Section: Radiology

Original Research Article

RADIOLOGICAL STUDY TO EVALUATE ROLE OF DIFFUSION WEIGHTED IMAGING AND PERFUSION IMAGING IN RECTAL MALIGNANCY

Manjeet Siddheshwar Kulkarni[1], Swenil Arun Shah[2], Makarand Kulkarni[3]

[1]Assistant Professor, Department of Radiology, RCSM Govt Medical College Kolhapur, India.
[2]Associate Professor, Department of Radiology, RCSM Govt Medical College Kolhapur, India.
[3]Ex Consultant Radiologist, Lilavati Hospital Mumbai, India.

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Corresponding Author:
Dr. Manjeet Kulkarni,
Email: manjeet.kulkarni@gmail.com
ORCID: 0000-0003-0563-534X

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Abstract

Background: Perfusion dynamic contrast material–enhanced MR imaging is increasingly applied noninvasively to assess the microvascular status of tumor tissue. Present study was aimed to evaluate role of diffusion imaging and perfusion imaging in patients of rectal malignancy. **Material and Methods:** Present study was prospective, observational study, conducted in patients referred to department of radiology (MRI), with a diagnosis of rectal carcinoma, based on manual palpation and proctoscopic results and confirmed by means of endoluminal biopsy. **Results:** In presents study, average age was 53.07 ± 14.36 years & 76.7% cases were males. 86.7% cases had Circumferential or Annular followed by 13.3% had Polypoidal tumor. 13.3% cases had sphincter involvement., 14.3% cases had CRM involvement & 90.0% cases were on CRT. 96.7% cases of pre-CRT had DWI in lesion which was significantly more as compared to 29.6% cases of post CRT. 90.0% cases showed lymph nodes in pre-CRT scans which were more as compared to 74.1% cases that showed lymph nodes on post CRT scan but the difference was insignificant. 88.9% cases showed restricted diffusion in lymph nodes in pre-CRT scans which was significantly more as compared to 30.0% cases who showed restricted diffusion in lymph nodes on post CRT scan. Mean ADC value was 1.10 among Responders which was significantly less than 1.29 among non-responders. 50.0% cases with DWI nodes had lymph nodes post CRT histopathology which more as compared to 20.8% cases who had no lymph nodes post CRT histopathology but the difference was not statistically significant. **Conclusion:** Number of lymph nodes showing diffusion restriction also reduced in post CRT scans as compared to pre-CRT and the difference was statistically significant. Number of lesions showing restricted diffusion also decreased in post CRT scans as compared to pre-CRT and the difference was statistically significant.

INTRODUCTION

Immense improvement has occurred over the past 2 decades in the surgical, radiologic, and oncologic treatment of rectal cancer. However, this neoplasm remains associated with a poor prognosis due to the high risk of metastases and local recurrence. After surgical treatment, local recurrence rates for rectal cancer can vary from 3% to 32%.[1]

Preoperative staging techniques for rectal cancer should allow identification of ^{extra} rectal and transmural spread, who might require preoperative chemoradiation therapy (CRT) and minimal or no sphincter involvement, who might be candidates for sphincter-sparing surgery. The post operative imaging modality should be able to differentiate between the post radiotherapy or post chemotherapy fibrosis and local recurrence as it is very important in treatment planning and affects patient survival.[2,3] Recently, perfusion dynamic contrast material–enhanced MR imaging is increasingly applied noninvasively to assess the microvascular status of tumor tissue. Regression of tumor microcirculation, as shown by using the perfusion index, is considered an important early prognostic factor for treatment response, before reductions in tumor volume. Thus, perfusion MR imaging can be used for prediction of CCRT response and for primary tumor staging. Recent data also suggests that dynamic imaging can help in differentiating residual tumor from fibrosis in post CRT patients.[4,5] Present study was aimed to

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evaluate role of diffusion imaging and perfusion imaging in patients of rectal malignancy.

MATERIAL AND METHODS

Present study was prospective, observational study, conducted in department of radiodiagnosis, at RCSM Govt Medical College Kolhapur, India. Study duration was of 1 year (December 2020 to December 2021). Study was approved by institutional ethical committee.

Inclusion Criteria

- All patients referred to department of radiology (MRI), with a diagnosis of rectal carcinoma, based on manual palpation and proctoscopic results and confirmed by means of endoluminal biopsy.

