MEDICINE UPDATES JOURNAL
Faculty of Medicine Port Said University
Volum: 18 No:2 PP:17 - 31

"Role of Diffusion MRI Study in Assessment of Colorectal Tumor Response after Chemoradiotherapy"

Authors
Khaled Abd El-Baky Ahmed [1] ,Mohamed Magdy Elrakhawy [2] , Ahmed Mohamed El shahat [3] ,Omnia Hassan Gohar [4] , Waleed Said Abo Shanab [5]

[1] Diagnostic Radiology Department Faculty of Medicine – Port said University [2] Diagnostic Radiology Department Faculty of medicine Mansoura University [3] Diagnostic Radiology Department Ministry of Health Specialized Damietta Hospital [4] Surgical Oncology Department, Ministry of Health, Damietta Oncology Institute [5] Assistant Professor of diagnostic radiology, faculty of medicine, Port Said University

Submitted: 26/03/2024
Accepted:05/04/2024

DOI: 10.21608/MUJ.2024.279453.1166

ISSN : 2682-2741

https://muj.journals.ekb.egdean@med.psu.edu.eg
vice_dean_postgraduate@med.psu.edu.eg

ABSTRACT:

Objective: To address the role of Diffusion-Weighted Image (DWI) Magnetic Resonance Imaging (MRI) in measurements of Apparent Diffusion Coefficient (ADC) [pre chemo-radiotherapy (CRT), post CRT] for pre-treatment prediction of outcome and early detection of response in patients having colorectal cancer.

Methods: The study was conducted on 40 cases selected from the patients who presented to Damietta Oncology Institute with colorectal cancer to whom DWI-MRI examinations of the lower abdomen before CRT and after CRT were performed. All patients underwent histopathological assessment of surgical specimens, which serve as the benchmark for local staging following CRT. The studied cases were classified into 3 groups according to response to CRT: stable disease (no response to treatment), partial response (decrease of at least one level in T or N staging in comparison to baseline MRI), and complete response (disappearance of any evidence of tumor cells in surgical specimen).

Results: For detection of colorectal cancer; the overall diagnostic accuracy of conventional MRI was calculated to be 66.5%, with sensitivity of 69% and specificity of 63.6%. The DWI MRI sequence showed overall diagnostic accuracy of 80%, and sensitivity of 72.7% and specificity of 82.7%. Our study proved significant statistical correlation between the ADC value and histopathological grade of the colorectal tumor as well as the tumor response after CRT ($p<0.05$); the ADC value is significantly lower in the poorly differentiated tumors. The estimated ADC post CRT cut off value for predication of complete colorectal tumor response is ≥ 1.18 × 10−3mm2/s with accuracy (92.5%), sensitivity (82%) .)and specificity (96.6%

Conclusion: The results of our study suggest that ADC exhibits significant utility in assessing the response of tumors following treatment, exhibiting exceptional diagnostic precision. Moreover, the use of ADC is highly advantageous in assessment of metastatic nodes, as lack of nodal disease in ADC serves as a dependable indicator of negative nodal metastases. Hence, ADC facilitates the development of a suitable treatment strategy and assists in identification of patients for organ preservation following CRT. In patients having locally advanced colorectal cancer, utilization of DWI with ADC value in conjunction with conventional MRI demonstrates superior accuracy compared to the exclusive reliance on conventional MRI. This improvement is observed in various aspects, including tumor grade correlation, staging, .together with evaluating response to neo-adjuvant CRT

Keywords: Apparent diffusion coefficient (ADC), Chemo-radiotherapy (CRT), Colorectal carcinoma, Mesorectal Fat (MRF), .)Circumferential Resection Margin (CRM

INTRODUCTION

Colorectal cancer is one of the lethal neoplasms. Risk factors include old age (as most cases are 65 years old or more), obesity, smoking, chronic inflammatory bowel disease with family history. More than 50% of these cancers originate from either sigmoid colon or from rectum and having 5-year survival rate is 50%. The main prognostic factors are local tumor stage, lymphatic or vascular invasion and preoperative carcino-embryonic antigen serum level [(1).]

Surgical excision is the main treatment option for colorectal cancer; however it is challenging in the rectum to obtain satisfactory marginal clearance to avoid local tumor recurrence without causing significant complications. Consequently, chemo-radiotherapy was used to lessen local recurrence [(2).]

During chemo-radiotherapy, assessment of response could re-direct non responding patients towards treatment amplification (e.g. escalation of the dose or addition of other agents) or to other management options (e.g. early surgery). Moreover, assessment of response may allow physicians to provide patients who accomplish complete response a less major surgery, as sphincter saving local excision, or even a wait and see technique with notable decrease of complications postoperatively, intestinal, bladder, sexual dysfunctions, permanent stoma care and mortality [(3).]

MRI is the most precise modality to define tumor invasion depth into rectum or MRF and to assess the progression of local malignancy and involvement of lymph nodes; both of which are fundamental for decision making regarding the treatment approach [(4)]. However, MRI; as a morphologic imaging modality; shows integral restrictions as the differentiation of diffuse fibrotic changes, desmoplastic reaction, and colloid from remaining viable tumor is difficult. Therefore, conventional MRI sequence is used; but cannot be used to predict complete response to chemo-radiotherapy [(5).]

Consequently, there is substantial eagerness for appointing DW-MRI as a functional imaging technique, which can elucidate microstructural changes of the tumor induced by CRT before morphological switches appear. DW-MRI permits performing quantitative measures as ADC; which provides biological data correlated to tumor cellularity and cell membranes integrity; can be used as non-invasive imaging evidence of tumor aggressiveness and to monitor and forecast tumor response to CRT [(6).]

MRI volumetric analysis, that encompasses estimation of mass volumes on a basis of DW-MRI, has also revealed promising results in forecasting complete tumor response. But, these outcomes are not consistent across all studies, and the precise role of DW-MRI for assessing response to CRT should be subjected to ongoing evaluation [(7).]

Inability to generalize the cutoff values of ADC may be due to small-scale studies with variable methodologies and contradictory conclusions; and absence of standardized imaging and measurement techniques which have led to wide range of results [(8).]

