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Gadolinium-Based Contrast Agent During Pelvic MRI: Contribution to Patient Management in Rectal Cancer

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Abstract

BACKGROUND—Few publications exist regarding Gadolinium-enhanced sequences in rectal MRI. None have evaluated its potential impact on patient management.

OBJECTIVE—This study aimed to assess if Gadolinium enhanced sequences, including dynamic contrast enhancement, change radiologic interpretation and clinical management of rectal cancer.

DESIGN—This is a retrospective analysis of 100 rectal MRIs (50 baseline and 50 post-neoadjuvant treatment), both without and with Gadolinium enhanced sequences. Treatment plans were rendered based on each radiologic interpretation for each case by a single experienced surgeon. Differences in radiologic interpretation and management were statistically analyzed.

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SETTING—Memorial Sloan Kettering Cancer Center

PATIENTS—Cases undergoing rectal MRI from 2011 to 2015 for baseline tumor staging and/or post-neoadjuvant re-staging.

MAIN OUTCOME MEASURES—Primary outcome measures were changes in radiologic tumor stage, tumor margins, and surgical planning with the use of Gadolinium at baseline and post-neoadjuvant time points.

RESULTS—At baseline, tumor downstaging occurred in 8/50 (16%) and upstaging in 4/50 (8%) with Gadolinium. Post-neoadjuvant treatment, upstaging occurred in 1/50 (2%) from T2 to T3a. At baseline, mean distances from tumor to anorectal ring, anal verge and mesorectal fascia were not statistically different with Gadolinium. However, in 7 cases, differences could have resulted in treatment changes, accounted for by changes in relationships to anterior peritoneal reflection (n=4), anorectal ring (n=2) or anal verge (n=1). Post-neoadjuvant treatment, distances to anorectal ring and anal verge (cm) were statistically smaller with Gadolinium (p=0.0017, p=0.0151), but could not have resulted in clinically significant treatment changes.

LIMITATIONS—Retrospective design

CONCLUSIONS—Use of Gadolinium at baseline MRI could have altered treatment in 24% of patients due to differences in tumor stage or position. Post-neoadjuvant treatment, Gadolinium resulted in statistically smaller distances to sphincters, which could influence surgical decision for sphincter preserving rectal resection.

See **Video Abstract** at <http://links.lww.com/DCR/AXXX>.

Keywords

Colorectal surgery; Gadolinium; MRI; Rectal cancer

Introduction

Gadolinium based contrast agents (hereafter “GAD”) are frequently used during pelvic MRI for malignant tumors due to their ability to improve visualization and conspicuity of tumors based on leaky neovascularization. To complicate matters, GAD may enhance normal tissue due to changes induced by chemoradiotherapy.^{1–3} Several publications have shown no clear advantage of GAD in T-staging MRI examinations for rectal cancer^{4–7} and recent ESGAR guidelines do not recommend its use. However, GAD is still used routinely at many institutions in both baseline and post-neoadjuvant settings.

Most prior publications on the use of GAD in rectal MRI have evaluated changes in diagnostic staging accuracy. In a study of 83 patients with rectal cancer, utilization of GAD did not yield improved accuracy over T2 weighted images in detecting tumor penetration through the rectal wall or tumor extension into mesorectal fascia.⁴ In a study of pre-operative assessments of 88 rectal cancer patients, comparison of A_z values in ROC analysis of T2 only, T1+GAD only, and combined T2 and T1+GAD for 2 readers, no significant differences in diagnostic accuracy were observed for tumor or nodal staging.⁵ In another retrospective study of 72 patients with advanced rectal cancer, utilization of combined T2

and T1+ GAD weighted sequences versus T2 alone yielded no advantage in interobserver agreement, accuracy in determining T-category or involvement of surrounding organs.⁸ Some centers also perform dynamic contrast enhanced (DCE) sequences. Evidence for the utility of DCE is conflicting, with some authors' suggesting a role in predicting complete pathological response.^{9–11}

