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Does Gadolinium-Based Contrast Material Improve Diagnostic Accuracy of Local Invasion in Rectal Cancer MRI? A Multireader Study

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Abstract

OBJECTIVE—The purpose of this study was to compare reader accuracy and agreement on rectal MRI with and without gadolinium administration in the detection of T4 rectal cancer.

MATERIALS AND METHODS—In this study, two radiologists and one fellow independently interpreted all posttreatment MRI studies for patients with locally advanced or recurrent rectal cancer using unenhanced images alone or combined with contrast-enhanced images, with a minimum interval of 4 weeks. Readers evaluated involvement of surrounding structures on a 5-point scale and were blinded to pathology and disease stage. Sensitivity, specificity, negative predictive value, positive predictive value, and AUC were calculated and kappa statistics were used to describe interreader agreement.

RESULTS—Seventy-two patients (38 men and 34 women) with a mean age of 61 years (range, 32–86 years) were evaluated. Fifteen patients had 32 organs invaded. Global AUCs without and with gadolinium administration were 0.79 and 0.77, 0.91 and 0.86, and 0.83 and 0.78 for readers 1, 2, and 3, respectively. AUCs before and after gadolinium administration were similar. Kappa values before and after gadolinium administration for pairs of readers ranged from 0.5 to 0.7.

CONCLUSION—On the basis of pathology as a reference standard, the use of gadolinium during rectal MRI did not significantly improve radiologists' agreement or ability to detect T4 disease.

Keywords

diagnostic accuracy; gadolinium; MRI; reader performance; rectal cancer

The superior intrinsic soft-tissue contrast of MRI compared with CT has led to greater diagnostic accuracy to distinguish tumor from normal tissue [1]. Consequently, unlike its fairly empirical use on CT, the requirement to add IV contrast material will vary more depending on the specific clinical indication. In spite of the theoretic advantage of IV-administered contrast material to improve tumor conspicuity because of leaky tumor neovascularity compared with normal tissues, in rectal cancer MRI, there are data to indicate that the use of gadolinium offers no advantage in the diagnostic accuracy of T-category determination for tumors limited to the bowel wall or the surrounding fat (T0 to T3) [2–5]. However there is limited information about its usefulness in determining invasion of surrounding organs, muscles, or bones.

Gadolinium-enhanced MRI sequences did not improve diagnostic accuracy for assessment of tumor penetration through the rectal wall and tumor extension into the mesorectal fascia in a retrospective study of 83 patients with operable rectal cancer [2]. In this study, 63 tumors were pT3 and 20 were pT2 or less. More recently, in a study including some patients with pT4 disease, 10 of 88 (11%) gadolinium-enhanced T1-weighted MRI studies also did not increase diagnostic yield for tumor and nodal staging. No site-specific data were available in this study [3].

As a large cancer referral center, performing 250 rectal cancer operations a year and more than 400 rectal MRI studies per year, we have a large number of advanced cases (i.e., T4), frequently requiring exenterations and operations requiring multiple subspecialty surgeons.

Given the extensive multiorgan resections for these patients, there is a need for highly accurate imaging for operative planning. Thus, we believe that a better assessment of the role of gadolinium is needed because it adds cost, time for additional sequences, and occasional morbidity. Therefore, the purpose of our study was to assess whether gadolinium administration can improve our diagnostic accuracy or interobserver variability for detecting T4 disease among radiologists with different levels of experience.

Materials and Methods

Patients

After a waiver of authorization from our institutional review board, we retrospectively searched the prospective colorectal cancer surgical database at our tertiary care cancer center. This database included patients who underwent open or laparoscopic radical pelvic resections for locally advanced primary or recurrent rectal cancer during the period from 1998 to 2008, including those patients who also underwent postneoadjuvant-treatment pelvic MRI for preoperative staging at our institution within the 10 weeks before surgery at our institution. Patients had to have T3 (uT3) or uT4 disease detected on endorectal ultrasound. All patients undergo endorectal ultrasound for baseline T categorization as the standard of care if the tumor location and patency are amenable. From this group of eligible patients, a random (RAND, Microsoft Excel 2007) selection of patients was made. A separate surgical database of resected locally recurrent rectal cancer at our institution was also used. This patient mixture is similar to other studies [1] and represents another important population with similar surgical staging questions. We desired an approximately equal mix of locally

advanced primary rectal cancer and locally advanced recurrent rectal cancer. MRI studies were anonymized to prevent recall bias.