2. Aim of the Work

To evaluate the role of DW-MRI in measurements of ADC (before and after CRT) for prediction of treatment outcome and for early detection of tumor response in patients with colorectal cancer

3. Materials and methods:

The study was conducted on 40 cases selected from the patients who presented to Damietta Oncology Institute with colorectal cancer to whom DWI-MRI examinations of the lower abdomen before and after CRT were performed. All patients underwent histopathological assessment, which serve as the benchmark for local staging following CRT. The estimated time for the thesis is 12 months.

The studied cases were classified into 3 groups according to response to CRT: stable disease (no response to treatment), partial response (decrease of at least one level in T or N staging in comparison to

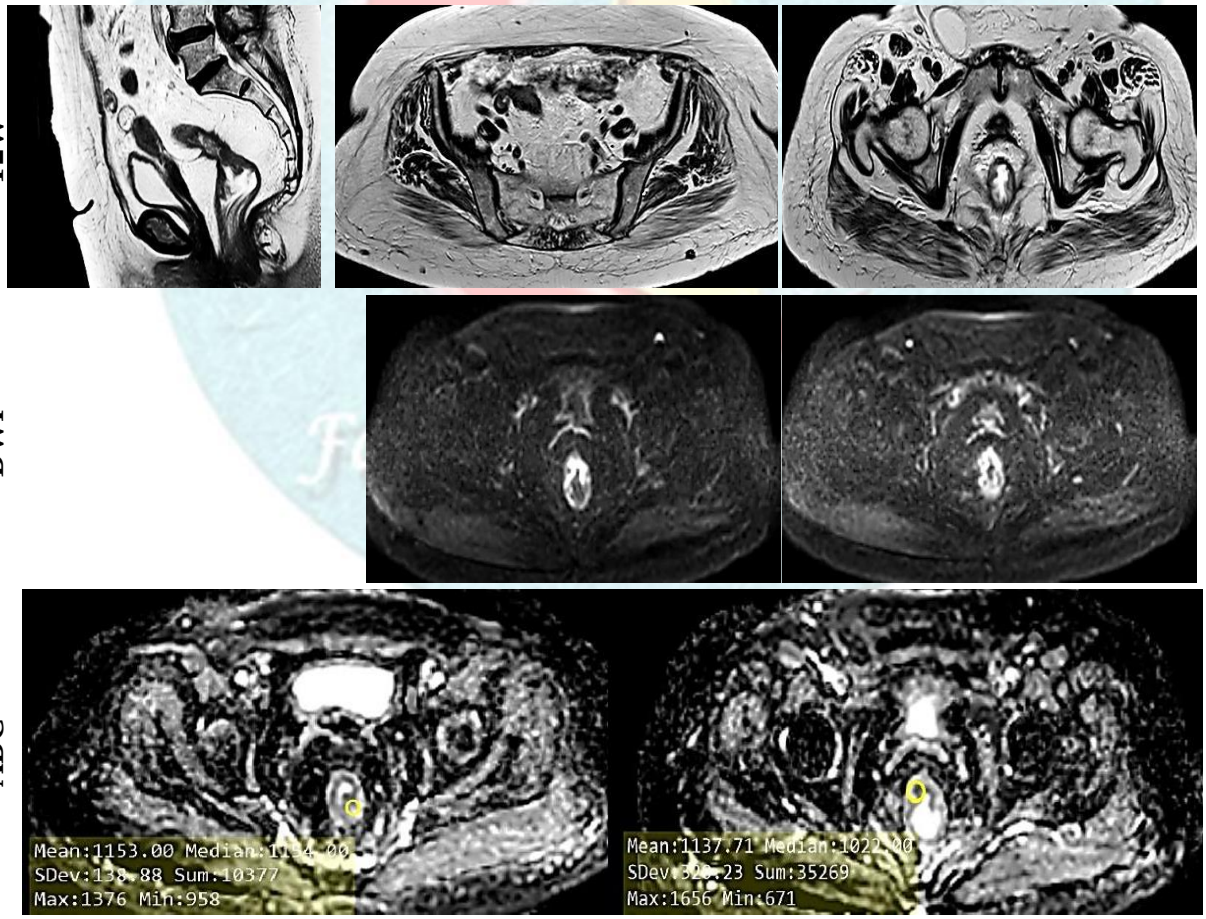
baseline MRI), and complete response (disappearance of any evidence of tumor cells in surgical specimen).

Inclusion criteria include Patients who were pathologically proven colorectal cancer, Patients who have completed full course of CRT and Patients who have undergone DW-MRI and pre- and post- CRT. Exclusion criteria include non-standardized MRI protocol, insufficient image quality (hip prosthetic artifacts, movement artifacts), or Previous CRT for colorectal cancer or tumors in other organs

MRI machine used in the study is 1.5-Tesla (Siemens Magnetom Sempra) with pelvic 8-channel phased array coil. Just before imaging, the patients were exposed to bowel cleansing by glycerin enema. The rectal lumen was filled 150–200 ml of barium sulfate. Hyoscine butylbromide (20 ml) was administrated intramuscularly to control the peristalsis. Sagittal scout images are obtained parallel to the coil

Qualitative analysis included: conventional MRI (T1 and T2-weighted morphological sequences and dynamic contrast-enhanced sequences and combined set of conventional and DWI. Quantitative analysis included: the mean ADC value (ΔADC) was calculated by the equation (ADCpost CRT – ADCpre CRT), and values of three groups of response (stable disease, partial response, complete response) were compared. ADC value was measured for the most solid component of the lesion. ADCpost CRT was calculated be after 4 months of CRT

Pre-treatment MRI



Post-treatment MRI (4 months)