Exclusion Criteria

- Patients who did not have surgery
- Patients whose surgical specimens did not have complete pathological data.
- Suboptimal imaging due to movement artifacts and suboptimal perfusion study.

Study was explained to patients in local language & written consent was taken for participation. MR imaging was performed at our institution at 3 T (Ingenia; Quasar Dual, Philips Medical Systems, the Netherlands). Subjects were positioned supine and in the head first position.

High-resolution T2-weighted imaging was used in this study. This sequence uses a high-resolution matrix, thin-section (3–5 mm) imaging, and a small field of view. Images were acquired in the axial, coronal, and sagittal planes to depict the length and extent of the tumor in all three dimensions.

- DIFFUSION WEIGHTED IMAGING was performed at the B values of 0, 400 and 800.
- DYNAMIC CONTRAST ENHANCED PERFUSION SEQUENCE (E-THRIVE): was performed after injection of 10-12 ml of intravenous gadolinium contrast agent. 8 acquisitions were taken in the region of interest.

The total imaging time was approximately 40 minutes. The different image series were evaluated by using the consensus of an experienced radiologist, unaware of the final surgical and histologic results. Radiologic staging was performed according to the TNM staging.

Tumor morphology- MRI reporting criteria for T and N staging of rectal carcinoma[4] -

1. T1 - A low signal mass within the bright mucosal/submucosal layer but with preservation of the muscularis propria.
2. T2 - A low signal mass within the submucosal layer causing loss of the interface between the submucosa and muscularis propria.
3. T3 - Tumor is of higher signal intensity than muscle. Breach of the outer rectal longitudinal muscle layer with broad based/ nodular extension of the tumor into the perirectal fat.
4. T4 - Extension of tumor signal intensity into adjacent structures or extension through peritoneal reflection in high anterior rectal tumors.

Nodal involvement - Presence of involved perirectal lymph nodes; tumor signal/ irregular contour. Lymph nodal size was taken as insignificant if it measured less than 4 mm, nodes between 4 -10 mm were regarded significant if they showed intermediate tumor signal or had spiculations. All nodes more than 1 cm were considered significant.

The patients were subjected to pre op RT and/or chemotherapy depending on clinical assessment and MR staging and subsequently taken up for surgery.

The MR imaging–based diagnosis (pre and post CRT) was compared with the histopathologic diagnosis-sensitivity, specificity, positive predictive value negative predictive value, were calculated for bowel wall invasion, prediction of metastatic adenopathy and residual disease. Chi square test and student t test were used to determine statistical significance as applicable to particular data set. Statistical analysis was performed by using the software package SPSS for Windows, release 10.0 (SPSS, Chicago, Ill).

RESULTS

In presents study, 30 patients were studied. Age of the patients were ranging from 26 - 77 years with average age being 53.07 ± 14.36 years. Majority of cases were from age group of 50- 70 years (60 %) followed by age group of 30-50 years (23.3%). 76.7% cases were males followed by 23.3% cases were females.

Table 1: Age & gender distribution

	No. of Cases (N=30)	Percentage (%)
Age (in years)		
< 30	03	10.0
30 - 50	07	23.3
50 - 70	18	60.0
> 70	02	06.7
Gender		
Male	23	76.7
Female	07	23.3

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46.7% cases had tumor in the middle third followed by 30.0% cases had tumor in the upper third and 23.3% cases had tumor in the lower third rectum.

Table 2: Location of tumor

Location	No. of Cases (N=30)	Percentage (%)
Upper third	09	30.0
Middle third	14	46.7
Lower third	07	23.3

In present study, 86.7% cases had Circumferential or Annular followed by 13.3% had Polypoidal tumor. 13.3% cases had sphincter involvement., 14.3% cases had CRM involvement & 90.0% cases were on CRT.

Table 3: Tumor morphology on MRI

Tumor morphology	No. of Cases (N=30)	Percentage (%)
Circumferential / Annular	26	86.7
Polypoidal	04	13.3
Other		
Sphincter involvement	04	13.3
CRM Involved (n=21)	03	14.3
Receiving CRT	27	90

In present study, 80.0% cases had moderately differentiated tumor followed by 20.0% cases had poorly differentiated tumor. 3.3% cases had distant metastasis.