MRI

All pelvic MRI studies for evaluation of rectal cancer were performed on either a 1.5-T ($n = 63$) or 3-T ($n = 9$) magnet (GE Signa and GE Horizon, GE Healthcare) using a pelvic phased-array coil with 4–32 elements. No endorectal coil, rectal cleansing preparation, or rectal contrast filling was performed. No spasmolytic was used. All studies included gadopentetate dimeglumine (Magnevist, Bayer HealthCare)–enhanced sequences for dynamic and static acquisitions. A dose of 2 mL/kg (0.1 mmol/kg) was injected at a rate of 2 mL/s followed by 25 mL of saline at the same rate using a power injector (Medrad, various models, Bayer HealthCare). Allowing for coverage of the tumor using this immediate postinjection dynamic contrast-enhanced (DCE) sequence resulted in the static contrast-enhanced axial images being obtained at approximately 6–7 minutes after gadolinium administration. Diffusion-weighted images were obtained variably once that technology became available. The standard protocol for the 1.5-T study consisted of axial, oblique axial, sagittal, and coronal T2-weighted fast recovery fast spin-echo (FRFSE, GE Healthcare) (TR range/TE, 4000–6000/102; fast spin-echo factor, 24; section thickness, 3 mm; intersection gap, 1 mm; number of signals acquired, 3; matrix, 320×192 ; and FOV, 18–26 mm), axial T1-weighted fast spin-echo (TR range/TE, 400–650/minimum; fast spin-echo factor, 3; section thickness, 5 mm; intersection gap, 1 mm; number of signals acquired, 2; matrix, 256×160 ; and FOV, 28–36 mm), sagittal perfusion (details omitted for brevity), and unenhanced and contrast-enhanced (after perfusion) axial T1-weighted ultra-fast spoiled gradient-echo sequences (LAVA [liver acquisition with volume acquisition] with fat saturation, GE Healthcare) (TR/TE, 3500/minimum; section thickness, 3 mm; intersection gap, 0 mm; number of signals acquired, 1; matrix, 192×320 ; and FOV, 28–36 mm). There were no known adverse effects reported for any MRI or endorectal ultrasound studies performed on this group of patients.

Readers and Strategy

All series, excluding the sagittal dynamic contrast-enhanced and the diffusion-weighted sequences were transferred to a 3D workstation after anonymization (AW, version 4.2, GE Healthcare). DCE is not commonly used, and if we had included it, the results might not be generalizable to other centers. Three board-certified radiologists, including a body imager specializing in gastrointestinal oncologic radiology and routinely attending colorectal multidisciplinary conferences, with 7 years of experience and subspecialization privileges of reading pelvic MRI only for rectal cancer (reader 1); a body imager with dedicated fellowship training in MRI with specialization in genitourinary-gynecologic imaging and privileges to read all genitourinary-gynecologic imaging and general screening pelvic MRI with 7 years of experience (reader 2); and an oncologic body imaging fellow in training (reader 3) independently observed all cases retrospectively, blinded to histopathology and surgical results but aware of study entry requirements. Only postneoadjuvant therapy MRI was evaluated. All cases were read twice and the interpretation of each patient's MRI was separated by a minimum interval of 4 weeks to avoid recall bias. Reading sessions either included or omitted the T1-weighted fat-saturated gadolinium-enhanced LAVA sequences

but always included all unenhanced non–diffusion-weighted sequences and T2-weighted sequences. A comparison of T1-weighted gadolinium-enhanced series alone with T2-weighted series alone was not performed. In the first reading session, some cases included gadolinium-enhanced sequences in which the corresponding second session excluded gadolinium, and some cases initially excluded gadolinium. In these cases, the complementary second session included the gadolinium-enhanced sequences. This was randomly assigned to avoid bias related to the order of reading cases. Prior CT and PET/CT studies that would be available in a clinical setting were not included in this review because both were thought to be of limited value in the determination of invasion of surrounding structures.