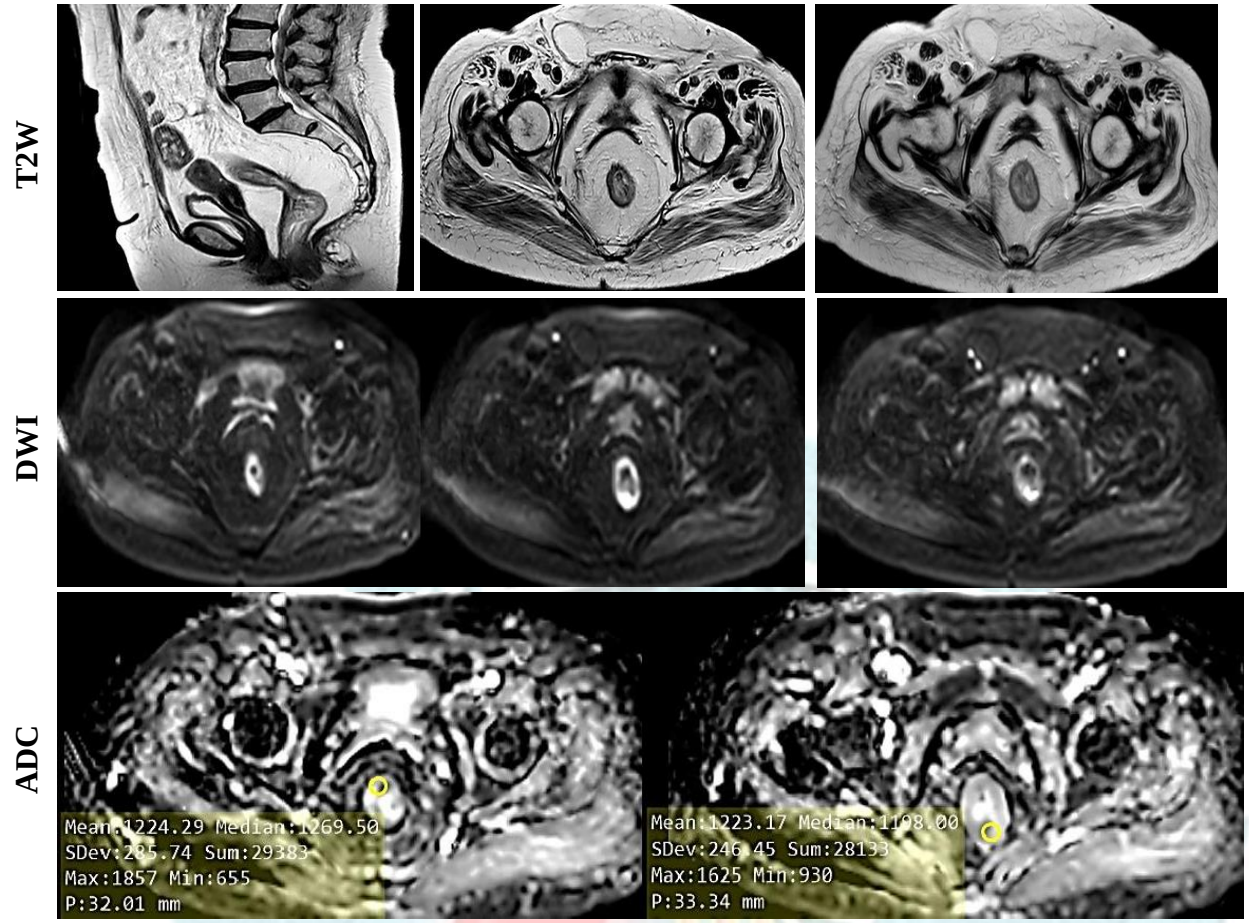


Figure (1): A 66-year old female patient presented with constipation and bleeding per rectum; Colonoscopy and biopsy revealed well-differentiated adenocarcinoma. Pretreatment MRI pelvis revealed irregular mucinous mass in upper and mid rectum and extending to recto-sigmoid; MRF invasion (T3); 6 mm beyond Musculosa Propria (T3c); CRM positive (< 1 mm); preserved fat plane between the mass & posterior uterine margin; no LNs involvement (N0); **ADC = 1.152 $\times 10^{-3}$ mm2/s** (consistent with well-differentiated tumor) → [T3c N0]. Post-treatment MRI pelvis (4 months later) revealed cancer in upper & mid rectum; decrease in size; MRF invasion (T3), 4.4 mm beyond Musculosa Propria (T3b); CRM negative 7.8 mm); no LNs involvement (N0); **ADC = 1.224 $\times 10^{-3}$ mm2/s** (consistent with regressive course); [**the mean ADC equation: 1.224 – 1.152 = 0.72 $\times 10^{-3}$ mm2/s**] → [T3b N0]. Post-treatment MRI pelvis (6 months later) reveled no recurrent masses and pathology report revealed no residual tumor, dense active inflammation and ulceration, free resection margins, free LNs **(complete therapy response)**