To our knowledge, no studies have evaluated the contribution of GAD at baseline or after neoadjuvant treatment (either static or DCE sequences) to changes in radiologic T-staging, measurement of specific tumor margins, and more importantly its potential impact on management of patients with rectal cancer. Clarification of the influence of GAD during MRI could impact medical and surgical management particularly in view of the increased utilization of MRI in lieu of endorectal ultrasound. Furthermore, its use incurs added magnet time and cost per patient, and occasional morbidity, including allergy, nephrogenic systemic fibrosis, and GAD accumulation in the brain.^{12–15} The purpose of this study is to assess: (1) if GAD use (especially using DCE-MRI) changes radiologic T-stage or tumor relationship to surrounding structures at baseline and/or post-neoadjuvant treatment MRI for primary rectal cancer; and (2) whether use of GAD could alter the overall treatment plan at baseline and/or the surgical approach recommended post-neoadjuvant chemoradiotherapy.

Materials and Methods

Demographics

Approval was obtained from the MSKCC Institutional Review Board for retrospective analysis of collected data in this study. All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2000 (5). For this type of study formal consent is not required.

A retrospective search of the institutional database identified the 100 most recent consecutive rectal MRIs, from December 2011 to January 2015. Inclusion criteria were: patients with histologically proven rectal adenocarcinoma who underwent pre-treatment (baseline) MRI and/or post total neoadjuvant treatment MRI. Total neoadjuvant treatment was defined as completion of induction chemotherapy followed by chemoradiotherapy (n=40), chemoradiotherapy alone (n=7), or chemotherapy alone (n=3). Exclusion criteria were: patients operated on by the surgical co-author, metastatic disease at time of diagnosis, poor quality MRI, and lack of DCE sequences.

The final cohort included 66 patients (mean age 59.0, range 29.2–84.9 years). Thirty-four had both baseline (BL) (mean age 55.5, range 29.2–81.1 years) and post treatment scans (PNT) (mean age 56.5, 29.5–84.9 years) scans. Sixteen patients had only BL scans and an additional 16 had only PNT scans. In total, 50 studies of BL staging MRI and 50 of PNT re-staging MRI were examined.

MRI Protocols

MRI examinations were performed on different MRI scanners manufactured by GE Healthcare (Waukesha, WI, USA) at a field strength of 1.5 Tesla or 3 Tesla using a

standardized MRI protocol that included standard high-resolution T2-weighted imaging in axial, sagittal, coronal and oblique orientation (TR: 4400–5000; TE: 90–110; echo train length: 12–24; slice thickness: 3–4 mm; interslice gap: 1 mm; FOV: 20 cm; matrix: 320 × 160; NEX: 2), an axial DW sequence (single-shot spin-echo EPI sequence, b-values: 0 and 750–1,000 s/mm²; TR: 1,800–5,550ms; TE: 60–112ms; slice thickness: 3–5 mm; interslice gap: 1 mm; FOV: 18–40 cm; matrix: 96–256 × 96–128; NEX: 3–6; mean acquisition time: 2.4 min) and sagittal DCE-MRI sequence (TR: 3.1–7.9 ms; TE: 0.9–4.2 ms; slice thickness: 4–10 mm; no interslice gap; FOV: 20–34 cm; matrix: 256–320 × 128–192; mean temporal resolution: 8.3 (5–11.5) s; 30–40 phases; mean acquisition time: 5.2 min). A bolus of Gd-DTPA (Magnevist, Bayer Schering, Berlin-Wedding, Germany) at a constant dose of 0.1 mmol/kg was power injected at a rate of 2 ml/s followed by a saline flush for all patients. After the DCE sagittal sequence, a standard axial post-Gd-DTPA spoiled 3D gradient echo sequence was obtained (Liver acquisition with volume acceleration [LAVA]); breath-hold; TR: default; TE: in phase; slice thickness: 3mm; no gap; FOV: 28–36 cm; 320 × 192; NEX: 1.

