for tumor penetration through rectal wall and tumor extension into mesorectal fascia. A confidence level scoring system was used, and receiver operating characteristic (ROC) curves were generated. Histologic findings were standard of reference. Difference in performance of T2-weighted and combined T2-weighted plus gadolinium-enhanced T1-weighted sequences was analyzed by comparing corresponding areas under ROC curves $(A_z)$ for each observer. Interobserver agreement was calculated by using linear weighted κ statistics.

**RESULTS:** Addition of contrast-enhanced T1-weighted to T2-weighted MR imaging did not significantly improve diagnostic accuracy for prediction of tumor penetration through rectal wall ($A_z$ of T2-weighted vs T2-weighted plus T1-weighted images for observer 1, 0.740 vs 0.764; observer 2, 0.856 vs 0.768) and tumor extension into mesorectal fascia ($A_z$ for observer 1, 0.962 vs 0.902; observer 2, 0.902 vs 0.911). Diagnostic performance $(A_z)$ of MR and interobserver agreement were high for prediction of tumor extension into mesorectal fascia (κ = 0.61, 0.74) but only moderate for penetration through rectal wall (κ = 0.47, 0.45).

**CONCLUSION:** Gadolinium-enhanced MR sequences did not improve diagnostic accuracy for assessment of tumor penetration through rectal wall and tumor extension into mesorectal fascia.


In recent years, surgeons and radiation therapists have directed their efforts at reducing the local recurrence rate after resection of primary rectal cancer. Incomplete removal of the lateral spread of tumor is generally recognized as the major cause of local recurrence rate, varying from 3% up to 32% (1–4). With a standardized surgical technique—total mesorectal excision—a distinct anatomic compartment called the mesorectum, containing the rectum and the mesorectal fat, is removed by means of sharp dissection along the mesorectal fascia. This results in a substantial reduction of the high local recurrence rate to less than 10% (5). Postoperative and especially preoperative radiation therapy have also shown a substantial reduction of local recurrence rates (6,7). A large randomized trial (8) showed that even with optimal surgical technique, a preoperative short course of radiation therapy even further reduces the local recurrence rate to less than 5%.

Although postoperative radiation therapy is still practiced widely in the United States, there is an increasing interest in applying it preoperatively on the basis of data that suggest an improved efficacy. At the same time, the idea of differentiated treatment is gaining ground: On the basis of the risk for local recurrence, patients could be treated with surgery only for cases of superficial tumors, with a short course of preoperative radiation therapy for intermediate cases, or with a long course of preoperative radiochemotherapy for locally advanced cases. This can be achieved only with good preoperative imaging of rectal cancer.

Magnetic resonance (MR) imaging is the most promising technique for the local staging of rectal cancer (9). The identification of tumors close to or invading the mesorectal fascia has become increasingly important, maybe even more important than the classic T stage determination (10).

High-spatial-resolution T2-weighted fast spin-echo (SE) MR sequences performed with a phased-array coil have been shown to produce a detailed depiction of the mesorectal fascia and allow accurate prediction of the circumferential resection margin (11,12). The role of contrast material–enhanced MR sequences is not clear. There are few publications on the use of contrast materials in MR imaging of rectal cancer (13–16). Most of these studies involve the comparison of contrast-enhanced MR imaging with nonenhanced MR imaging for the prediction of T stage, but because of the different techniques applied, these studies are difficult to compare. To our knowledge, there is no report on the benefit of contrast-enhanced MR sequences for the prediction of tumor invasion into the mesorectal fascia.

The purpose of this study was to determine retrospectively whether the addition of gadolinium-enhanced T1-weighted MR sequences to T2-weighted turbo SE MR sequences is valuable for preoperative assessment of T stage and circumferential resection margin in patients with primary rectal cancer.

## MATERIALS AND METHODS

The local institutional review board approved this study and waived informed consent for retrospective review of clinical patient data. Between July 1997 and April 2001, a total of 83 consecutive patients with primary operable rectal cancer who underwent surgery following standard preoperative MR imaging that included gadolinium-enhanced sequences were included retrospectively. There were 61 male patients with a mean age of 64 years (age range, 15–85 years) and 22 female patients with a mean age of 66 years (age range, 36–86 years).

### Imaging Techniques

MR imaging was performed with a 1.5-T system (Gyroscan, Powertrack 6000, NT release 6.2.1 with 23.0 mT/m, rise time of 0.2 msec, and slew rate 105 T/m/sec; Philips Medical Systems, Best, the Netherlands). The patients were positioned supine with feet in the first position with the pelvis centered on the proximal end of a quadrature phased-array spine coil (Synergy spine coil; Philips Medical Systems).

The following MR imaging sequences were applied: a precontrast T1-weighted two-dimensional turbo (fast) SE sequence (repetition time msec/echo time msec, 656/10; echo train length of five, 8-mm section thickness, 0.8-mm gap, four signals acquired, 166 × 256 matrix, 25-cm field of view, and acquisition time of 1.4 minutes), a gadolinium-enhanced (0.2 mL per kilogram of body weight, Magnevist; Schering, Berlin, Germany) T1-weighted two-dimensional turbo (fast) SE sequence (612/15, echo train length of five, 3-mm section thickness, 0.3-mm gap, eight signals acquired, 383 × 512 matrix, 20-cm field of view, 0.6-mm$^3$ voxel size, and acquisition time of 9.0 minutes), and a T2-weighted two-dimensional turbo (fast) SE sequence (3427/150, echo train length of 25, 3-mm section thickness, 0.3-mm gap, eight signals acquired, 175 × 256 matrix, 20-cm field of view, 2.64-mm$^3$ voxel size, and acquisition time of 6.5 minutes).

The T1-weighted precontrast MR sequence was performed in the transverse plane, and the first T2-weighted MR sequence was performed in the sagittal plane. These images were used to plan the T2-weighted sequences in the transverse and coronal planes. The transverse and coronal planes were angled exactly perpendicular to the long axis of the rectal tumor. Gadolinium-enhanced T1-weighted sequences were performed in the transverse and coronal planes.

Patients did not receive bowel preparation, air insufflation, or intravenous spasmolytic medication. The total imaging time was approximately 45 minutes.

### Image Evaluation

The MR images were evaluated retrospectively by two radiologists, who were blinded to each other and to the histologic results. Observer 1 was a dedicated pelvic MR imaging radiologist (R.G.H.B.T.) who had more than 10 years of experience in reading pelvic MR images. Observer 2 was a general radiologist (R.F.A.V.) who had 5 years of experience in reading MR images.

Both observers scored the MR images independently for tumor penetration through the muscular rectal wall and tumor extension into the mesorectal fascia by using a confidence level scoring system. The following confidence levels were used: definitely absent, probably absent, possibly present, probably present, and definitely present.