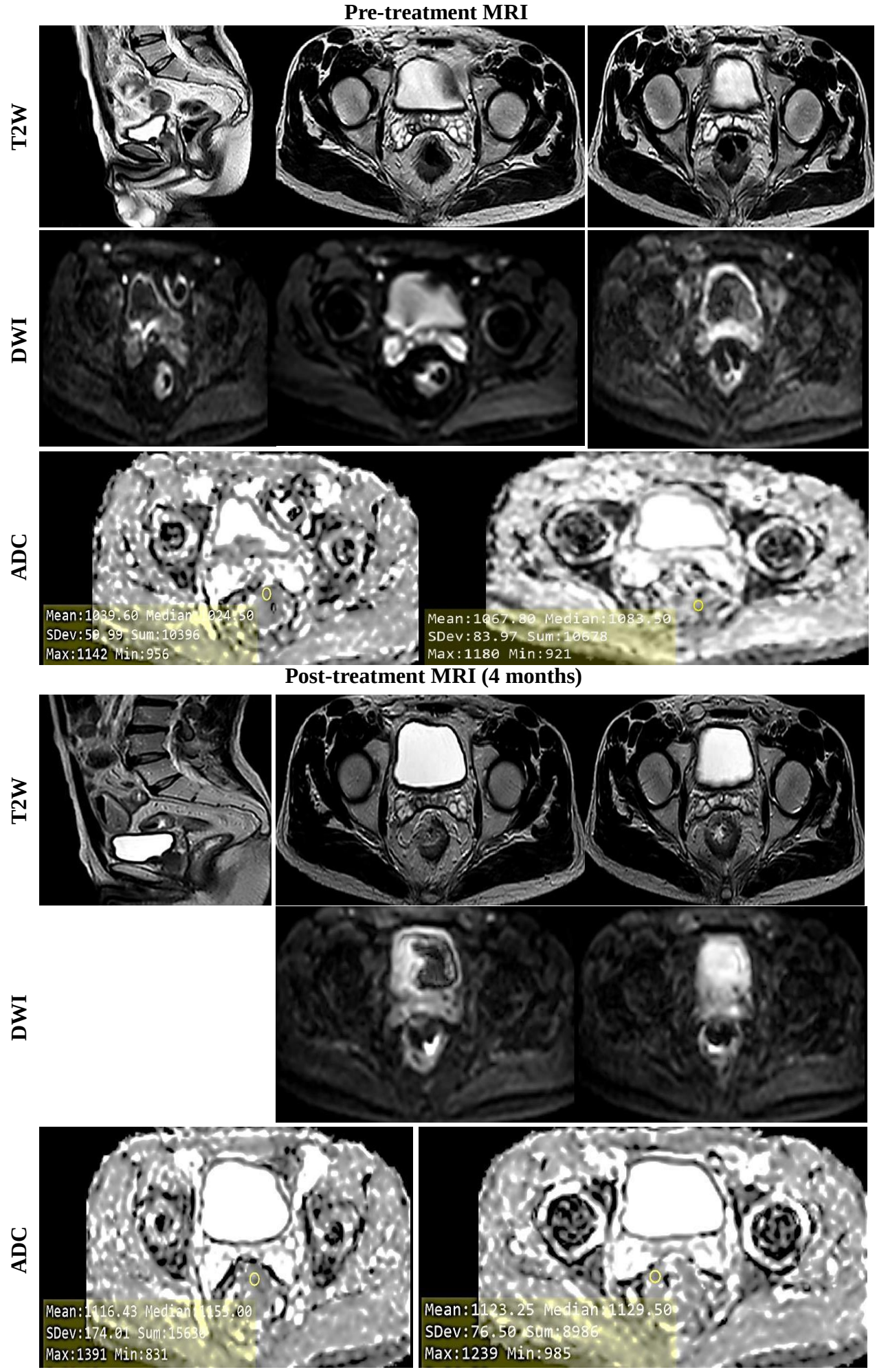
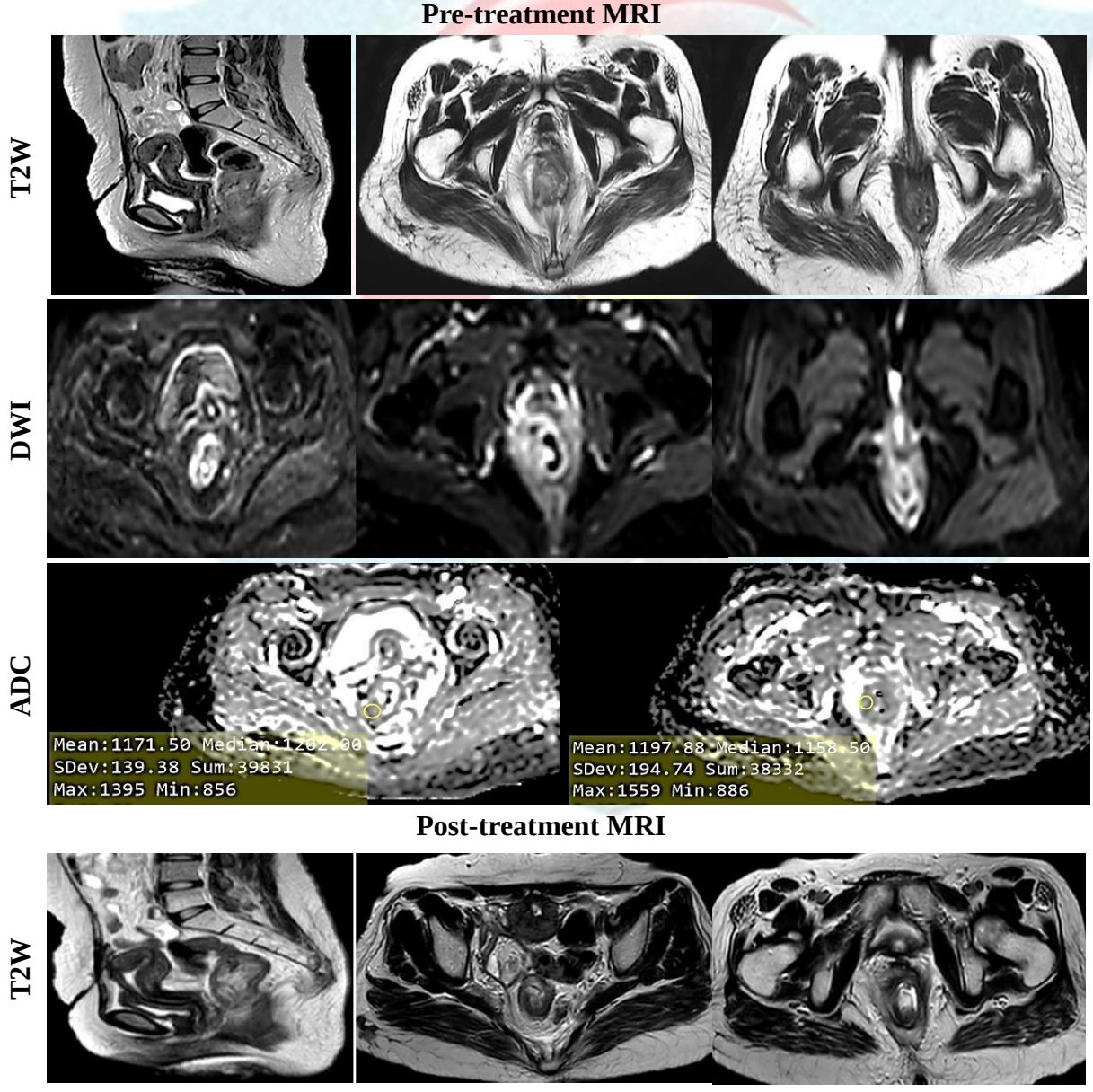