Table 4: Histopathology findings

Grade on pathology	No. of Cases (N=30)	Percentage (%)
• Poorly differentiated	06	20.0
• Moderately differentiated	24	80.0
Distant metastasis	01	03.3

96.7% cases of pre-CRT had DWI in lesion which was significantly more as compared to 29.6% cases of post CRT. 90.0% cases showed lymph nodes in pre-CRT scans which were more as compared to 74.1% cases that showed lymph nodes on post CRT scan but the difference was insignificant. 88.9% cases showed restricted diffusion in lymph nodes in pre-CRT scans which was significantly more as compared to 30.0% cases who showed restricted diffusion in lymph nodes on post CRT scan.

Table 5: DWI in lesions pre and post CRT

Stage	Pre CRT (N=30)	Post CRT (N=27)	
Restricted Diffusion in Lesions	29 (96.7 %)	08 (29.6 %)	0.001
Lymph Nodes Involvement	27 (90 %)	20 (74.1 %)	> 0.05
Restricted Diffusion in Lymph Nodes	24 (88.9 %)	06 (30 %)	< 0.05

This analysis states that, 80.0% cases of pre-CRT showed Type IV perfusion curve which was significantly more as compared to 14.8% cases of post CRT.

Table 6: Type of perfusion curve

Type of curve	Pre CRT (N=30)	Post CRT (N=27)	P value
Type I	0	0	0.009
Type II	0	08 (29.6 %)	
Type III	06 (20 %)	15 (55.6 %)	
Type IV	24 (80 %)	04 (14.8 %)	
Type V	0	0	

In this study group, 40.8% cases showed TRG 1 followed by 25.9% cases showed TRG 2 and 22.2% cases showed TRG 0.

Table 7: Profile of post CRT tumor regression grade on histopathology

TRG	No. of Cases (N=27)	Percentage (%)
0	06	22.2
1	11	40.8
2	07	25.9
3	03	11.1

Mean ADC value was 1.10 among Responders which was significantly less than 1.29 among non-responders.

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Table 8: Comparison of mean ADC value among responder and non-responder

Groups	Mean ADC value	p value
Responder (N=17)	1.10 ± 0.08	*0.001
Non-responder (N=10)	1.29 ± 0.08	

In present study, 50.0% cases with DWI nodes had lymph nodes post CRT histopathology which more as compared to 20.8% cases who had no lymph nodes post CRT histopathology but the difference was not statistically significant.

Table 9: Association between DWI nodes and lymph nodes post CRT

DWI nodes	No. of Cases	% Of cases with lymph nodes post CRT		p value
		Yes	*0.001	
Yes	06	03 (50.0 %)	03 (50 %)	>0.05
No/NA	24	05 (20.8 %)	19 (79.2 %)	

On comparison of tumor regression with HPE by perfusion curve, parameters were Sensitivity 47.17 %, Specificity: 100%, Positive Predictive Value: 100% & NPV 27.27%.

Table 10: New Method: Perfusion Curve

	By Curve Positive	By Curve negative	TOTAL
Histopath/TRG positive	05	16	21
Histopath/TRG negative	00	06	06

Parameters on comparing restricted diffusion in lesion post CRT & residual disease on HPE were sensitivity = 38.10%, specificity= 100%, PPV = 100% & NPV = 31.58%.

Table 11: Relation between restricted diffusion in lesion post CRT & residual disease on HPE

	HP RESIDUAL +	HP RESIDUAL -	TOTAL
DWI R	8	0	8
DWI NR	13	6	19

DISCUSSION

At present, Total Mesorectal Excision (TME) is the treatment of choice for rectal cancer, being associated with a recurrence rate of less than 10% when used as a single-modality therapy.[6.7] In patients with involvement of the mesorectal fascia at presentation, the use of preoperative radiation therapy is useful and has been shown to reduce the recurrence rate from 8.2% to 2.4% at 2 years.[6] This therapeutic approach mandates meticulous preoperative tumor staging—namely, detection of rectal carcinoma infiltration into the mesorectal fat, involvement of the mesorectal fascia, and nodal involvement.