During a first reading only, the T2-weighted fast SE MR sequences in three orientations (sagittal, coronal, and transverse) were evaluated. During a second reading after at least a 1-week interval and in a different order, both T2-weighted turbo SE images and gadolinium-enhanced T1-weighted images (transverse and coronal) were evaluated. When there were MR images available that were obtained before radiation therapy in the group of patients that received preoperative irradiation, these images were scored for the prediction of tumor penetration through the rectal wall and extension into the mesorectal fascia.

The confidence levels for the prediction of tumor penetration through the rectal wall on MR images were defined as follows: definitely absent, completely intact muscular rectal wall; probably absent, disruption of the muscular rectal wall without extension beyond the contour of the rectal wall; possibly present, subtle spiculations in the perirectal fat or a minimal bulging tumor margin beyond the contour of the rectal wall; probably present, spiculations in the perirectal fat or a bulging tumor margin beyond the contour of the rectal wall; and definitely present, nodular invasion of the perirectal fat or diffuse stranding from the tumor into the perirectal fat with complete disruption of the muscular rectal wall.

On MR images, the mesorectal fascia was defined as the fine linear structure enveloping the mesorectum that was hypointense on T2-weighted images and isointense to muscle on contrast-enhanced T1-weighted images. The confidence levels for the prediction of tumor (or nodal) extension into the mesorectal fascia were defined as follows: definitely absent, a wide fat plane between the tumor and the mesorectal fascia; probably absent, a thin fat plane between the tumor and the mesorectal fascia; possibly present, a thin fat plane between the tumor and the fascia with subtle spiculations from the tumor reaching the

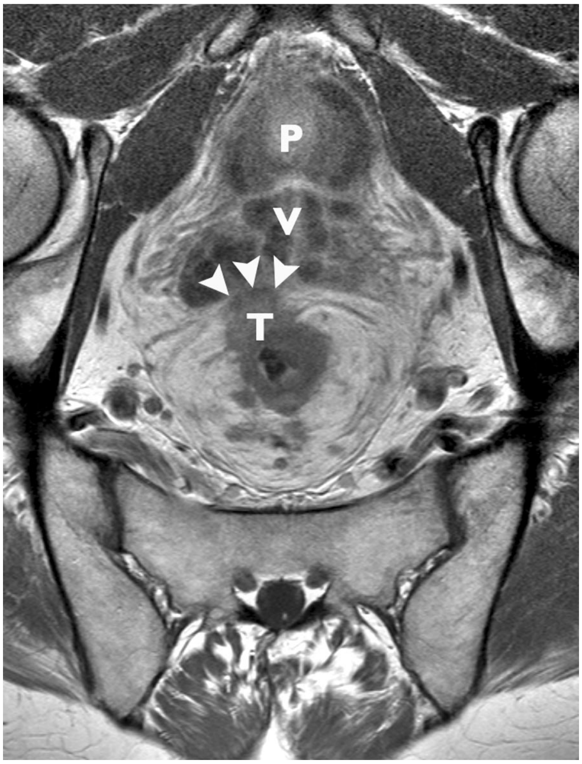



**Figure 1.** Clear invasion of mesorectal fascia. Transverse gadolinium-enhanced T1-weighted MR image (612/15) of rectal tumor *(T)* with penetration (arrowheads) through rectal wall into mesorectal fat and fascia. There is no fat plane between anterior penetrating tumor and nodular thickened mesorectal fascia, which suggests invasion of this structure. This was confirmed at histologic examination. *P* = prostate, *V* = seminal vesicle.

mesorectal fascia; probably present, clear spiculations from the tumor reaching the mesorectal fascia or a minimal fat plane between the tumor, tumor deposit, or a suspected lymph node and the mesorectal fascia; and definitely present, diffuse stranding from the tumor into the mesorectal fascia, a nodular tumor mass encroaching the mesorectal fascia (Fig 1), or a tumor deposit or suspected lymph node in direct contact with the mesorectal fascia.

On the combined T2-weighted plus gadolinium-enhanced T1-weighted MR images, observer 1 assessed whether there was a nodular advancing tumor margin present in the perirectal fat or an advancing tumor margin consisting of spiculations into the perirectal fat. This was done to define the predictive value of these patterns of invasion of the perirectal fat for the prediction of tumor penetration through the rectal wall. A nodular advancing tumor margin was defined as bulky tissue extending from the tumor into the perirectal fat. An advancing tumor margin consisting of spiculations was defined as fine strands of tissue extending from the tumor into the perirectal fat.

## Preoperative Radiation Therapy and Surgery

The standard surgical resection was a total mesorectal excision (5). Forty-two patients underwent sphincter-sparing total mesorectal excision, and six patients underwent non–sphincter-sparing abdominoperineal resection. In 29 patients, the surgical resection was extended to include surrounding pelvic structures or organs to obtain a free resection margin. Two patients underwent transanal resection because of a superficial rectal tumor. Four patients underwent explorative laparotomy with biopsy because of noncurable extensive disease. Twenty-seven patients received preoperative radiation therapy because of *(a)* suspected extensive rectal cancer, for which a long course of radiation therapy was administered in an attempt to downstage the tumor, or *(b)* participation in the Dutch randomized Total Mesorectal Excision trial, in which a short course of radiation therapy was administered (5 × 5 Gy) (8). Six of the 27 patients underwent MR imaging before radiation therapy only, 10 of 27 patients underwent MR imaging after radiation therapy only, and 11 of 27 patients underwent MR imaging both before and after radiation therapy.

## Histologic Examination

Since the mid-1990s, the histologic evaluation of rectal cancer excision specimens has been standardized according to the protocol of Quirke et al (3). All evaluations are performed or supervised by dedicated pathologists with more than 10 years of experience in gastrointestinal pathology. The circumferential resection plane of the specimen was stained, and the specimen was opened anteriorly and fixed in formalin for 24 hours. The specimen was then sliced transversely at 0.5-cm intervals. The extent of lateral tumor spread into the mesorectal fat was assessed macroscopically on each slice, and the shortest distance between the tumor or involved lymph node and the mesorectal circumferential resection plane was measured.

When at macroscopy the circumferential resection margin was close to or involved with tumor tissue, the distance between the tumor and the circumferential stained resection plane was measured at microscopy. When adjacent organs were resected or when a resection was outside the plane of the mesorectal fascia, the relationship between the tumor and the mesorectal fascia was reconstructed. When a tumor response to radiation therapy was noted, the area of the obvious tumor necrosis and fibrosis was considered as the former tumor extent. In a few patients, the tumor appeared to be nonresectable at surgery. The distance of the tumor to the mesorectal fascia was reconstructed on the basis of intraoperative findings and biopsy results.

## Statistical Analysis

Tumor penetration through the muscular rectal wall and tumor extension into the mesorectal fascia at histologic examination were used as the standard of reference against which MR findings were compared (R.G.H.B.T., R.F.A.V.). A histologically measured distance of up to 1 mm between the tumor or a pathologic lymph node and the mesorectal fascia was considered to be tumor extension into the mesorectal fascia.