Figure (2): A 52-year old male patient presented with abdominal pain and altered bowel habits. Colonoscopy and biopsy showed moderately-differentiated adenocarcinoma. Pretreatment MRI pelvis

revealed circumfrential non-mucinous mass in recto-sigmoid and upper rectum with narrowing of the lumen; MRF invasion (T3); 7.1 mm beyond Musculosa Propria (T3c); CRM negative (3.5 mm); preserved fat plane between the mass & posterior wall of urinary bladder, seminal vesicles and prostate; no enlarged pelvic LNs; **ADC = 1.039 $\times 10^{-3}$ mm^2/s (consistent with moderately-differentiated tumor) → [T3c N0**]. Post-treatment MRI pelvis (4 months later) revealed irregular mural thickening in recto-sigmoid and upper rectum MRF invasion (T3); 8.2 mm beyond Musculosa Propria (T3c); CRM negative (2.4 mm); preserved fat plane between the mass & posterior wall of urinary bladder, seminal vesicles and prostate; no enlarged pelvic LNs; **ADC = 1.123 $\times 10^{-3}$ mm^2/s** (consistent with stationary course) [**the mean ADC equation: 1.123 – 1.039 = 0.84 $\times 10^{-3}$ mm^2/s**] → [T3c N0]. Post-treatment MRI pelvis (6 months later) revealed irregular mural thickening in recto-sigmoid and upper rectum MRF invasion (T3); 7.6 mm beyond Musculosa Propria (T3c); CRM negative (3 mm); preserved fat plane between the mass & posterior wall of urinary bladder, seminal vesicles and prostate; no enlarged pelvic LNs; **ADC = 1.099 $\times 10^{-3}$ mm^2/s (consistent with stationary course) → [T3c N0].**



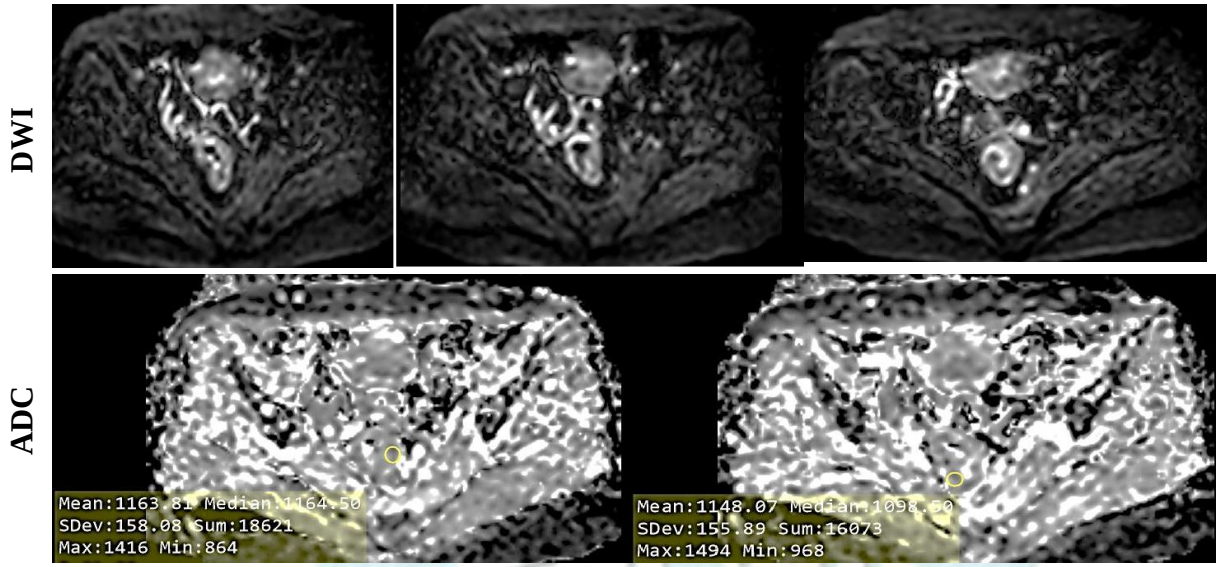


Figure (3): A 50-year old female patient presented with abdominal pain & bleeding per rectum since 6 months. Colonoscopy and biopsy showed moderately-differentiated adenocarcinoma. Pretreatment MRI pelvis revealed irregularly marginated moderately circumferential mucinous mass in mid and lower rectum with narrowing of the lumen; 2.2 cm from anal verge, with invasion of external anal sphincter; MRF invasion (T3); 12 mm beyond Musculosa Propria (T3c); CRM positive (< 1 mm); preserved fat plane between the mass & posterior uterine margin; 3 mesorectal LNs (suspicious for metastasis) (N1); **ADC = 1.197 $\times 10^{-3}$ mm^2/s** (consistent with moderately-differentiated tumor) → [T3c N1]. Post-treatment MRI pelvis (4 months later) revealed irregularly marginated moderately circumferential mucinous mass in mid and lower rectum with narrowing of the lumen; 3 cm from anal verge, with invasion of external and internal anal sphincters with left intersphincteric marginally cavity; MRF invasion; 23 mm beyond Musculosa Propria (T3d); CRM positive (< 1 mm); absent fat plane between the mass & posterior vaginal wall (recto-vaginal fistula) (T4d); 2 mesorectal LNs (suspicious for metastasis) (N1); **ADC = 1.148 $\times 10^{-3}$ mm^2/s** [**the mean ADC equation: 1.148 – 1.197 = –0.49 $\times 10^{-3}$ mm^2/s]** → [T4d N1]. **(Progressive course)**

4. Results:

Table (1): Basic demographic data of the studied patients

	(n = 40)
Age (years)	
Range	31.0 – 75.0
Mean ± SD	52.2 ± 13.5
Gender (no,s %)	
Male	33(82.5%)
Female	7(17.5%)

The mean age of our population is (52.2 ± 13.5 years old) ranged from 31 to 75 years old with male predominance (82.5%)

Table (2): Distribution of histopathology results of all lesions (n=40).

	(n = 40)
Well-differentiated adenocarcinomas (n,%)	12(30%)
Moderately differentiated adenocarcinomas (n,%)	21(52.5%)
Poorly differentiated adenocarcinomas (n,%)	7(17.5%)

Out of 40 cases, 7 (17.5%) have been poorly differentiated, 21 (52.5%) have been moderately differentiated, and 12 (30%) were well differentiated histologically.

Table (3): Mean ADC value of histological types of lesions (n=40).