Interpretation Methods

Readers were asked to rate image quality on a 3-point scale: poor, good, and excellent. These were subjective terms not strictly defined but left to each observer's judgment. Assessment of organ involvement or invasion was rated on a 5-point scale (with an additional NA for genitourinary organs in which the site was not present in that particular sex or was surgically absent): 0, not invaded; 1, probably not invaded; 2, possibly invaded; 3, probably invaded; and 4, definitely invaded. Finally an estimated T category [1–4] was recorded as defined by the 7th edition American Joint Committee on Cancer (AJCC) system. In patients with recurrent disease not involving the anastomosis, lack of invasion of an adjacent structure was described as T3 and invasion of an adjacent structure was described as T4 for simplicity. The organs and structures included bladder, pelvic sidewall (pyriformis, obturator internus), sacrum, pelvic floor (levator ani, sacrospinous or sacrotuberous ligaments, ischiococcygeus), sciatic nerve, internal or external anal sphincter, ureter, prostate, seminal vesicles, uterus, cervix, and vagina. Invasion of any of these structures (excluding the internal anal sphincter) is considered T4 status using the TNM staging criteria. The criteria for invasion were not strictly defined because these are not standardized in the literature and are very subjective. These were left to the observers' experience from general radiologic principles. Typically, loss of a fat plane, irregular borders with an organ, signal intensity of tumor infiltrating broadly or irregularly into an organ with different signal intensity, or enhancement similar to tumor infiltrating broadly or irregularly into an organ with different signal intensity indicated varying degrees of invasion, whereas preservation of a fat plane or sharp borders or differing T2 signal intensity or enhancement qualities indicated noninvasion or possibly only anatomic contiguity without invasion. Nodal category assessment was not performed.

Surgical Guidelines

Surgical resections were performed by one of five colorectal specialty surgeons, and primary resections were performed according to the principles of total mesorectal excision, which could include anterior resections, abdominoperineal resections, or exenterations. For recurrent disease, local limited and exenterative resections were performed. Patients who underwent transanal excision or transanal endoscopic microsurgery were excluded. Surgeons ordered pelvic MRI variably (with increased use as published staging accuracy data became available) and used the MRI interpretations as a general guideline after discussions in multidisciplinary conferences, to plan the extent of resection, or to determine

unresectability. Findings at surgery ultimately dictated the necessary extent of the resection, even if these findings differed from the radiologic interpretation. Surgeons were not blinded to the MRI results. Laparoscopic and robotic resections were allowed.

Pathologic Definitions

A board-certified pathologist specializing in gastrointestinal oncologic pathology who was a regular participant in the colorectal multidisciplinary conferences assisted the radiology fellow in recording a datasheet on the basis of the complete pathologic report from the electronic medical record. From the same organ and structure list, for each site the following were recorded: whether the organ or structure was present in the specimen and whether there was gross (macroscopic) involvement of this organ or structure by the tumor. Subsequently, by microscopy, four degrees of involvement or invasion were possible: no invasion, microscopic involvement by acellular mucin only, microscopic evidence of fibrous reaction, and microscopic tumor invasion. The following information pertains to pathologic standards and definitions at our institution: If a recognizable organ or structure (such as the urinary bladder or bone) is included in a pelvic resection, it is always sectioned and analyzed histologically. Soft tissue and muscle attached to the specimen are always examined grossly and representative sections are examined histologically. If fibrous reaction is found in an organ and there was prior treatment, this is considered to be possible evidence of completely regressed tumor; if there was no prior treatment, then it is considered to be non-specific. In this study, for the purposes of consistency, fibrous invasion, whether with or without prior treatment, was considered invasion. The levator ani and other muscles were not specifically named in the pathology reports but if “skeletal muscle [was] involved,” it was considered a match when the radiologist rated a named muscle as 2, 3, or 4.

Reference Standard

Histopathology was the reference standard using a binomial collapse of the 5-point rating scale of the radiologist for organ involvement (0 and 1, not invaded; 2, 3, and 4, invaded) and comparing the rating with pathology using the schema in Table 1.