Radiologic Interpretation

Two board certified radiologists retrospectively interpreted MRI blinded to details of clinical history for each case. Observer 1 was an academic senior radiologist subspecializing in gastrointestinal oncologic radiology. Observer 2 was a junior radiologist with fellowship training in oncologic radiology. Observer 1 interpreted BL cases only and observer 2 interpreted PNT only. For BL and PNT readings, MRI cases were interpreted twice; first using the T2-weighted sequence alone (GAD–) and subsequently interpreted up to 48 hours later with T1-weighted GAD (GAD+) sequences (combined spoiled gradient echo [“static”] + DCE). For each study, the radiologist recorded T-stage, distance from the inferior tumor border to the anal verge (AV), distance from the inferior tumor border to sphincter apparatus/anorectal ring (ARR), and distance to mesorectal fascia (circumferential resection margin). The relationship to the anterior peritoneal reflection (above, below, straddles), sphincter involvement, and tumor size (craniocaudal length and thickest wall) were also recorded at BL.

Clinical/Surgical Interpretation

Radiologic interpretations were systematically and anonymously presented to the single experienced surgeon who did not operate on any case in 4 sessions, separated by 4 weeks or more, along with a clinical history proforma for clinical management assessment. The surgeon was blinded to whether radiologic interpretations provided were GAD– or GAD+.

The proforma contained chief complaint, history of present illness, physical exam, digital rectal exam, labs, medications, Eastern Cooperative Oncology Group performance score,¹⁶ colonoscopy and images, biopsy, endorectal ultrasound, and results of other imaging studies. Clinical proformas for PNT cases revealed the actual treatment and clinical course up to the time of PNT MRI.

For BL MRI interpretations, the surgeon selected a theoretical initial treatment plan: direct to surgery, preoperative treatment (induction/chemoradiation therapy), palliative treatment or

non-operative management. For PNT MRI interpretations, the surgeon selected a theoretical PNT surgical plan: no surgery (non-operative management or inoperable), transanal excision (TAE), total mesorectal excision (TME), low anterior resection (LAR), abdominoperineal resection (APR), intersphincteric resection (ISR), exenteration, or other.

Definitions and Criteria

Radiologic T-stage was reported according to the 7th edition American Joint Committee on Cancer system. Current surgical recommendations at our institution for T1/T2 tumors are to proceed directly to surgery with either TAE or TME, unless there are suspicious lymph nodes, or tumor is adjacent to the sphincter apparatus. For T3 and T4 tumors, patients are recommended for long course chemoradiotherapy often with induction chemotherapy followed by surgery.¹⁷ Clinical complete response was defined as having no residual tumor present on PNT imaging and no mass on digital rectal exam and/or endoscopy.

Statistics

Differences in GAD– and GAD+ radiologic interpretations were analyzed using the Student's Paired T-test, 2-tailed, for all continuous variables. Descriptive statistics and frequency distribution were conducted for T-stage. Differences in treatment plans rendered based on GAD– versus GAD+ were reported using descriptive statistics. Statistics were conducted using Graph Pad Prism 7 and IBM SPSS Software. A p-value of 0.05 was selected to determine significance with confidence interval of 95%.

Results

Clinical and Pathologic Tumor Stage

For the 100 cases (50 BL and 50 PNT), the distribution of clinical Tumor and Node stage (cTN), post-treatment pathologic Tumor and Node stages (ypTN), and actual treatment received is detailed in Table 1.

MRI Reading

BL—Results of tumor stage are reported in Figure 1. Table 2 details the changes using GAD + for tumor height, size, and distance to mesorectal fascia. At BL, differences in distances to AV, ARR and MRF, as well as wall thickness and tumor size were not statistically significant (Table 2).

PNT—Results of PNT tumor stage are reported in Figure 1. T-stage changes occurred in 2% (1/50) with use of GAD+, with upstaging from T1/2 to T3a. Statistically significant differences were found in measurements of distance to the anal verge ($p=0.0017$) and to the anorectal ring ($p=0.0151$) with GAD+, depicted in Table 3.