	(n = 40)	P-value
Well-differentiated adenocarcinomas mean ADC value± SD ($\times10^{-3}mm^2/s$)	1.309 ± 0.021	**<0.001***
Moderately differentiated adenocarcinomas mean ADC value± SD ($\times10^{-3}mm^2/s$)	1.122 ± 0.159	
Poorly differentiated adenocarcinomas mean ADC value± SD ($\times10^{-3}mm^2/s$)	0.983 ± 0.176	
Paired t test used *Statistically significant as p<0.05.		

The mean ADC in poorly differentiated tumors was 0.983 ± 0.176 ($\times10^{-3}mm^2/s$). The mean ADC value in moderately differentiated cases was 1.122 ± 0.159 ($\times10^{-3}mm^2/s$). The mean ADC value in well-differentiated malignancies was 1.309 ± 0.021 ($\times10^{-3}mm^2/s$) with statistical significant difference (p<0.001).

Table (4): Post-CRT/APR Response Evaluation Criteria in Solid Tumors of the patients (n=40).

	(N=40)
Complete Response	11(27.5%)
Partial Response	24(60%)
Stable Disease	3(7.5%)
Progressive Disease	2(5%)

Out of these 40 cases, 3 (7.5%) had Stable disease, 24 (60%) showed Partial response, and two patients (5%) had progressive disease.

Table (5): Post-CRT MRI versus histopathology assessment of T staging of the lesions

	Post-CRT Histopathology					K
		T2	T3	T4	No residual	
Post-CRT MRI	T2	7	0	0	0	0.782
	T3	3	12	0	3	
	T4	0	0	7	0	
	No residual	0	0	0	8	
Abbreviations: CRT: chemoradiotherapy. Kappa result be interpreted as follows: values ≤ 0 as indicating no agreement and 0.01–0.20 as none to slight, 0.21–0.40 as fair, 0.41– 0.60 as moderate, 0.61–0.80 as substantial, and 0.81–1.00 as almost perfect agreement.						

There is substantial agreement between histopathological results and MRI staging post CRT as K=0.782.

Table (6): Post-CRT MRI versus histopathology assessment of N staging of the lesions

	Post-CRT Histopathology				K
		N0	N1	N2	
Post-CRT MRI	N0	12	4	0	0.812
	N1	2	13	0	
	N2	0	0	9	
Abbreviations: CRT: chemoradiotherapy. Kappa result be interpreted as follows: values ≤ 0 as indicating no agreement and 0.01–0.20 as none to slight, 0.21–0.40 as fair, 0.41– 0.60 as moderate, 0.61–0.80 as substantial, and 0.81–1.00 as almost perfect agreement.					

There is perfect agreement between histopathological results and MRI staging post CRT as K=0.812.

Table (7): The estimated minimum and maximum values for ADC before and after neo-adjuvant therapy

	(n = 40)	P-value
Before RCT	0.971 ± 0.132 0.567 – 1.283	**<0.001***
After CRT	1.78 ± 0.167 1.22– 2.34	
Paired t test used. *Statistically significant as p<0.05.		

This table indicates the minimum and maximum values of the ADC before and after CRT. At these qualities compared when there may be light of help there may be expand in the comparing ADC.

Table (8): Conventional MRI versus pathology in the studied group

Characteristics		Pathology		*P*-value
		CRs (No. = 11)	**Non-CRs (No. = 29)**	
Conventional MRI	**CRs (No. = 16)**	7 (63.6%) TP	9 (31%) FP	0.001*
	Non-CRs (No. = 24)	4 (36.4%) FN	20 (69%) TN	
$\chi 2$=Chi-square test *Statistically significant as p<0.05.				

The concordance between the conventional MRI and the pathology was as follows: in complete responder (CR) patients, 7 patients had true-positive results and 9 patients had false-positive results. In non-complete responder (non-CR) patients, 20 patients had true-negative results and 4 patients had false-negative results.

Table (9): DW-MRI versus pathology in the studied group

Characteristics		Pathology		*P*-value
		CRs (No. = 11)	**Non-CRs (No. = 29)**	
DW-MRI	**CRs (No. = 13)**	8 (72.7%) TP	5 (17.2%) FP	0.001*
	Non-CRs (No. = 27)	3 (29.3%) FN	24 (82.7%) TN	
$\chi 2$=Chi-square test *Statistically significant as p<0.05.				

The correlation between the DWI MRI and the pathology was as follows: true-positive results were identified in 8 patients (CRs) and false-positive results were identified in 5 patients; true-negative results

were identified in 24 patients (non-CRs); and false-negative results were identified in 3 patients (non-CRs).

Table (10): ADC versus pathology in the studied group

Characteristics		Pathology		*P*-value
		CRs (No. = 11)	**Non-CRs (No. = 29)**	
ADC	**CRs (No. = 10)**	9 (82%) TP	1 (3.4%) FP	0.001*
	Non-CRs (No. = 30)	2 (20%) FN	28 (96.6%) TN	
χ2=Chi-square test *Statistically significant as p<0.05.				

The ADC exhibited the following concurrence with the pathology: 9 patients (CRs) exhibited true-positive outcomes, with 1 patient had false-positive outcomes. Conversely, 28 patients (non-CRs) exhibited true-negative outcomes, with 2 patients experiencing false-negative outcomes.