Biostatistics

Measurement accuracy and detectability of T3 and T4 disease using MRI were analyzed at the patient level as well as at the site level. If any site was invaded, the patient was deemed to have T4 disease. Measures of accuracy for determination of T3 and T4 disease were estimated at the cutoff point between 1 (probably not invaded) and 2 (possibly invaded) for each reader, including sensitivity, specificity, positive predictive value, and negative predictive value, along with the 95% CI. The variance of measures of accuracy at the patient level was estimated using the method by Zhou et al. [6] for clustered data. Empirical ROC curve and the AUC were estimated for organ involvement or invasion reading on MRI with gadolinium and without gadolinium for each reader. The AUCs with gadolinium and without gadolinium at the patient level were compared using the method proposed by DeLong et al. [7] to take into account multiple sites per patient. Because treatment groups were heterogeneous, which could potentially confound readings (e.g., due to fibrosis from radiation), AUC estimates were also performed and compared among different treatment groups (none, chemotherapy only, chemoradiotherapy).

Interreader agreement on organ involvement between pairs of readers was assessed using weighted kappa with quadratic weights at the patient level and at the site level. Kappa values were interpreted as follows: 0.00–0.20, slight agreement; 0.21–0.40, fair agreement; 0.41–0.60, moderate agreement; 0.61–0.80, substantial agreement; and 0.81–1.00, almost perfect agreement. We compared the kappa values with gadolinium and without gadolinium at the patient level using the weighted least-squares approach proposed by Barnhart and Williamson [8] for correlated data. Statistical analyses were performed in software packages SAS 9.2 (SAS Institute) and R, version 2.13 (R Foundation for Statistical Computing).

Results

Patients and Demographics

There were 72 patients (38 men and 34 women; median age, 61 years; range, 32–86 years) with locally advanced primary rectal cancer ($n = 44$) and locally advanced recurrent rectal cancer ($n = 28$). As rated by reader 1, the scans were of excellent ($n = 17$), good ($n = 53$), or poor quality ($n = 2$). The median time between MRI and surgery was 25 days (range, 2–70 days), and the interquartile range was 17–42 days. Tumor depth of invasion at pathology was T4 ($n = 15$), T3 ($n = 44$), and T2 ($n = 13$). Most patients underwent preoperative therapy ($n = 41$), including chemotherapy ($n = 14$) or chemoradiotherapy ($n = 27$). All therapy occurred before the index MRI. Thirty-one patients, mainly those with recurrent disease, did not undergo further treatment because treatment options had been exhausted during remote tumor treatment.

Surgical Procedures

Surgical procedures were all radical and consisted of low anterior resection or anterior resection ($n = 34$), abdominoperineal resection ($n = 37$), and sacrectomy ($n = 1$).

Surgical Findings

Among 72 patients, 16 patients had 123 organs removed either due to surgical assessment of involvement ($n = 54$), to obtain an adequate margin ($n = 64$), or due to adherence with the tumor ($n = 5$) (Table 2).

Histopathology

Among 123 sites or organs received at pathology, true tumor cellular invasion was found in 25, fibrous invasions in three, acellular mucinous invasion in four, and no invasion in 91 (Table 2). Histopathology was used as the reference standard (Fig. 1).

Global T4 Assessment

Table 3 and Figure 1 show global T4 assessment. All three readers performed similarly when examining the area under the ROC curve in their overall assessment of T4 invasion of surrounding structures without gadolinium administration (reader 1, 0.79; reader 2, 0.91; and reader 3, 0.83). There was no statistically significant difference between each reader's AUC for global T4 determination with the addition of gadolinium (reader 1, 0.77; reader 2, 0.86; and reader 3, 0.78).

AUC values were slightly higher in the subgroup of patients with locally advanced primary rectal cancer compared with locally advanced recurrent rectal cancer, but this difference was not significant. For a given reader, the AUC without gadolinium administration and with gadolinium administration for locally advanced primary rectal cancer and locally advanced recurrent rectal cancer were as follows: reader 1, 0.87, 0.82 and 0.69, 0.70; reader 2, 0.93, 0.91, and 0.87, 0.81 and, reader 3, 0.85, 0.81 and 0.83, 0.74. AUC values for all readers with and without gadolinium administration among groups with no treatment, chemotherapy, and chemoradiotherapy treatment showed no significant differences.

Site-specific T4 assessment—Table 4 and Figures 2–4 show site-specific T4 assessment.