Receiver operating characteristic (ROC) curves were constructed (A.G.H.K., R.F.A.V.) with the confidence level scores (0 = absent, 1 = probably absent, 2 = possibly present, 3 = probably present, and 4 = present) at both readings (T2-weighted MR images and T2-weighted plus gadolinium-enhanced T1-weighted MR images) and for both observers for the detection of tumor penetration through the muscular rectal wall and for tumor extension into the mesorectal fascia.

The difference in performance between T2-weighted MR sequences only and the combined T2-weighted plus gadolinium-enhanced T1-weighted MR sequences was analyzed (A.G.H.K., R.F.A.V.) by means of comparison of the corresponding areas under the ROC curves *($A_z$)* for each observer (17).

For the analysis of the influence of preoperative radiation therapy, age, and sex on the results, a subgroup analysis was performed (A.G.H.K., R.F.A.V.). The following subgroups were analyzed: patients with versus those without preoperative radiation therapy, male versus female patients, and age less than 60 years versus age more than 60 years. In each subgroup, ROC curves were constructed, and the difference in performance of T2-weighted and the combined T2-weighted plus gadolinium-enhanced T1-weighted sequences was evaluated by comparing $A_z$ values for the prediction of penetration through the rectal wall and tumor extension into the mesorectal fascia for each observer (17).

Findings that were missed on MR images at one or both readings for the whole group of patients and the subgroups were reviewed (R.G.H.B.T., R.F.A.V.) to find a specific cause.

For the calculation (A.G.H.K., R.F.A.V.) of the accuracy, sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of MR imaging for the prediction of tumor extension into the mesorectal fascia and penetration through the rectal wall, the confidence level scores of each reading were dichotomized. The cutoff point was assigned between possibly present and probably present (between confidence levels of 0–2 and 3–4).

The accuracy, sensitivity, specificity, PPV, and NPV of a nodular advancing tumor margin into the perirectal fat and a tumor margin consisting of spiculations into the perirectal fat visualized on the combined T2-weighted plus gadolinium-enhanced T1-weighted MR images for the prediction of tumor penetration through the rectal wall were calculated (A.G.H.K., R.F.A.V.) for observer 1.

**TABLE 1**
**Prediction of Tumor Penetration of the Rectal Wall and Invasion of the Mesorectal Fascia**

| | Observer 1 | | Observer 2 | |
|---|---|---|---|---|
| Parameter | T2-weighted | CE T1- and T2-weighted | T2-weighted | CE T1- and T2-weighted |
| Tumor penetration of rectal wall | | | | |
| $A_z$ | 0.74 | 0.76 | 0.86 | 0.77 |
| 95% CI | 0.61, 0.87 | 0.63, 0.90 | 0.75, 0.96 | 0.63, 0.91 |
| Accuracy (%) | 69 (57/83) | 81 (67/83) | 83 (69/83) | 84 (70/83) |
| Sensitivity (%) | 78 (49/63) | 87 (55/63) | 91 (57/63) | 98 (62/63) |
| Specificity (%) | 40 (8/20) | 60 (12/20) | 60 (12/20) | 40 (8/20) |
| PPV (%) | 80 (49/61) | 87 (55/63) | 88 (57/65) | 84 (62/74) |
| NPV (%) | 36 (8/22) | 60 (12/20) | 67 (12/18) | 89 (8/9) |
| Invasion of mesorectal fascia | | | | |
| $A_z$ | 0.97 | 0.90 | 0.90 | 0.91 |
| 95% CI | 0.93, 1.01 | 0.83, 0.98 | 0.83, 0.98 | 0.84, 0.98 |
| Accuracy (%) | 93 (77/83) | 88 (73/83) | 87 (72/83) | 87 (72/83) |
| Sensitivity (%) | 88 (30/34) | 85 (29/34) | 82 (28/34) | 79 (27/34) |
| Specificity (%) | 96 (47/49) | 90 (44/49) | 90 (44/49) | 92 (45/49) |
| PPV | 94 (30/32) | 85 (29/34) | 85 (28/33) | 87 (27/31) |
| NPV | 90 (44/49) | 92 (47/51) | 88 (44/50) | 87 (45/52) |

Note.—Numbers in parentheses are raw data. CE = contrast enhanced (T1-weighted sequence only). There were no significant differences between $A_z$ values.

The interobserver agreement of the MR imaging evaluation was calculated (A.G.H.K., R.F.A.V.) by using linear weighted κ statistics (18). κ values can range from 0 (no agreement) to 1.00 (perfect agreement) and can be interpreted as poor (0), slight (0.01–0.20), fair (0.21–0.40), moderate (0.41–0.60), substantial (0.61–0.80), and almost perfect (0.81–1.00) (19).

Statistical analysis was performed (A.G.H.K., R.F.A.V.) by using the software package SPSS for Windows, release 10.0 (SPSS, Chicago, Ill). *P* values less than .05 were considered to indicate a significant difference.

## RESULTS

### Tumor Penetration of the Rectal Wall

The accuracy, sensitivity, specificity, PPV, and NPV of T2-weighted images and combined T2-weighted plus gadolinium-enhanced T1-weighted MR images for the prediction of tumor penetration of the rectal wall for observers 1 and 2 are given in Table 1.

The $A_z$ values with 95% confidence intervals (CIs) of T2-weighted MR images only and T2-weighted plus gadolinium-enhanced T1-weighted MR images were 0.74 (95% CI: 0.61, 0.87) and 0.76 (95% CI: 0.63, 0.90), respectively, for observer 1 and 0.86 (95% CI: 0.75, 0.96) and 0.77 (95% CI: 0.63, 0.91), respectively, for observer 2 (Table 1, Fig 2). There was no significant difference between the $A_z$ values of T2-weighted MR images only and T2-weighted plus contrast-enhanced T1-weighted MR images for both observers ($P$ = .71 for observer 1 and $P$ = .17 for observer 2).

Subgroup analysis of patients with versus those without preoperative radiation therapy, male versus female patients, and age less than 60 years versus age more than 60 years showed that there was only a significant difference between the $A_z$ values of T2-weighted MR sequences and gadolinium-enhanced T1-weighted MR sequences in the group of patients with preoperative radiation therapy for observer 2. T2-weighted sequences performed significantly better than the combined T2-weighted plus gadolinium-enhanced T1-weighted sequences in this subgroup of patients ($P < .05$). The $A_z$ values with 95% CIs, accuracy, sensitivity, specificity, PPV, and NPV of T2-weighted images and combined T2-weighted plus gadolinium-enhanced T1-weighted images for the prediction of tumor penetration of the rectal wall in the group of patients with and those without preoperative radiation therapy for both observers are given in Tables 2 and 3.