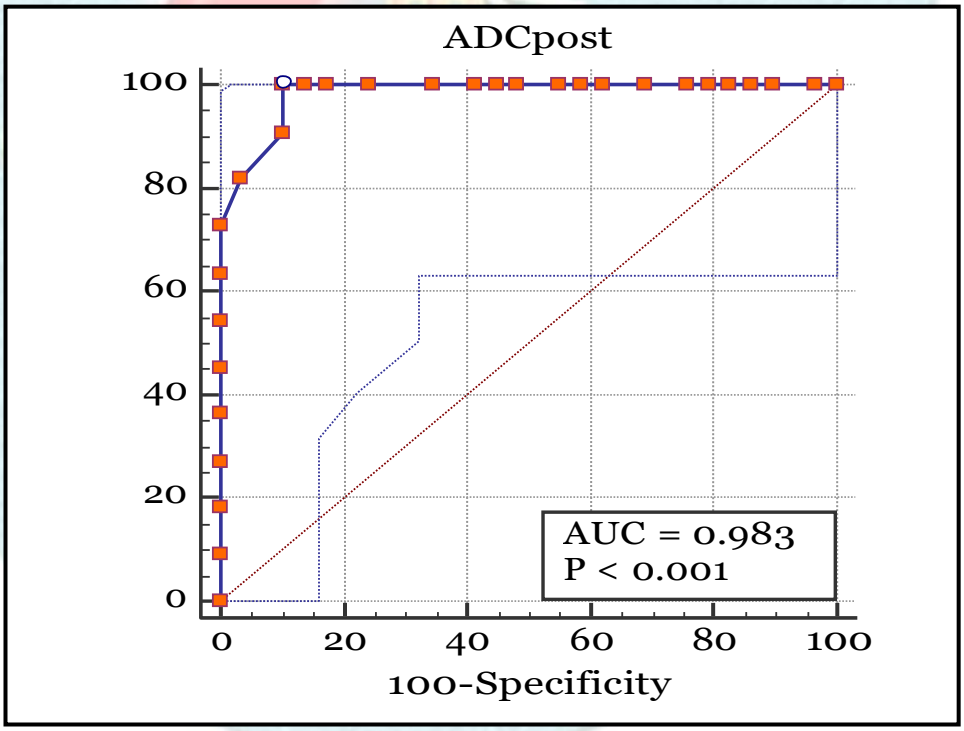


Figure (1): ROC curve analysis of ADCpost of CR group versus non-CR.

ROC curve was created by plotting ADCpost values in CR group against those in non-CR group. The estimated ADC post CRT cut off value for predication of complete colorectal tumor response is ≥ $1.18 \times 10^{-3} mm^2/s$ with accuracy (92.5%), sensitivity (82%), specificity (96.6%), positive predictive value (90%), negative predictive value (93.3%) and Area under the curve (AUC) is 0.983

Table (11): Diagnostic indices (sensitivity, specificity, PPV, NPV, and accuracy) of MRI (conventional, DWI, and ADC) in the studied group

	Sensitivity	Specificity	PPV	NPV	Accuracy
Conventional	7/11 (63.6%)	20/29 (69%)	7/16 (43.7%)	20/24 (83.3%)	27/40 (67.5%)
DWI	8/11 (72.7%)	24/29 (82.7%)	8/13 (61.5%)	24/27 (88.8%)	32/40 (80%)
ADC	9/11 (82%)	28/29 (96.6%)	9/10 (90%)	28/30 (93.3%)	37/40 (92.5%)
PPV: Positive Predictive Value *NPV*: Negative Predictive Value					

Overall diagnostic accuracy of conventional MRI was calculated to be 67.5%; the sensitivity was 63.6%, specificity was 69%. Overall diagnostic accuracy of DWI-MRI sequence was calculated to be

80%; the sensitivity was 72.7%, specificity was 82.7%. Overall diagnostic accuracy of ADC was calculated to be 92.5%; the sensitivity was 82%, specificity was 96.6%.

5. Discussion:

Various cross-sectional imaging methods, like CT (computed tomography), PET/CT (positron emission tomography/ computed tomography), and MRI, are frequently employed for the initial assessment, staging, and follow-up of cancer therapy response [9,10].

While contrast enhanced MRI is considered a standard method for local staging colorectal cancer, it is invasive, time-consuming, and requires adequate cooperation in the breath hold technique. It also has contraindications and contrast media adverse effects. Tumor aggressiveness is indicated by ADCs, which are the quantitative expressions of the diffusion properties that decreased with increased tissue cellularity. An imaging technique called DW- MRI can be used to examine the in vivo diffusion process, which differs depending on the tissue [11].

When staging and restaging rectal carcinomas and selecting the best course of action for treatment, radiology is a crucial component. MRIs are typically used to stage and restage rectal tumors. Lately, there has been an increase in the use of DWI for rectal cancer restaging [12].

The DWI diagnostic performance has significantly improved with the advent of newly designed MRI systems having high gradient amplitude. However, selection of b values within the context of DWI is a compromise. Because of the contamination from different types of intravoxel incoherent motion, low b values result in larger ADC values, whilst high b values reduce the signal-to-noise ratio (SNR) but necessitate longer acquisition periods [13,14].

Therefore, the purpose of the study was to assess utility of diffusion-weighted MR imaging in assessing ADC (pre- and post-CRT) for the purpose of predicting treatment outcome and identifying tumor response early in patients having colorectal cancer.

The DWI study utilized b values of 0, 400, and 800 s/mm^2. By employing the breath triggering technique with parallel imaging, we were able to achieve a satisfactory picture quality using a 1.5-T scanner, while still maintaining an acceptable acquisition time.

The present study revealed that sensitivity of DWI in identifying colorectal cancer residual was 80%.

This is consistent with findings which reported a sensitivity of 92.5% (37/40) for DWI in detecting colorectal cancer [1]. This finding is consistent with previous study conducted by Ichikawa et al., which documented MRI-DWI had a sensitivity of 91% in detecting rectal cancer (30/33) [11].

Our research demonstrated a noteworthy correlation between ADC value and the tumor's histological grade. The ADC value is significantly lower in the poorly differentiated tumors.

Similarly, Sabry et al. discovered that the ADC value is considerably diminished in tumors that lack differentiation [1]. These findings were consistent with those of the research conducted by Gu et al. together with Curvo-Semedo et al [15,16].

In our study, the conventional MRI had an overall diagnostic accuracy of 67.5%, with sensitivity of 63.6% and specificity of 96%. The DWI-MRI sequence showed overall diagnostic accuracy of 80%, and sensitivity of 72.7% and specificity of 82.7%. ROC curve was created by plotting ADC post values in CR group against those in non-CR group. The optimal cutoff value was 1.18×10^{-3} mm^2/s which rendered an

overall diagnostic accuracy of 92.5%, with sensitivity of 82%, specificity of 96.6% and Area under the ROC curve (AUC) of 0.983.

The study delivered by Sabry et al. found that utilizing a cut-off ADC value of $1.20 \times 10^{-3} mm^2/s$ to distinguish between complete responders (CR) and non-complete responders (non-CR) resulted in a 100% net present value (NPV) in 8 out of 8. This supports use of ADC values in accurately differentiating between responders and non-responders [(1).]