Histopathology reference standard—Thirty-two organs or sites were invaded including 10 vaginas, six prostates, four sidewalls, four sphincters, two in uterus or cervix, two bladders, two seminal vesicles, one ureter, and one sacrum (Table 4). Site-specific ROC analyses were not performed using histopathology as a reference standard because of the small number of cases involved at each site.

Interrater agreement—Interobserver agreement values were calculated between individual observers (weighted quadratic kappa) and indicated a similar range of agreement between readers whether gadolinium was or was not used. Without contrast administration, for readers 1 and 2, 1 and 3, and 2 and 3, the kappa values were 0.69, 0.51, and 0.63, respectively. With contrast administration, for readers 1 and 2, 1 and 3, and 2 and 3, the kappa values were 0.67, 0.63, and 0.70, respectively (*p*, not significant for all pairs). No consistent pattern of increase or decrease in agreement was seen using gadolinium.

Reader overall T category staging—Overall, reader 1 overstaged 23 and 21 cases and understaged three and three cases without and with gadolinium administration, respectively; reader 2 overstaged 16 and 16 cases and understaged seven and eight cases without and with gadolinium administration, respectively; and reader 3 overstaged 23 and 24 cases and understaged 11 and 10 cases without and with gadolinium administration, respectively.

Discussion

In this retrospective study of patients with locally advanced and recurrent rectal carcinoma imaged at our cancer center by MRI including gadolinium administration as the standard of care, three radiologists with different levels of experience did not improve their accuracy or their interobserver agreement for the diagnosis of surrounding organ or structure involvement (T4) using gadolinium sequences combined with T2-weighted sequences when compared with T2-weighted sequences alone. AUCs for overall T4 disease assessment among all three readers ranged from 0.79 to 0.91 without gadolinium administration and from 0.77 to 0.86 with gadolinium administration. Overall, among the various reader pairs examined with the kappa method, interobserver agreement ranged from 0.51 to 0.69 without gadolinium administration and from 0.63 to 0.70 with gadolinium administration, revealing no significant difference. At a site-specific level, there were no anatomic sites in which gadolinium improved accuracy. In spite of our experience that led us to a subjective

impression that gadolinium helped us more accurately assess the invasion of surrounding structures, our data indicate that no such improvement occurs even for an inexperienced junior observer. Because we did not compare T1-weighted gadolinium-enhanced images alone against T2-weighted images, but rather the combination versus T2-weighted images alone, a reasonably sensible interpretation is that the intrinsic contrast already achieved with the T2-weighted sequences is adequate and optimal for differentiation between tumors and normal structures or fibrosis and that it is hard to improve on this method. Adding contrast-enhanced imaging may have added another layer of complexity to the interpretation of the findings and has been reported to lead to false-negative interpretations of tumor, which may be poorly vascularized, and to false-positive interpretations of fibrosis, which may be well vascularized [3, 4]. This could be especially true in patients who have received chemoradiotherapy, which can induce cell death and devascularization as well as fibrosis. Interestingly, with respect to the possible confounding effects on interpretation due to postradiotherapy fibrosis, our analysis of AUC for all readers, both with or without gadolinium administration, between different treatment groups consisting of chemotherapy only, chemoradiotherapy, or no treatment, revealed no differences. With respect to reader experience and performance, it is interesting to note that the radiologist with the greatest overall experience in reading pelvic MRI, though not the same radiologist responsible for reading all rectal MRI had the best overall accuracy. When considering the number of cases that were over- and understaged, more cases were understaged by this reader than the dedicated rectal MRI reader, likely explaining the difference in accuracy. We speculate that the dedicated rectal MRI reader has probably adjusted his interpretations to err on the side of overstaging so as not to deny patients adequate treatment, whether neoadjuvant chemoradiotherapy or surgical extirpation. This practice is common and generally thought to be the safer approach given the morbidity of incomplete tumor resection and of recurrent disease.