Sixty-three tumors breached the rectal wall, and 20 tumors were confined to the rectal wall. On T2-weighted MR images only, observers 1 and 2 over-

**TABLE 2**
**Subgroup Analysis of Patients without Preoperative Radiotherapy for the Prediction of Tumor Penetration of the Rectal Wall and Invasion of the Mesorectal Fascia**

| | Observer 1 | | Observer 2 | |
|---|---|---|---|---|
| Parameter | T2-weighted | CE T1- and T2-weighted | T2-weighted | CE T1- and T2-weighted |
| Tumor penetration of rectal wall | | | | |
| $A_z$ | 0.70 | 0.80 | 0.83 | 0.83 |
| 95% CI | 0.55, 0.85 | 0.66, 0.95 | 0.70, 0.96 | 0.69, 0.97 |
| Accuracy (%) | 70 (39/56) | 73 (41/56) | 79 (44/56) | 84 (47/56) |
| Sensitivity (%) | 67 (26/39) | 72 (28/39) | 77 (30/39) | 90 (35/39) |
| Specificity (%) | 77 (13/17) | 76 (13/17) | 82 (14/17) | 71 (12/17) |
| Invasion of mesorectal fascia | | | | |
| $A_z$ | 0.98 | 0.90 | 0.83 | 0.89 |
| 95% CI | 0.94, 1.00 | 0.79, 1.00 | 0.68, 0.99 | 0.75, 1.00 |
| Accuracy (%) | 91 (51/56) | 84 (47/56) | 86 (48/56) | 88 (49/56) |
| Sensitivity (%) | 85 (11/13) | 85 (11/13) | 77 (10/13) | 85 (11/13) |
| Specificity (%) | 93 (40/43) | 84 (36/43) | 88 (38/43) | 84 (36/43) |

Note.—Numbers in parentheses are raw data. CE = contrast enhanced (T1-weighted sequence only). There were no significant differences between $A_z$ values.

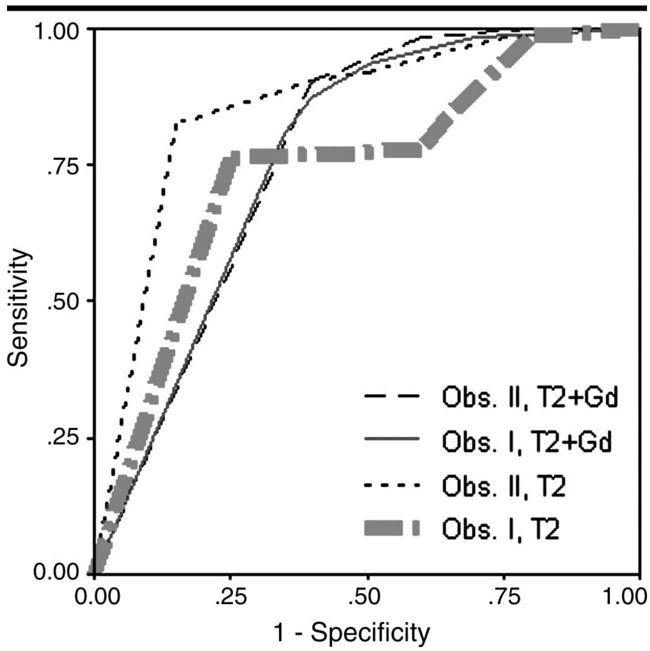



**Figure 2.** Diagnostic performance represented by ROC curves of T2-weighted MR sequences *(T2)* and T2-weighted sequences plus contrast-enhanced T1-weighted MR sequences *(T2+Gd)* for prediction of tumor penetration through rectal wall for observers 1 *(Obs. I)* and 2 *(Obs. II)*. There was no significant difference ($P > .05$) between $A_z$ values of T2-weighted sequences and combined T2-weighted sequences plus contrast-enhanced T1-weighted sequences. Diagnostic performance of MR imaging for prediction of rectal wall penetration for both observers appeared to be moderate: $A_z = 0.74–0.86$.

staged 12 and eight tumors and understaged 14 and six tumors, respectively. After the addition of gadolinium-enhanced T1-weighted images, observers 1 and 2 overstaged eight and 12 tumors and understaged eight tumors and one tumor, respectively.

Most cases of inaccurate staging were caused by difficulties of the interpretation of spiculations into the perirectal fat (Fig 3a, 3b). This occurred in patients without preoperative radiation therapy, as well as in a few irradiated patients with superficial tumors. These spiculations consisted histologically of a desmoplastic tumor reaction or radiation-induced fibrosis with or without tumor nests that could not be discriminated on T2-weighted MR images or on gadolinium-enhanced T1-weighted MR images. No specific cause could be found for the better performance of T2-weighted sequences in the group of patients with preoperative radiation therapy for observer 2.

The accuracy, sensitivity, specificity, PPV, and NPV of a nodular advancing tumor margin into the perirectal fat (Fig 3c) or a tumor margin consisting of spiculations (Fig 3a, 3b) for the prediction of tumor penetration through the rectal wall, as assessed by observer 1 on T2-weighted plus gadolinium-enhanced T1-weighted MR images, were 71% (59 of 83 patients), 64% (40 of 63 patients), 95% (19 of 20 patients), 98% (40 of 41 patients), and 45% (19 of 42 patients), respectively, for a nodular tumor margin and 34% (28 of 83 patients), 27% (17 of 63 patients), 55% (11 of 20 patients), 65% (17 of 26 patients), and 19% (11 of 57 patients), respectively, for a margin consisting of spiculations.

The interobserver agreement expressed by the linear weighted κ statistic with 95% CIs was 0.47 (95% CI: 0.31, 0.64) for T2-weighted MR images and 0.45 (95% CI: 0.25, 0.65) for combined T2-weighted plus gadolinium-enhanced T1-weighted MR images.

## Tumor Extension into Mesorectal Fascia

The accuracy, sensitivity, specificity, PPV, and NPV of T2-weighted MR images versus combined T2-weighted plus gadolinium-enhanced T1-weighted MR images for the prediction of tumor extension into the mesorectal fascia for observers 1 and 2 are given in Table 1.

The $A_z$ values with 95% CIs of T2-weighted images only versus T2-weighted plus gadolinium-enhanced T1-weighted images were 0.97 (95% CI: 0.93, 1.01) and 0.90 (95% CI: 0.83, 0.98), respectively, for observer 1 and 0.90 (95% CI: 0.83, 0.98) and 0.91 (95% CI: 0.84, 0.98), respectively, for observer 2 (Table 1, Fig 4). There was no significant difference between $A_z$ values for T2-weighted images only and T2-weighted images plus gadolinium-enhanced T1-weighted images for both observers ($P = .052$ for observer 1 and $P = .77$ for observer 2) for the prediction of tumor extension into the mesorectal fascia.

There was tumor extension into the mesorectal fascia in 34 patients (41%).

Thirty-five patients (42%) had a circumferential resection margin larger than 10 mm. On T2-weighted MR images, observers 1 and 2 overestimated two and five tumors, respectively, as tumor extension into the mesorectal fascia and underestimated four and six tumors, respectively. After the addition of gadolinium-enhanced T1-weighted MR imaging to T2-weighted sequences, observers 1 and 2 overestimated five and four tumors and underestimated five and seven tumors, respectively.