Our study, states that, 80.0% cases of pre-CRT showed Type IV perfusion curve which was significantly more as compared to 14.8% cases of post CR. Type IV curve is suggestive of malignancy and type II and III are suggestive of nonmalignant pathology. As evident by the table above 80% of the patients showed type IV curve in pre-CRT phase which reduced significantly to 14.8% in post CRT phase indicating response to CRT. These changes clearly indicate shift from probably malignant type of curve to probably benign and benign type of curve.

Parameters of perfusion curve as a new method to predict the residual disease as compared to the histopathology as standard method were Sensitivity: 47.17%, Specificity: 100%, Positive Predictive Value: 100%, Negative Predictive Value: 27.27%.

Cause for this low sensitivity and negative predictive value lies in the method of deriving the perfusion curve. We used ROI method for perfusion analysis which gives the averaged perfusion characteristics in the region of interest and this method can miss small number of scattered viable tumor cells which corresponds to TRG.[8] This can be avoided by meticulous analysis using pixel by pixel method.

On comparison of mean ADC value, mean ADC value was 1.10 among Responders which was significantly less than 1.29 among non-responders. By using pre-CRT ADC values it is possible to predict response to CRT beforehand and accordingly we can adjust the dose or duration of CRT. Although we agree that this needs further evaluation with a study having large number of patients.

Our findings are in agreement with Andrzej Dzik-Jurasz et al.,[9] who showed that mean pretreatment tumor water ADC is correlated with the degree of tumor response after chemotherapy and chemoradiation and, responders seemed to have a lower ADC at presentation than non-responders.

In present study, 50.0% cases with restricted diffusion in nodes had metastatic lymph nodes on histopathology which is more as compared to 20.8% cases who had no restricted diffusion in lymph nodes post CRT but the difference was not statistically significant. This suggests that only diffusion restriction cannot be used to predict the

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metastatic lymph node involvement and it is not a reliable indicator for the same.

Relation between restricted diffusion in lesion post CRT and residual disease on histopathology had sensitivity 38.10 %, specificity 100%, PPV 100% & NPV 31.58%. This shows that persistent restricted diffusion in the lesion post CRT has high specificity and positive predictive value (100%). However, it has low sensitivity and negative predictive value (38.1 and 31.58% respectively).

In present study, 96.7% cases of pre-CRT had DWI in lesion which was significantly more as compared to 29.6% cases of post CRT. 90.0% cases showed lymph nodes in pre-CRT scans which were more as compared to 74.1% cases that showed lymph nodes on post CRT scan but the difference was insignificant. 88.9% cases showed restricted diffusion in lymph nodes in pre-CRT scans which was significantly more as compared to 30.0% cases who showed restricted diffusion in lymph nodes on post CRT scan. 84.0% cases of pre-CRT had nodal size < 10 mm which was less as compared to 100.0% cases of post CRT but the difference was not significant.

DW (diffusion weighted)-MRI is the only imaging method that can evaluate the diffusion process in vivo. Apparent diffusion coefficients (ADCs), which are quantitative expressions of diffusion characteristics of tissues, are related to the proportion of extracellular and intracellular components. They tend to decrease with increased tissue cellularity or cell density. Conversely, the cell density may be indicative of tumor aggressiveness.[10,11,12]

Seung Ho Kim et al found that Adding DW MR imaging to conventional MR imaging yields better diagnostic accuracy than use of conventional MR imaging alone in the evaluation of CR to neoadjuvant CRT in patients with locally advanced rectal cancer.[2]

DCE-MRI techniques inform on tissue perfusion and vascular leakage and have been used in several clinical settings including novel drug evaluation. T1- or relaxivity based MR sequences are sensitive to the presence of dilute contrast medium in the extravascular–extracellular space. In most tumors, low-molecular-weight contrast media readily diffuse from the blood into the extravascular–extracellular space (also called leakage space) at a rate determined by perfusion and the capillary permeability and surface area.