Our findings are in line with those of prior studies indicating no advantage of gadolinium for determining T category, including cases with surrounding organ invasion (T4). Okizuka et al. [4] tested the accuracy of fat-suppressed T1-weighted gadolinium sequences to improve accuracy over T2-weighted imaging in a prospective study of 32 patients. Their study was limited to one patient with T4 disease. Additionally, all patients underwent biopsy 7–10 days before MRI, which could complicate the findings. Those authors saw two advantages of interest in their study: Tumor conspicuity increased with gadolinium, and the fat suppression performed as part of the T1-weighted sequence with gadolinium overcame the motion artifact associated with T2-weighted sequences in which unsuppressed fat caused phase ghosting [4]. Vliegen et al. [2] tested the ability of T1-weighted gadolinium-enhanced sequences to improve accuracy over T2-weighted sequences for T categorization and for determining invasion of the mesorectal fascia and found no improvement among two radiologists, one with 5 and one with 10 years of experience in interpreting such studies. Unfortunately, no details on the number of T4 cases were provided. Furthermore, some MRI studies were performed before radiotherapy and the reader strategy included only a 1-week separation between sessions, possibly leading to recall bias [2]. In contrast to both of these studies, we believe that the organ-by-organ analysis in our investigation and the greater number of T4 lesions conferred greater strength to our study. In a study by Jao et al. [3],

designed similarly to our study, more T4 lesions were tested ($n = 10$) but no site-by-site analysis was published. Nonetheless, two radiologists achieved AUC with and without contrast administration of 0.84 and 0.87 and 0.80 and 0.79, respectively, results that are similar to ours. Other studies investigating the added value of gadolinium were more focused on early-stage tumors [5, 9, 10], rectal filling, or the ability to differentiate tumor from fibrosis in the setting of potentially recurrent disease.

We also performed a detailed analysis of radiologists' performances on a site-by-site basis with and without gadolinium administration in light of the need to include subspecialty surgeons in complex radical resections. Quite frequently in our disease management team meetings, questions arise regarding our level of confidence of invasion of particular structures. We had hoped that gadolinium might improve on the poor muscle invasion accuracy in the pelvis by enhancing the tumor greater than the normal muscle (pelvic sidewall or sphincter apparatus), but this was not borne out in our data. Comparison with the study by Dresen et al. [11], who investigated tumor invasion of pelvic structures with four readers using T2-weighted sequences in 40 patients, is somewhat limited because the authors grouped organs together. Furthermore, 28 pretreatment MRI cases were combined with 40 posttreatment MRI cases, which might have improved overall assessment secondary to a lack of treatment-induced fibrosis compared with our strategy. The most experienced reader in that study had experience far exceeding anyone in our group, and the inter-slice gap used was 0.3 mm or 10%, whereas ours was 1 mm or 33% of our slice thickness. However, accuracy for pelvic sidewall assessment was lower than for other sites, but overall AUCs were higher than our results. The authors indicate that assessment failures were mainly because of misinterpretation of diffuse fibrosis [11].

The clinical implications of our data would seem to indicate that we can forego the use of gadolinium when performing MRI of locally advanced or recurrent rectal cancer. Is there any role for gadolinium in rectal cancer evaluation? As we and others have noted [4], in some clinical settings, the tumor conspicuity is greater using gadolinium than in using T2-weighted sequences. Despite the known limitations of posttreatment MRI for evaluation of response of the primary rectal tumor to chemoradiation [12], it is routinely performed, but tumor shrinkage can be so significant that the tumor becomes hard to recognize. This is especially true in a partially or fully collapsed rectum. Given the lack of routine rectal distention during scanning and the recent European guidelines indicating that this is not necessary [13], we have informally observed that these small residual tumor foci can be made more conspicuous once IV contrast material has been administered. Whether this indication justifies the use of an expensive and potentially harmful intervention would require formal investigation. Another potential indication for gadolinium, requiring the burden of proof, may be as a quantitative functional assessment of treatment response. Although there are some promising early results investigating dynamic contrast-enhanced MRI for rectal cancer [14, 15], the use of gadolinium as such remains as a research tool and awaits validation.