For PNT cases, a comparison to the gold standard pathologic stage was conducted. Pathologic stage data was unavailable for 12/50 (24%) cases, which underwent non-operative management. Eight of these 12 were clinical complete responses, 2 refused surgery and 2 did not undergo surgery due to extensive disease or significant cardiac comorbidity. For 29/38 cases (76%), both GAD– and GAD+ accurately assessed T-stage.

For 5/38 cases (13%), both GAD– and GAD+ overstaged tumors and for 3/38 (8%), both understaged tumors. For one case of 38, GAD– accurately assessed a T1/2 tumor while GAD+ overstaged it as T3.

Changes in Treatment Planning

BL—At baseline, 12 total T-stage changes occurred with GAD. However, changes in baseline treatment planning only occurred for 4 of these 12 changes, 3 T-upstages and 1 T-downstage (Table 4). Because of upstaging from T1/2 (with no nodes) to T3a (n=2) or T3b (n=1), these patients were recommended for chemoradiotherapy (CRT), per our reviewing surgeon and our institutional treatment standards. Because 1 case downstaged from T3b to T1/2 (with no nodes), the patient was recommended for surgery directly rather than preoperative CRT. Figure 2 depicts 2 cases in which changes in radiologic T-stage and corresponding changes in treatment plans were rendered with GAD.

Using quantitative analysis instead of numerical means, which did not differ statistically with GAD, in 7 cases, the differences were clinically significant enough to warrant a change in treatment (Table 4). Relationships to the anterior peritoneal reflection (n=4), anorectal ring (n=2) or anal verge (n=1) accounted for treatment changes. In 3 cases of stage T1/2 rectal cancer not requiring CRT, radiation for tumor shrinkage was no longer warranted with use of GAD, since the tumor was measured as farther from the sphincters, thus not requiring downstaging for sphincter preservation. In one case the tumor was interpreted as above the anterior peritoneal reflection; also a relative contraindication for radiation. In the remaining 3 cases, the tumor changed from above to below the anterior peritoneal reflection, thus instead of a direct-to-surgery plan, CRT was recommended. Figure 3 depicts a baseline case that demonstrates improved delineation of the anterior peritoneal reflection with GAD.

PNT—Changes in PNT readings occurred in 2% (1/50) with use of GAD, with upstaging from T2 to T3a. Since this patient had already received treatment and did not have a major stage change, there was no resultant change in treatment.

Although statistically different measurements of distance from the inferior tumor border to AV (p=0.0017) and to ARR (p=0.0151) were observed with GAD, no clinically significant changes were noted that altered treatment as recommended by our reviewing surgeon, since patients already qualified for neoadjuvant treatment. GAD did not result in clinically significant alterations in tumor location with respect to the anterior peritoneal reflection, ARR or AV to warrant a change in surgical approach.

Overall, discordant treatment assessments were made in 11 patients, all at baseline; 4 due to changes in radiologic T-stage with GAD and 7 due to tumor height in the rectum.

Discussion and Conclusion

In this retrospective study of rectal cancer patients imaged by MRI with GAD per our institutional standard of care, and interpreted blindly with and without GAD sequences, the use of GAD in baseline MR altered T-staging in 24% of cases. These changes would not have altered treatment in the majority of these cases due to the nodal status. Of greater

impact, was the change in location of tumor using GAD, wherein treatment in 7 cases would still have changed. At PNT, only 1 T-stage change occurred with GAD, and this would not have affected treatment. Even though significant differences were noted in average distances to the AV and ARR using GAD, no individual case resulted in a change in treatment, and thus, GAD had no potential effect on patient management in the PNT setting.

While the clinical consequence of stage T2 vs T3a with a clear CRM alone might not necessarily indicate a change in treatment based on current guidelines, neoadjuvant CRT can be administered for locally advanced cancer (cT3 or T4) in order to increase the probability of sphincter preserving resections, which is recommended at our institution, as compared to patients with T2 tumors who are recommended for direct surgery. It is also important to consider that additional factors in conjunction with stage could also contribute to the decision for CRT versus direct surgical intervention, such as nodal status and tumor location/proximity to sphincters, as well as CRM involvement.