There has been some work evaluating response to CRT of primary CRC. Rectal tumors with higher Ktrans values at presentation appear to respond better to CRT than those with lower values. After CRT, Ktrans values in general are reduced, with persistent raised values indicating residual active disease. DCE-MRI has been reported by many authors as a tool potentially able to permit an evaluation of pre-CRT effectiveness basing on the strict relationship between tumor growth and angiogenesis.[13,14,15]

IMAGES

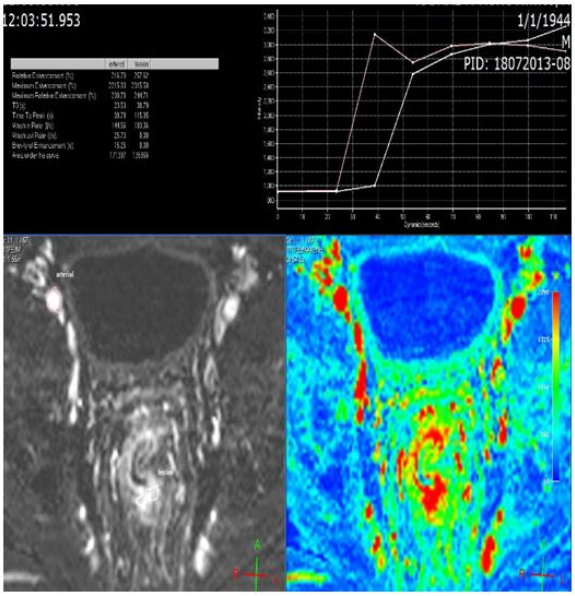

Figure 1

Method of computing perfusion curve, as shown in the figure above one ROI is taken on the external iliac artery(red ROI) and the other one is kept on the lesion in the rectum(white ROI).

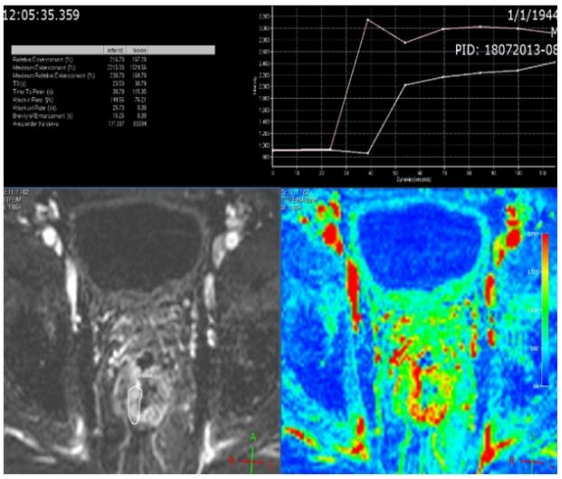

Figure 2

Type III perfusion curve is seen in the above example in the lesion after the administration of the CRT

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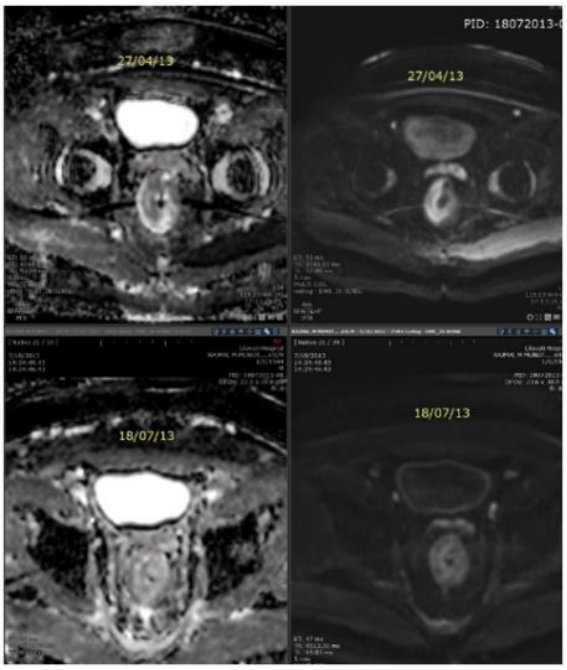

Figure 3

Pre and post CRT images of a patient showing changes in diffusion restriction. The images in the upper half (pre CRT) show restricted diffusion in the rectal lesion. Images in the lower half (post CRT) show no evidence of restricted diffusion indicating response to CRT.