Subgroup analysis of patients with versus those without preoperative radiation therapy, male versus female patients, and age less than 60 years versus age more than 60 years showed that there was only a significant difference between T2-weighted MR sequences and gadolinium-enhanced T1-weighted MR sequences in the group of patients older than 60 years and only for observer 1 ($P < .05$). T2-weighted sequences performed significantly better than the combined T2-weighted plus gadolinium-enhanced T1-weighted sequences ($P < .05$) in this subgroup. The $A_z$ values with 95% CIs, accuracy, sensitivity, specificity, PPV, and NPV of T2-weighted MR images and combined T2-weighted plus gadolinium-enhanced T1-weighted MR images for the prediction of tumor extension into the mesorectal fascia in the group of patients with and those without preoperative radiation therapy for both observers are given in Tables 2 and 3.

Analysis of false-positive and false-negative findings showed that there was no specific cause for these failures. Two cases were misinterpreted with both T2-weighted and gadolinium-enhanced T1-weighted imaging because of difficulty in the interpretation of spiculations reaching the mesorectal fascia (Fig 5a, 5b). These spiculations could consist of fibrosis with or without tumor cells, and the observers were not able to discriminate between the two on images obtained with either sequence. Interpretation difficulties of spiculations in the mesorectal fat obviously do not occur strictly with postradiation MR imaging, as these two specific cases were found in the subgroup of nonirradiated patients. Another reason for the false predictions occurred in a few cases of low anteriorly located bulky tumors. These bulky tumors caused a mass effect on the surrounding pelvic structures, which stretched the fat plane in between (Fig 5c). When there was a normal signal intensity of the surrounding pelvic organs, it was difficult to discriminate mass effect from invasion into this organ. This problem existed on both T2-weighted and gadolinium-enhanced T1-weighted MR images, but for unknown reasons, fewer interpretation problems occurred on T2-weighted images for observer 1 in the patient group older than 60 years.

**TABLE 3**
**Subgroup Analysis of Patients with Preoperative Radiotherapy for the Prediction of Tumor Penetration of the Rectal Wall and Invasion of the Mesorectal Fascia**

| | Observer 1 | | Observer 2 | |
|---|---|---|---|---|
| Parameter | T2-weighted | CE T1- and T2-weighted | T2-weighted | CE T1- and T2-weighted |
| Tumor penetration of rectal wall | | | | |
| $A_z$ | 0.78* | 0.48* | 0.92† | 0.46† |
| 95% CI | 0.45, 1.00 | 0.14, 0.82 | 0.82, 1.00 | 0.13, 0.79 |
| Accuracy (%) | 89 (24/27) | 85 (23/27) | 85 (23/27) | 81 (22/27) |
| Sensitivity (%) | 92 (22/24) | 96 (23/24) | 92 (22/24) | 92 (22/24) |
| Specificity (%) | 67 (2/3) | 0 (0/3) | 33 (1/3) | 0 (0/3) |
| Invasion of mesorectal fascia | | | | |
| $A_z$ | 0.96* | 0.87* | 0.95* | 0.90* |
| 95% CI | 0.88, 1.00 | 0.67, 1.00 | 0.86, 1.00 | 0.78, 1.00 |
| Accuracy (%) | 93 (25/27) | 85 (23/27) | 89 (24/27) | 78 (21/27) |
| Sensitivity (%) | 95 (20/21) | 86 (18/21) | 90 (19/21) | 76 (16/21) |
| Specificity (%) | 83 (5/6) | 83 (5/6) | 83 (5/6) | 83 (5/6) |

Note.—Numbers in parentheses are raw data. CE = contrast enhanced (T1-weighted sequence only).
* No significant difference between $A_z$ values.
† Significant difference ($P < .05$) between $A_z$ values.

The interobserver agreement between both observers expressed by the linear weighted κ statistic with 95% CIs was 0.75 (95% CI: 0.63, 0.86) on T2-weighted MR images only and 0.61 (95% CI: 0.48,0.74) for the combined T2-weighted plus gadolinium-enhanced T1-weighted MR images.

## DISCUSSION

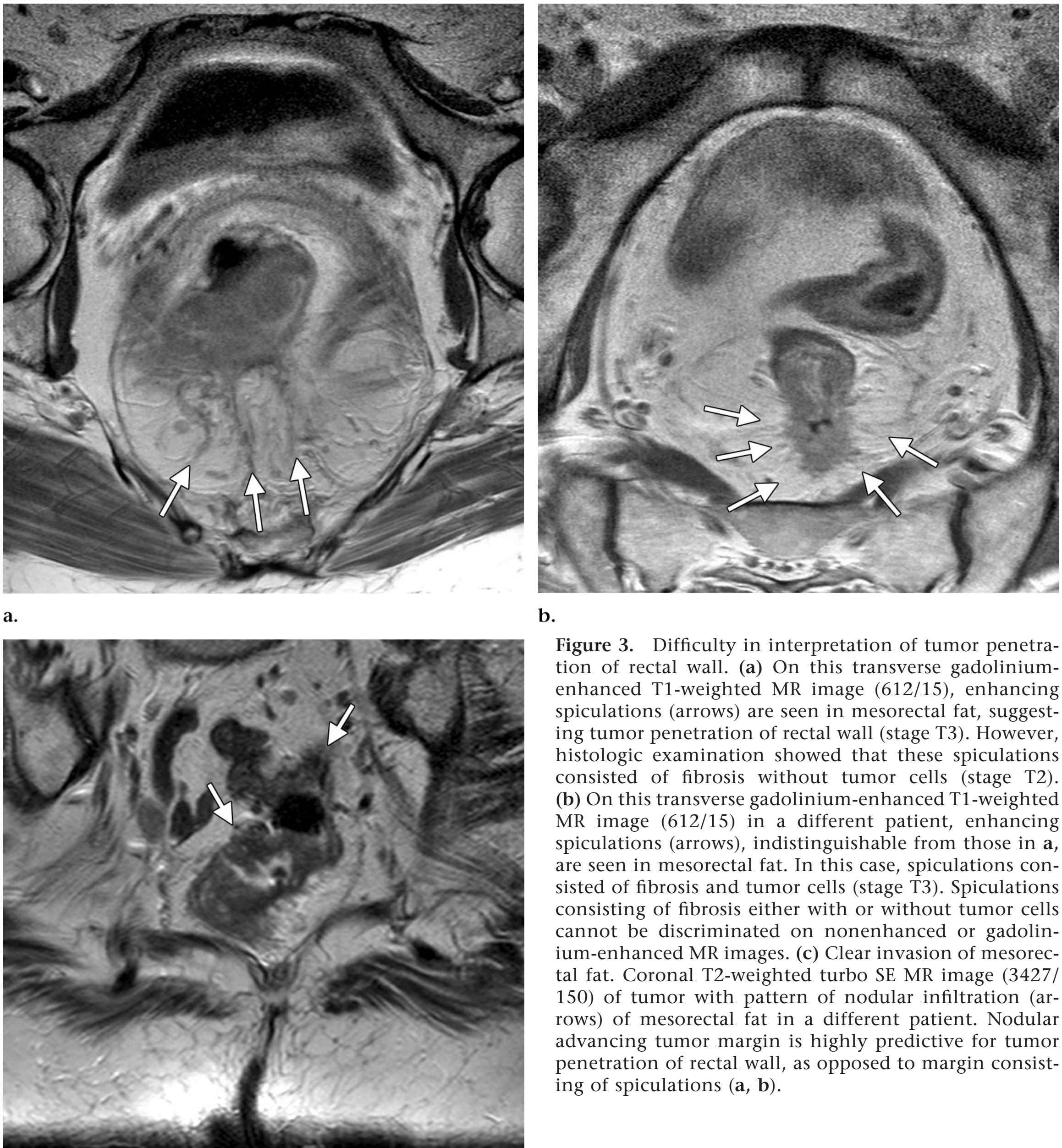
### T1-weighted MR Sequences and Rectal Wall Penetration