There are limitations to our study other than its retrospective nature. Gadolinium-enhanced imaging performed by others is usually timed at between 1 and 3 minutes after injection, sometimes capturing multiple time points, as is done in dynamic liver studies, but because of

our intervening perfusion sequence, our static images were obtained at about 6–7 minutes. This limits comparison with other studies because the tumor will have further washed out in our cases at this later time point. Unlike other authors, we did not explicitly predefine tumor invasion but rather allowed each reader to use the general principles of imaging to guide the interpretation. The cutpoint we used lay between probably not involved and possibly involved, which sets the bar on the low side for radiologist performance. In spite of these limitations, we believe that our methodology was robust using three readers of different training, using a 4-week separation interval between datasets, and presenting and correlating highly specific invasion definitions as clinically used in pathology.

In summary, three radiologists of varying levels of experience when comparing post-treatment T2-weighted MR images combined with T1-weighted gadolinium-enhanced images versus T2-weighted images alone did not improve accuracy or interobserver agreement for the invasion of surrounding structures (T4) in patients with locally advanced or recurrent rectal cancer. Our data, in agreement with prior more-limited studies, imply therefore that gadolinium administration is not necessary for the purpose of determining T4 invasion in rectal cancer. Other indications for the use of gadolinium in the evaluation of rectal cancer are not proven at this time and require further investigation and validation.

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Fig. 1.

Graph shows ROC analysis for global T4 determination by three readers with histopathology as reference standard.

Fig. 2. 62-year-old man with rectal cancer who underwent radiotherapy and chemotherapy. Pathology showed involvement of prostate by acellular mucin only

A, Axial fast spin-echo T2-weighted pelvic MR image shows tumor nodule near left peripheral zone (*arrow*). Readers rated as 2, 3, and 1.

B, Axial gradient-recalled echo T1-weighted MR image after gadolinium injection shows low signal intensity rim-enhanced tumor nodules abutting posterior midline and left prostate peripheral zone (*arrow*). Readers rated as 4, 3, and 1.

Fig. 3. 48-year-old woman with rectal cancer who underwent chemoradiotherapy. Pathology showed invasion of skeletal muscle. Axial fast spin-echo T2-weighted MR image shows high-T2-signal intensity mucinous tumor invading right levator ani muscles (*arrows*). Reader ratings were 4, 4, and 4.

Fig. 4. 62-year-old woman who underwent neoadjuvant chemoradiation and low anterior resection 2 years ago. Patient presented with recurrent rectal cancer and is being considered for pelvic exenteration. Sacral biopsy was negative for tumor. Vaginal specimen was positive for gross and microscopic tumor

A, Sagittal fast spin-echo T2-weighted MR image of pelvis shows mass in posterior pelvis with thickening of upper posterior vaginal wall (*arrow*). Reader ratings for involvement were 1, 4, and 4.

B, Axial gradient recalled-echo T1-weighted MR image after gadolinium administration show contrast-enhanced mass obliterates normal vaginal outline superiorly (*arrow*). Reader ratings for involvement were 4, 4, and 2.

TABLE 1

Matching Schema and Definitions Using Pathology as Reference Standard

Radiology	Pathology	Definition of Radiologic Interpretation
2, 3, 4	Microscopic tumor invasion	True positive
	Microscopic evidence of fibrous reaction	True positive ^a
	Acellular mucin	True positive
	None	False positive
0, 1	Microscopic tumor invasion	False negative
	Microscopic evidence of fibrous reaction	False negative ^a
	Acellular mucin	False negative
	None	True negative

Note—Radiology scale: 0 = not invaded, 1 = probably not invaded, 2 = possibly invaded, 3 = probably invaded, 4 = definitely invaded.

^aMicroscopic evidence of fibrous reaction is considered evidence of tumor invasion if there has ever been treatment and of unclear meaning if there has never been treatment. We chose not to distinguish on a per-case basis but rather to empirically consider this to be invasion.