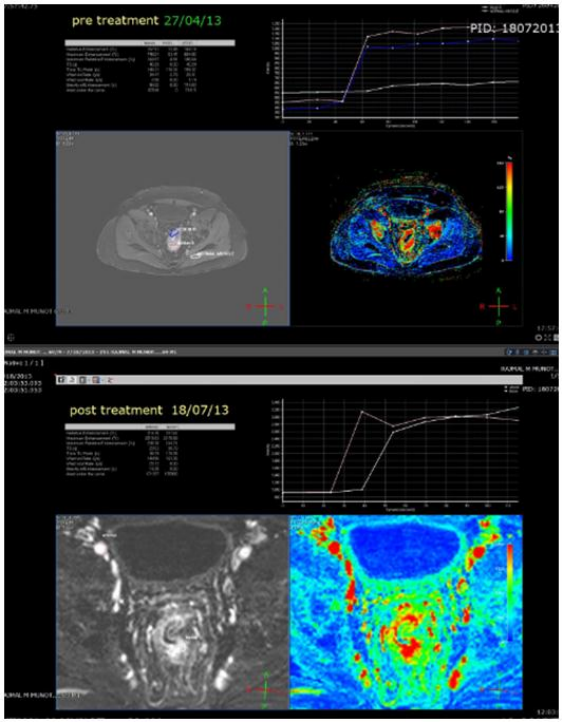

Figure 4

Change in the perfusion curves in pre and post CRT scans: images in the upper half (pre CRT) show type IV perfusion curve however images in the lower half show type III perfusion curve indicating decrase in vascular density.

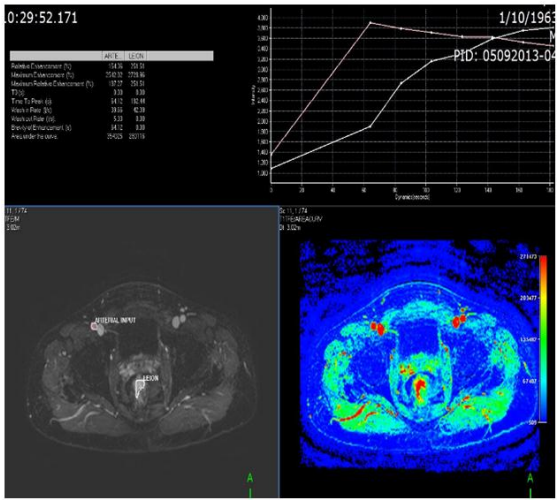

Figure 5

mage showing type II perfusion curve in a post CRT scan which correlated with TRG 0 on histopathology which means no residual disease.

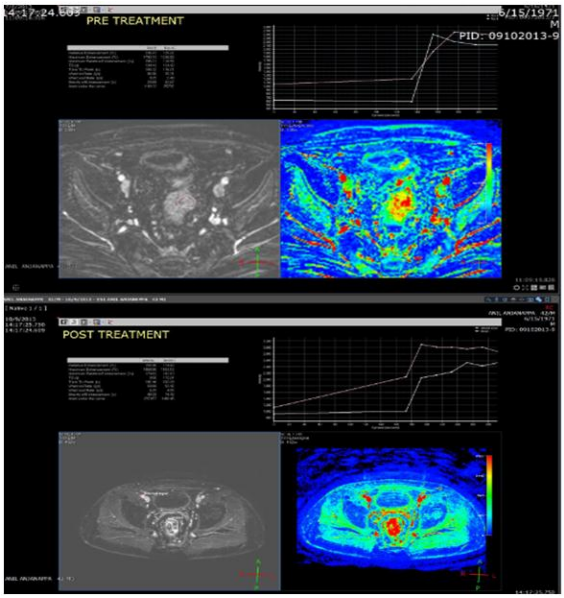

Figure 6

Pre and post CRT changes in the type of perfusion curve . images in the upper half show type V curve which changed to type III in the post CRT images (in the lower half)

CONCLUSION

There was significant decrease in patients showing type IV perfusion curve in post CRT scans as compared to pre-CRT scans. Number of lymph nodes showing diffusion restriction also reduced in post CRT scans as compared to pre-CRT and the difference was statistically significant. Number of lesions showing restricted diffusion also decreased in post CRT scans as compared to pre-CRT and the difference was statistically significant. High resolution T2 weighted images proved to be the best imaging sequence for prediction of rectal wall

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anatomy as well as determination of tumor stage. Review of literature revealed comparable sensitivity of imaging with 3 tesla MR when compared to 1.5 Tesla MR.

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