The results of the present study show that the addition of gadolinium-enhanced T1-weighted MR sequences to T2-weighted fast SE MR sequences did not significantly improve the diagnostic accuracy for the prediction of tumor penetration through the rectal wall. The accuracy of MR imaging for the evaluation of tumor penetration through the rectal wall remained moderate for both observers, with accuracies of 69%–84%.

A standard protocol for MR imaging of rectal cancer consists of high-resolution T2-weighted fast SE sequences (11,12). Different opinions exist about the value of contrast-enhanced MR sequences in rectal cancer staging. In a study of 32 patients, Okizuka et al (13) reported no improvement for T staging after addition of gadolinium-enhanced fat-suppressed MR imaging to conventional T1- and T2-weighted MR imaging. Although in their study, contrast-enhanced MR imaging allowed better tumor detection and delineation, it tends to lead to overstaging of stage T1 and T2 tumors because of peritumoral inflammatory reaction. In a study of 106 patients with rectal cancer, Maier et al (14) showed that the tumor could be better identified and delineated by using a double-contrast technique of intravenous gadolinium-based contrast material combined with an enema of ferristene. However, overstaging difficulties occurred in most of the stage T1 tumors (six of 10 tumors) and T2 tumors (13 of 22 tumors).

Wallengren et al (16) also used the double-contrast technique and found improved identification of the individual rectal wall layers and tumor delineation. The authors applied a conventional low-spatial-resolution MR technique, however, which may explain the superior performance of their contrast-enhanced sequences. Vogl et al (15) studied 35 patients with superficial tumors and found a high accuracy for stage T1 tumors when a dynamic contrast-enhanced MR technique was applied by using an endorectal coil. Stage T2 and T3 tumors were staged accurately, however, by using nonenhanced T2-weighted sequences only. Contrast-enhanced sequences did not provide additional benefit.

Overall, our findings support the literature that there is at present no real benefit of the use of gadolinium-based contrast material in the staging of rectal



a. b. c.

**Figure 3.** Difficulty in interpretation of tumor penetration of rectal wall. **(a)** On this transverse gadolinium-enhanced T1-weighted MR image (612/15), enhancing spiculations (arrows) are seen in mesorectal fat, suggesting tumor penetration of rectal wall (stage T3). However, histologic examination showed that these spiculations consisted of fibrosis without tumor cells (stage T2). **(b)** On this transverse gadolinium-enhanced T1-weighted MR image (612/15) in a different patient, enhancing spiculations (arrows), indistinguishable from those in **a**, are seen in mesorectal fat. In this case, spiculations consisted of fibrosis and tumor cells (stage T3). Spiculations consisting of fibrosis either with or without tumor cells cannot be discriminated on nonenhanced or gadolinium-enhanced MR images. **(c)** Clear invasion of mesorectal fat. Coronal T2-weighted turbo SE MR image (3427/150) of tumor with pattern of nodular infiltration (arrows) of mesorectal fat in a different patient. Nodular advancing tumor margin is highly predictive for tumor penetration of rectal wall, as opposed to margin consisting of spiculations (**a**, **b**).

cancer with a phased-array MR technique. The moderate accuracy in T staging does not improve with contrast-enhanced sequences. Overstaging as a result of desmoplastic tumor reaction still occurs, and identification of the individual rectal wall layers, particularly the submucosal layer, can still be difficult after contrast enhancement (9,13,14,20). For superficial rectal cancer, either MR imaging with an endorectal coil or endorectal ultrasonography in experienced hands is probably more accurate than MR imaging with a phased-array coil.

The moderate accuracy for the prediction of tumor penetration through the rectal wall is in concordance with other studies. In a study of 49 patients, Blomqvist et al (21) showed an accuracy of 76% for the prediction of tumor penetration through the rectal wall on T2-weighted fast SE MR images. In their study, most of the staging failures were caused by peritumoral tissue reaction that simulated tumor penetration through the rectal wall. The studies in which gadolinium-enhanced MR sequences were used in combination with T2-weighted sequences have the same staging difficulties with accuracies of only 76%–82% (13,14,20).

Difficulties with the interpretation of spiculations in the mesorectal fat on both nonenhanced T2-weighted and contrast-enhanced T1-weighted images were responsible for most of the staging failures in our study. These failures occurred for both observers, independent of their reading experiences. Neither reader was able to distinguish *(a)* spiculations in mesorectal fat caused by fibrosis that contained tumor cells from *(b)* spiculations that contained fibrosis only on either nonenhanced or contrast-enhanced MR images. When the pattern of tumor growth through the rectal wall into the mesorectal fat was nodular, however, the PPV increased to 98%, compared with 65% for a spiculated pattern.

In other fields of MR imaging (ie, musculoskeletal imaging), fat-suppressed MR sequences can help increase the contrast between pathologic and normal surrounding tissues. This is not the case with MR imaging of rectal cancer. Rectal MR imaging involves high natural contrast between the tumor and the perirectal fat. With a fat-suppressed MR technique, the contrast between the hypointense mesorectal fascia and the mesorectal fat disappears, and the anticipated resection margin is difficult to evaluate. The value of fat suppression for the prediction of tumor penetration through the rectal wall is unclear.

A study by Okizuka et al (13) showed that gadolinium-enhanced T1-weighted MR sequences in conjunction with a fat-suppressed technique did not improve the performance of MR imaging for staging of rectal cancer. In their study, as well as in the present study, the main staging problems were caused by desmoplastic tumor reaction, a problem apparently not solved with a fat-suppressed technique.