TABLE 2

Surgical Removal and Histopathologic Involvement by Individual Site

Organ Removed	Total	Histopathology			
		Tumor Invasion	Fibrous Invasion	Mucin Invasion	No Invasion
Bladder	5	2	0	0	3
Sidewall	41	4	0	0	37
Sacrum	1	1	0	0	0
External anal sphincter–internal anal sphincter	37	2	0	2	33
Ureter	3	0	1	0	2
Prostate	11	5	0	1	5
Seminal vesicle	11	2	0	0	9
Uterus-cervix	2	2	0	0	0
Vagina	12	7	2	1	2
Total	123	25	3	4	91

TABLE 3
Measures of Accuracy of Invasion at Any Site on MRI Using Histopathologic Reference (Global T4 Assessment)

Total (<i>n</i> = 72)	Cutoff Point	Sensitivity	Specificity	PPV	NPV	AUC	<i>p</i> (Comparing AUC)
Reader 1 Without contrast administration	> 1	0.90 (0.68–0.98)	0.59 (0.45–0.73)	0.46 (0.30–0.63)	0.94 (0.80–0.99)	0.79 (0.68–0.90)	0.766
	> 1	0.80 (0.56–0.94)	0.57 (0.43–0.71)	0.42 (0.26–0.59)	0.88 (0.72–0.97)	0.77 (0.65–0.90)	
Reader 2 Without contrast administration	> 1	0.95 (0.75–0.99)	0.71 (0.57–0.83)	0.56 (0.38–0.73)	0.97 (0.86–0.99)	0.90 (0.82–0.99)	0.08
	> 1	0.85 (0.62–0.96)	0.75 (0.61–0.86)	0.57 (0.37–0.75)	0.93 (0.81–0.99)	0.86 (0.76–0.96)	
Reader 3 Without contrast administration	> 1	0.70 (0.46–0.88)	0.69 (0.55–0.81)	0.47 (0.28–0.66)	0.86 (0.71–0.95)	0.83 (0.73–0.94)	0.65
	> 1	0.70 (0.46–0.88)	0.78 (0.65–0.89)	0.56 (0.35–0.76)	0.87 (0.74–0.95)	0.78 (0.66–0.90)	

Note—Data in parentheses are 95% CI. PPV = positive predictive value, NPV = negative predictive value.

Site-Specific Performance per Reader With and Without Gadolinium Administration With Cutoff Point Less Than 1 ($n = 80$)

TABLE 4

Performance	Gadolinium Administration							
	Sensitivity		Specificity		PPV		NPV	
	Without	With	Without	With	Without	With	Without	With
Reader 1								
Bladder	0.50	0.50	0.97	0.97	0.033	0.33	0.99	0.99
Pelvic sidewall	0.50	0.50	0.88	0.88	0.20	0.20	0.97	0.97
External anal sphincter–internal anal sphincter	0.50	0.25	0.94	0.89	0.33	0.125	0.97	0.95
Prostate	0.83	0.67	0.88	0.90	0.56	0.57	0.97	0.93
Seminal vesicles	0.50	1.00	0.67	0.69	0.08	0.15	0.96	1.00
Vagina	0.50	0.70	0.87	0.88	0.63	0.70	0.80	0.88
T category	0.98	0.97	0.25	0.33	0.87	0.88	0.75	0.67
Reader 2								
Bladder	0.50	0.0.50	0.97	0.96	0.33	0.25	0.99	0.99
Pelvic sidewall	0.50	0.50	0.96	0.94	0.40	0.33	0.97	0.97
External anal sphincter–internal anal sphincter	0.50	0.50	0.83	0.88	0.15	0.20	0.97	0.97
Prostate	0.83	1.00	0.94	0.90	0.71	0.67	0.97	1.00
Seminal vesicles	0.50	0.50	0.78	0.77	0.11	0.011	0.97	0.96
Vagina	0.80	0.90	0.87	0.92	0.73	0.82	0.91	0.96
T category	0.92	0.93	0.33	0.50	0.87	0.90	0.44	0.60
Reader 3								
Bladder	0.50	0.00	0.96	0.97	0.28	0.00	0.99	0.97
Pelvic sidewall	0.25	0.50	0.94	0.91	0.20	0.25	0.96	0.97
External anal sphincter–internal anal sphincter	0.50	0.50	0.93	0.94	0.50	0.70	0.97	0.97
Prostate	0.40	0.40	0.94	0.97	0.50	0.67	0.91	0.91
Seminal vesicles	0.00	0.00	0.83	0.77	0.00	0.00	0.97	0.96
Vagina	0.60	0.40	0.87	0.96	0.67	0.80	0.83	0.78
T category	0.85	0.92	0.25	0.42	0.85	0.88	0.25	0.50

Note—PPV = positive predictive value, NPV = negative predictive value.