Since T-stage changes using GAD at baseline showed no consistent pattern, little could be concluded in our small study. Nonetheless, more cases were downstaged than upstaged after GAD. We believe this is because tumors perfuse and de-enhance with GAD earlier than normal tissue. The de-enhanced tumor allowed better definition of its borders as low signal intensity not extending beyond the rectal wall (T2); whereas without GAD, nonspecific spiculations penetrating the wall and extending into mesorectal fat (potential T3) could have either represented tumor or reactive changes. The lack of a gold-standard limits our ability to prove this theory, but we know from the literature that radiologists tend to overstage tumor up to 43% of the time.¹⁸ Treatment changes that would have occurred for the above downstaged cases consisted mainly of conversion from the need for neoadjuvant treatment to the lack thereof, appropriate to the new T-stage.

Using a similar explanation for tumor relationships to anterior peritoneal reflection, ARR, and AV, although no statistical difference was shown with the use of GAD, in 7 individual cases, by virtue of the enhancement/de-enhancement phenomenon, an apparent change in relationship with these structures would have resulted in treatment changes in which greater distances of tumor from the AV or ARR would have allowed avoidance of preoperative CRT, used to downsize tumor and retract it from the internal anal sphincter. The critical assessment of the upper and lower tumor margins with respect to the anterior peritoneal reflection, ARR and AV, absent in prior publications, can affect treatment more significantly than would small changes in the middle rectum.

Although tumor distances to these important anatomic landmarks were statistically smaller with GAD after neoadjuvant treatment, this would not have led to a change in treatment in any patient in our PNT cohort. This may have been due to our particular mix of patients, since several millimeters difference in a tumor close to the sphincters could influence a surgeon's decision for sphincter preservation. We hypothesize that these shorter distances resulted from hyper-enhancing radiated mucosa mimicking tumor, which is known to become more permeable to flow.^{5,6} Also, in the PNT setting, there was little if any tumor left to be delineated by the "washout" de-enhanced appearance we were able to appreciate at baseline.

In concert with existing research that has demonstrated that GAD does not improve T-stage accuracy at baseline staging MRI,^{3,4} our study supports that GAD does not alter the majority of patients' T-stages, and based on T-stage alone would not often alter therapy. However, unlike published literature, we went beyond T-stage to assess other tumor features important for treatment planning. Additionally, as re-staging MRI has only recently become widespread, our study provides new data that would need further validation.

There are numerous clinical implications of this study that might spur further investigations. For example, the implication that a potentially smaller number of sphincter preserving surgeries might be conducted with the implementation of GAD in PNT rectal MRI since tumor seemed to be closer to the sphincters. Imaging is but one data point input to patient care and it is important to acknowledge that the type of surgery performed is dependent on the clinical judgment of the surgeon at the time of surgery, during which alternate methods of assessing tumor location are used (e.g., intraoperative endoscopy and digital exam). Imaging is important in determining which patients require neoadjuvant therapy and is a consideration in the decision to proceed with APR versus LAR. However, intraoperative localization of the tumor plays a larger role and remains the same, whether minimally invasive or open, as lesions are low enough to palpate with digital exam.

The limitations of this study are its retrospective nature and small sample size. Furthermore, our method of GAD use includes DCE-MRI, not widely used, and subsequent static GAD images. We also did not separately compare the effects of the static images and the DCE images on our tumor staging versus no GAD. A final limitation is the artificial assessment that our surgeon was able to conduct from only reading the clinical proforma we provided in the absence of the critically valuable, and more realistic input of a direct history and physical exam on the patient, supplemented by discussion of each patient's complexities in a multidisciplinary tumor board.