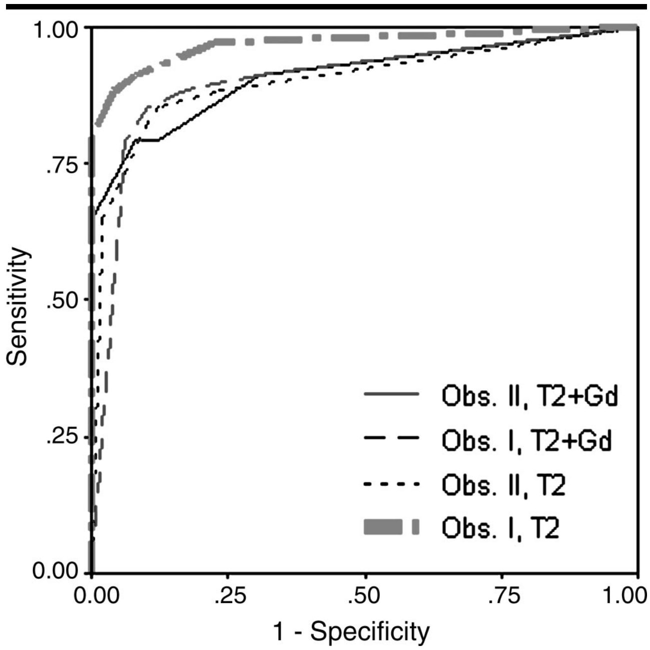



**Figure 4.** Diagnostic performance represented by ROC curves of T2-weighted MR sequences *(T2)* and T2-weighted plus gadolinium-enhanced T1-weighted MR sequences *(T2+Gd)* for prediction of tumor invasion of mesorectal fascia for observers 1 *(Obs. I)* and 2 *(Obs. II)*. There was no significant difference ($P > .05$) between $A_z$ values of T2-weighted sequences and combined T2-weighted plus gadolinium-enhanced T1-weighted sequences. Diagnostic performance of MR imaging for prediction of involvement of mesorectal fascia for both observers was high: $A_z > 0.90$.

### T1-weighted MR and Tumor Extension into Mesorectal Fascia

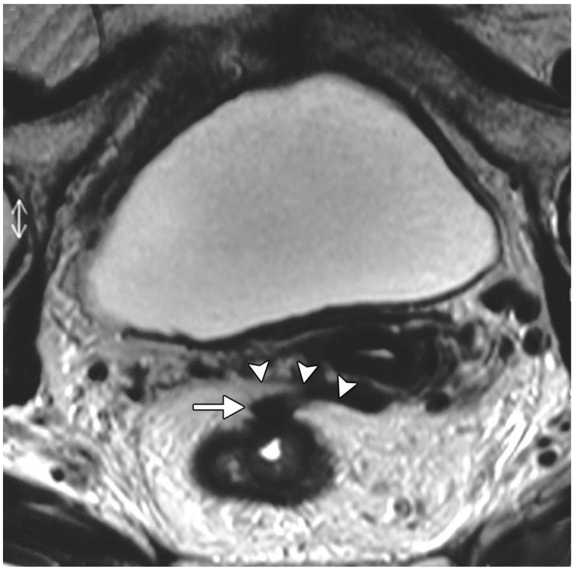
Results of the present study show that the addition of gadolinium-enhanced T1-weighted MR imaging does not improve the high accuracy (approximately 90%) of T2-weighted fast SE MR imaging for the evaluation of tumor invasion in the mesorectal fascia. The gadolinium-enhanced MR sequences can therefore be omitted, thus saving acquisition time and examination costs and avoiding potential allergic reactions.

The clinical importance of the relationship of the tumor to the mesorectal fascia should be emphasized. The ideal plane of dissection during a resection of the rectum is along the mesorectal fascia. When the tumor is close to or invading the mesorectal fascia, there is a risk for a positive resection margin with a high risk of local recurrence. Although the T stage is a strong predictor for overall prognosis, for local recurrence, the circumferential resection margin is probably a more important prognostic indicator (4,22). On the basis of the encouraging results of preoperative radiation therapy, a differentiated preoperative treatment according to the risk for local recurrence becomes an attractive option when there is a reliable imaging test. Patients with a low risk could be treated with surgery only, patients with an intermediate risk could be treated with a short course of preoperative radiation therapy, and patients with a locally advanced tumor could be treated with an extensive radiochemotherapy schedule to allow for downsizing.

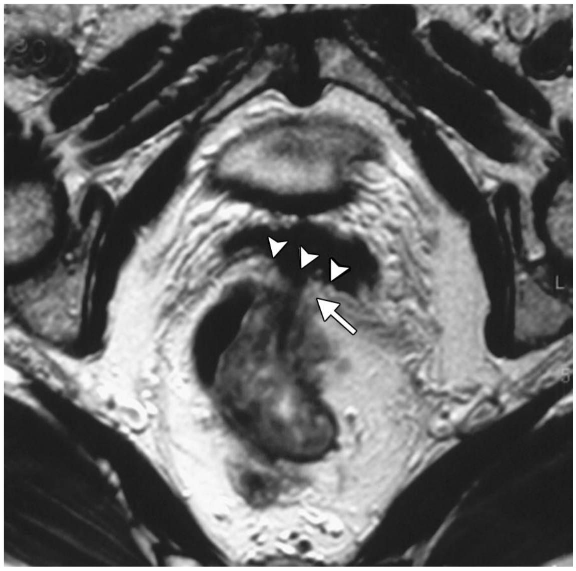
In several studies, MR imaging has allowed accurate prediction of tumor extension into the mesorectal fascia and the surrounding organs (12,20,23–25). In a study of 76 patients, Beets-Tan et al (20) reported that an involved circumferential resection margin could be predicted with an accuracy of 100% in 12 stage T4 tumors, and a tumor-free circumferential resection margin could be predicted with an accuracy of more than 90% in 29 tumors with a wide margin at MR imaging. For the remaining tumors that were close to the mesorectal fascia, a linear regression curve showed that a margin of 1 mm could be predicted with high certainty when the measured distance between the tumor and the mesorectal fascia at MR was at least 5 mm.

In a study of 26 specimens obtained after total mesorectal excision, Blomqvist et al (24) showed a sensitivity and specificity of 100% and 61%, respectively, for the prediction of involvement of the circumferential resection margin. In a study of 43 patients with rectal cancer, Bissett et al (12) found an accuracy, sensitivity, and specificity of 95%, 67%, and 100%, respectively, for prediction of the circumferential resection margin. In a study of 98 patients, Brown et al (25) showed agreement in 95% ($\kappa$ = 0.81) of cases between MR imaging and histologic findings for the prediction of circumferential resection margin. Only in the first-mentioned study by Beets-Tan et al (20) was a gadolinium-enhanced MR sequence added to the high-resolution T2-weighted fast SE MR sequence. The latter three studies reported equally good results without the use of gadolinium-enhanced sequences (12,24,25). The results of the present study support the idea that gadolinium-based contrast material is not essential for the determination of tumor extension into the mesorectal fascia.