In conclusion, from our data, the effect of GAD on baseline tumor interpretation could have potentially changed treatment in 24% of patients, mostly due to differences in tumor position with respect to critical anatomic landmarks (e.g. ARR, AV, and anterior peritoneal reflection). In only a fraction of these cases would initial treatment recommendations have changed due to either unchanged N-stage or lack of other pivotal differences to warrant a different treatment approach. In the post neoadjuvant setting, GAD resulted in statistically smaller distances between the lower tumor edge and the ARR and AV, which might suggest potential for fewer sphincter-preserving operations when using GAD. However, in our particular patients, this never led to a change in treatment planning, perhaps due to the chance location and distribution of tumors in our cohort. Given the theoretical and retrospective nature of our study, we believe that further investigation into the value of GAD would have to be prospective, but is unlikely to be pursued due to the safety profile, low cost and overall acceptance of GAD. Finally, the question of GAD use may become less trivial if newly discovered toxicities, such as the recent revelation of GAD brain deposition, prove to confer long-term harm to patients.

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Figure 1. Contribution of GAD to changes in T-category

Note: Abbreviations: GAD=Gadolinium

Figure 2. Contribution of T1-W +GAD Sequences to Radiologic T-Stage Interpretation at BL
 Upper panel: Sagittal T2-weighted MRI [A] and T1-weighted MRI +GAD [B] for Case X with differences in interpretation of tumor height. The T2-W image [A] shows high signal intensity in mucosa isointense to mass (arrow) with distance to ARR measured as 0 cm. T1-W +GAD [B] distance to ARR measured 2.6 cm due to improved delineation of tumor (arrow) and resulted in change in BL treatment decision from induction CRT (GAD-) to LAR (GAD+).

Lower panel: Axial T2-W MRI [C] and T1-W +GAD [D] for Case Y. The T2-W image [C] shows tumor purely confined to wall (arrow), interpreted as T1/2. The T1-W +GAD [D]

image shows spiculations of tissue interpreted as T3 extension into fat (arrow). Difference in interpretation of tumor stage resulted in change in BL treatment plan from LAR (GAD-) to induction/CRT (GAD+). Left image.

Note: Abbreviations: BL= baseline, GAD= Gadolinium, ARR= anorectal ring, CRT= chemoradiotherapy, LAR= low anterior resection.

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Figure 3. Delineation of tumor relationship with GAD

68 year old male presenting with 3.5 month history of rectal bleeding. Colonoscopy revealed an 1.5cm ulcerated rectal lesion at 10–12 cm from the anal verge.

A: Sagittal FSE T2-weighted MRI revealing intermediate T2 signal mass-like tissue likely representing tumor-region (white arrows). Vaguely apparent thin fascial line represents anterior peritoneal reflection (APR, black arrow). Part of the tumor is above and part below the APR based on this sequence.

B: Sagittal dynamic contrast enhanced (DCE) depicting early mass-like enhancement demarcating tumor as well as diffuse mucosal enhancement. A dynamic viewing of this

data-set [approximately 30–40 images over time at this location] better reveals the mass-like early enhancement quite distinctly (not shown). Upper border of early enhancement demarcated by black arrow. Anterior peritoneal reflection (white arrow) is at level of tumor upper border. Therefore, tumor lies entirely below APR. Note the incidental increased conspicuity of APR as a result of thicker slice (slab).

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Table 1

Clinical and Pathologic Stage and Surgical Outcomes

BL Cases		PNT Cases		PNT True Surgical Outcomes		PNT Pathologic Stage	
cTN Stage	Total	cTN Stage	Total	Surgical approach	Total	pTN Stage	Total
T2N0	1	T0N0	9	LAR	24	ypT1N0	3
T2N+	5	T0Nx	2	NOM	12	ypT0	5
T3N0	6	T1N0	2	APR	9	ypT2N0	7
T3N+	31	T1Nx	1	Robotically assisted LAP w/ diverting ileostomy	2	ypT2N1	1
T3Nx	1	T1/2N0	1	TAE	1	ypT2N1a	2
T4N0	2	T2N0	5	LAP R hemicolectomy	1	ypT2	4
T4N+	3	T3N0	4	Robotically assisted LAP	1	ypT3N0	3
TxN+	1	T3N+	6	Grand Total	50	ypT3N1a	2
Grand Total	50	T3Nx	6			ypT3N1b	2
		T4N+	2			ypT3N2a	2
		T4Nx	2			ypT3N2b	1
		TxN0	3			ypT3	4
		TxN+	1			ypT4bN0	1
		TxNx	6			ypT4	1
		Grand Total	50			N/A *	12
						Grand Total	50

Note:

* indicates N/A made up of 8 cCR, 4 no surgery for other reasons.