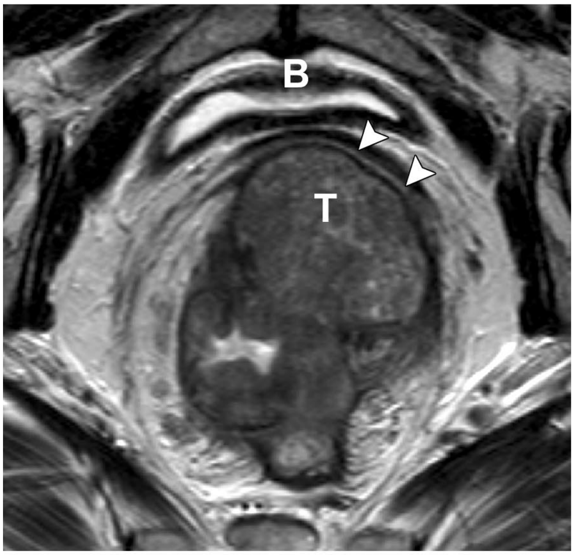
On the high-resolution T2-weighted fast SE MR images, even thin structures such as the mesorectal fascia can be well delineated from the mesorectal fat because of the natural difference in signal intensity between the hypointense fascia and the adjacent hyperintense fatty tissues. It is therefore relatively easy to estimate the width of the circumferential re-




a.



b.




c.

**Figure 5.** Difficulty in interpretation of tumor invasion of mesorectal fascia. **(a)** Transverse T2-weighted turbo SE MR image (3427/150) of tumor with spiculations (arrow) reaching normal-appearing mesorectal fascia anteriorly (arrowheads). On contrast-enhanced T1-weighted MR images, these spiculations enhanced (not shown). Histologic examination of surgical specimen showed that these spiculations consisted of fibrosis without tumor cells (no invasion of mesorectal fascia). **(b)** Transverse T2-weighted turbo SE MR image (3427/150) of tumor with spiculations (arrow) reaching normal-appearing mesorectal fascia anteriorly (arrowheads) in a different patient. On contrast-enhanced MR images, these spiculations enhanced (not shown). As opposed to **a**, spiculations consisted of fibrosis and tumor cells. Contrast-enhanced or nonenhanced MR imaging does not allow differentiation of fibrosis either with or without tumor cells. Therefore, mesorectal fascia must be considered potentially invaded with tumor. **(c)** Transverse T2-weighted turbo SE MR image (3427/150) of bulky (voluminous) low anteriorly located tumor in a different patient. This tumor *(T)* causes a mass effect on surrounding pelvic structures (arrowheads indicate vagina) and stretches fat plane in between these structures. When surrounding pelvic organs have normal signal intensity, it can be difficult to differentiate compression from tumor invasion. In this case, histologic examination showed invasion of vagina. *B* = bladder.

section margin after a total mesorectal excision procedure, since it is the width of the hyperintense fat plane between the hypointense mesorectal fascia and the isointense tumor.

Interpretation difficulties remain when a tumor shows a spiculated tumor extension that reaches close to the mesorectal fascia. As shown from the results of our subgroup analysis, this does not occur strictly for postradiation MR imaging but can also occur for primary MR images of nonirradiated rectal cancer, especially of tumors that show an extensive desmoplastic reaction. It is difficult to predict whether the spiculations consist of desmoplastic reaction only or desmoplastic reaction that contains tumor nests. In our experience, even contrast-enhanced dynamic MR sequences will not always depict this microscopic tumor load.

Another type of tumor in which the distance to the mesorectal fascia may be difficult to predict is the low anteriorly located rectal cancer. The distal anterior part of the mesorectum contains less mesorectal fat, and when a tumor breaches the muscular rectal wall anteriorly, it is invariably close to or invades the mesorectal fascia. This is especially so for low bulky tumors, where the fat plane between the tumor and the adjacent structures can be obliterated because of the mass effect of the tumor. In these circumstances, it can be difficult to distinguish compression of adjacent organs (posterior vaginal wall, seminal vesicles, prostate) from tumor invasion into these organs.

When considering the results of the present study, one must keep in mind that the design of the study has some limitations. They relate to the use of an MR technique with an external coil, the reconstruction of the histologic standard of reference in locally advanced rectal cancers, and the inclusion of patients with preoperative radiation therapy. Endorectal coils are more accurate for the staging of superficial tumors than are phased-array coils. The use of an endorectal coil in the present study could have influenced the accuracy for the prediction of tumor penetration through the rectal wall. The results of Vogl et al (15), however, who found no beneficial effect of gadolinium-enhanced MR sequences for staging of stage T2 and T3 tumors with an endorectal coil technique, suggest that the use of different coils would have no substantial effect on the final results of the present study.

The second limitation concerns the histologic standard of reference. The routine histologic evaluation after rectal cancer surgery includes the measurement of the distance from the tumor to the circumferential margin. Most patients underwent standard total mesorectal excision, and the circumferential resection margin coincides with the mesorectal fascia. For the more advanced tumors, however, more extensive surgery was performed, and the distance from the tumor to the mesorectal fascia had to be reconstructed retrospectively by correlating the complete pathologic report with the surgical findings. Although most of these cases were easy to interpret because an advanced tumor with invasion in a surrounding structure by definition has invaded the mesorectal fascia, in some patients this could have resulted in errors of the exact histologic distance of the tumor to the mesorectal fascia (most notably after extensive preoperative radiation therapy, see the following).

The third limitation is related to the inclusion of patients after preoperative radiation therapy. Radiation therapy can induce a fibrotic reaction both in normal tissue and in areas of tumor necrosis. For most patients, MR images obtained before radiation therapy were available, and these were used for comparison with histologic findings. When present, areas of clear necrosis and fibrosis at histologic examination were considered former tumor extensions. This may have caused some measurement inaccuracies, as discussed earlier. For the small group of patients that underwent postradiation MR imaging only, interpretation of the images was difficult. Fibrosis that occurs after radiation therapy can sometimes be seen as hypointense spiculations in the perirectal fat. It is difficult to differentiate between postradiation fibrosis, fibrosis that contains viable tumor, and a primary desmoplastic tumor reaction. This can lead to diagnostic errors for the prediction of rectal wall penetration and tumor extension into the mesorectal fascia. To evaluate the effect of the inclusion of patients with preoperative radiation therapy, we performed a subgroup analysis of patients who had undergone radiation therpy and those that had not. Basically, this did not change the results of the study.

The high performance of both readers for the prediction of invasion of the mesorectal fascia with both MR sequences and the high interobserver agreement shows that this can be done with a high accuracy and consistency, as opposed to the prediction of tumor penetration through the rectal wall. This is in concordance with a previous study (20). Striking observations include that even for a more specialized MR reader, it was difficult to predict the T stage, and that a less specialized MR reader performed equally well when predicting invasion of the mesorectal fascia.

In conclusion, the addition of a gadolinium-enhanced T1-weighted sequence to T2-weighted fast SE MR imaging did not improve the diagnostic accuracy for prediction of tumor penetration through the rectal wall and tumor involvement of the mesorectal fascia. When the protocol for local staging includes high-resolution T2-weighted fast SE images, in our opinion, contrast-enhanced sequences can be omitted. The present study confirms previous reports that the performance of phased-array MR imaging is high for the prediction of tumor extension into the mesorectal fascia but only moderate for penetration of the rectal wall, independent of the experience of the reader.

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