Abbreviations: cTN= clinical tumor and nodal stage, pTN=pathologic tumor and nodal stage, BL= baseline, PNT= post-neoadjuvant treatment, LAR= low anterior resection, NOM= non-operative management, APR= abdominoperineal resection LAP= laparotomy, R= right, x=unable to assess presence of absence of cancer due to clinical, imaging, or specimen limitations.

Table 2

Assessment of Tumor Margins and Size at Baseline

Parameter measured (cm)	GAD– Mean (SD)	GAD+ Mean (SD)	Difference with use of GAD Mean (SD)	P Value, significance
Distance to Anal Verge	6.44 (3.70)	6.60 (3.43)	0.15 (1.83)	p=0.57, ns
Distance to Anorectal Ring (ARR)	3.20 (3.19)	3.30 (2.94)	0.10 (1.31)	p=0.59, ns
Sub-analysis: tumors 0.0–2.0cm from ARR	0.15 (0.35)	0.71 (1.465)	0.56 (1.428)	p=0.09, ns
Distance to Mesorectal Fascia	0.57 (0.85)	0.77 (0.96)	0.20 (0.55)	p=0.09, ns
Craniocaudal length	4.99 (2.15)	5.05 (2.08)	0.06 (1.15)	p=0.72, ns
Thickest wall	1.90 (1.89)	2.05 (1.94)	0.15 (0.91)	p=0.27, ns

Note: Results from paired Student's T test, 2-tailed, 95% CI, n=50 pairs. P value for significance=0.05. All measurements are reported in centimeters.

Abbreviations: GAD=Gadolinium, ARR= anorectal ring

Table 3

Assessment of Tumor Margins Post-Neoadjuvant Treatment

Parameter measured (cm)	GAD– Mean (SD)	GAD+ Mean (SD)	Difference with use of GAD Mean (SD)	P-Value
Distance to Anal Verge	7.45 (4.08)	7.19 (3.98)	–0.27 (0.47)	p=0.0017 *
Distance to Anorectal Ring	4.20 (3.22)	4.08 (3.19)	–0.12 (0.28)	p=0.0151 *
Distance to Mesorectal Fascia	0.56 (0.99)	0.53 (1.0)	–0.030 (0.13)	p=0.35, ns

Note: Results from paired Student's T test, 2-tailed, 95% CI, n=50 pairs. P value for significance=0.05. All measurements are reported in centimeters.

Abbreviations: GAD= Gadolinium; ns= not significant;

*
=significant

Table 4

Treatment changes at Baseline with Use of Gadolinium

Treatment changes- Baseline			
4 treatment changes due to T stage			
T stage		Treatment	
GAD–	GAD+	GAD–	GAD +
T1/2 (2)	T3a (2)	LAR (2)	CRT (2)
T1/2	T3b	LAR	CRT
T3b	T1/2	CRT	LAR
7 treatment changes due to height			
Height		Treatment	
GAD–	GAD+	GAD–	GAD+
Tumor above anterior peritoneal reflection (3)	Tumor straddles (2)/below anterior peritoneal reflection (1)	LAR (3)	CRT (3)
Tumor straddles anterior peritoneal reflection	Tumor above anterior peritoneal reflection	CRT	LAR
Tu-AV: 2.7cm	6.0 cm	CRT	Proctocolectomy
Tu-ARR: 0cm	2.6 cm	CRT	LAR
IAS involved	IAS not involved	CRT	LAR

Abbreviations: GAD=Gadolinium; Tu-AV= distance from inferior tumor border to anal verge; IAS= internal anal sphincter; Tu-ARR=distance from inferior tumor border to anorectal ring/sphincter complex; LAR= low anterior resection; CRT= chemoradiotherapy. Parenthesis indicate number of cases if greater than 1.