Moreover, Blažić, et al. reported that ADC values for adequate tumor response was $0.98 \times 10^{-3} mm^2/s$ for the most cellular region and 1.29×10^{-3} mm^2/s for the entire lesion. He also reported the cut-off values for the mean ADC: 0.18×10^{-3} mm^2/s and 0.28×10^{-3} mm^2/s [(17)]

The findings of our study align with prior study done by Kim et al., which documented a 100% negative predictive value (23 out of 23 cases) while employing an ADC of 1.20×10^{-3} mm^2/s as threshold value for distinguishing the CR group from the non-CR group [(18).]

Prior research has demonstrated that relying just on conventional MRI is insufficient in reliably distinguishing between fibrotic alterations and remaining tumor tissue [(16,19).]

In a recent study, it was found that DWI plays significant role for assessing response of tumors after treatment, achieving a diagnostic accuracy of 91% [(12)]. Qureshi et al. (year) also noted a statistically significant increase in the mean ADC levels among patients with a complete response (CR) in comparison to those without a CR [(12).]

In a separate research, van Heeswijk et al. also supported use of DWI for identifying patients for organ preservation following CRT. They proposed that lack of lymph nodes in locally advanced tumor after neo-adjuvant CRT, as assessed by restaging DWI, could serve as a dependable indicator of negative nodal condition [(20).]

DW MRI is a reliable method for distinguishing between complete and poor responders. However, this does have certain drawbacks. The accuracy of distinguishing between CR and near CR and distinguishing inactive mucin pools from remaining tumor tissue in the mucinous type, is not entirely precise. In addition, it is unable to address the diversity in the tumor response to neo-adjuvant CRT. Even when using high-spatial-resolution ADC mapping with small voxels, it is not possible to evaluate the tumor response at the cellular level of each person. Furthermore, it should be noted that DW MRI has restricted spatial resolution and a comparatively diminished signal-to-noise ratio when the b value is high [(19).]

There are certain limitations inherent in our study. Initially, it is imperative to validate the findings of our study, which were based on a limited sample size, by more extensive clinical investigations. Furthermore, ADC measurements acquired were obtained by measuring 3 regions of interest (ROIs), which might not sufficiently reflect overall tumor profile. However, we opted for that approach due to the time-consuming nature of outlining the entire tumor volume and the challenges associated with performing it in daily clinical practice. We attempted to replicate the daily clinical procedures by utilizing a more efficient and straightforward method to get ADC values.

6. Conclusion:

ADC is very useful in the evaluation of post-treatment tumor response with excellent diagnostic accuracy with the optimal cutoff value was $1.18 \times 10^{-3} mm^2/s$ which rendered an overall diagnostic accuracy of 92.5%, with sensitivity of 82%, specificity of 96.6%

ADC is also very valuable in the evaluation of metastatic nodes, and aids in making an appropriate treatment plan and helps in the selection of patients for organ preservation after CRT.

The addition of DW imaging with ADC value to conventional MRI yields better diagnostic accuracy than using conventional MR imaging alone in detection, correlation with tumor histologic grade, initial staging, and response evaluation to neo-adjuvant CRT in patients with locally advanced colorectal cancer.

7. Abbreviations:

- Diffusion-Weighted Image (DWI)
- Magnetic Resonance Imaging (MRI)
- Apparent Diffusion Coefficient (ADC)
- Chemo-radiotherapy (CRT)
- Complete Responder (CR)
- Non-Complete Responder (non-CR)
- Receiver Operating Characteristic (ROC)
- Positive Predictive Value (PPV)
- Negative Predictive Curve

8. References:

1. Sabry MS, Rady AEE, Niazi GEM, Ali SA. Role of diffusion-weighted MRI in diagnosis and post therapeutic follow-up of colorectal cancer. Egypt J Radiol Nucl Med [Internet]. 2021;52(1). Available from: http://dx.doi.org/10.1186/s43055-021-00561-7
2. Ha H Il, Kim AY, Yu CS, Park SH, Ha HK. Locally advanced rectal cancer: diffusion-weighted MR tumour volumetry and the apparent diffusion coefficient for evaluating complete remission after preoperative chemoradiation therapy. Eur Radiol [Internet]. 2013;23(12):3345–53. Available from: http://dx.doi.org/10.1007/s00330-013-2936-5
3. Foti PV, Privitera G, Piana S, Palmucci S, Spatola C, Bevilacqua R, et al. Locally advanced rectal cancer: Qualitative and quantitative evaluation of diffusion-weighted MR imaging in the response assessment after neoadjuvant chemo-radiotherapy. Eur J Radiol open [Internet]. 2016;3:145–52. Available from: https://pubmed.ncbi.nlm.nih.gov/27489868
4. Maas M, Nelemans PJ, Valentini V, Das P, Rödel C, Kuo L-J, et al. Long-term outcome in patients with a pathological complete response after chemoradiation for rectal cancer: a pooled analysis of individual patient data. Lancet Oncol [Internet]. 2010;11(9):835–44. Available from: http://dx.doi.org/10.1016/s1470-2045(10)70172-8
5. Liu Z, Zhang X-Y, Shi Y-J, Wang L, Zhu H-T, Tang Z, et al. Radiomics Analysis for Evaluation of Pathological Complete Response to Neoadjuvant Chemoradiotherapy in Locally Advanced Rectal Cancer. Clin Cancer Res [Internet]. 2017;23(23):7253–62. Available from: http://dx.doi.org/10.1158/1078-0432.ccr-17-1038
6. Enkhbaatar N-E, Inoue S, Yamamuro H, Kawada S, Miyaoka M, Nakamura N, et al. MR Imaging with Apparent Diffusion Coefficient Histogram Analysis: Evaluation of Locally Advanced Rectal Cancer after Chemotherapy and Radiation Therapy. Radiology [Internet]. 2018;288(1):129–37. Available from: http://dx.doi.org/10.1148/radiol.2018171804

7. Kalisz KR, Enzerra MD, Paspulati RM. MRI Evaluation of the Response of Rectal Cancer to Neoadjuvant Chemoradiation Therapy. RadioGraphics [Internet]. 2019;39(2):538–56. Available from: http://dx.doi.org/10.1148/rg.2019180075
8. Bassaneze T, Gonçalves JE, Faria JF, Palma RT, Waisberg J. Quantitative Aspects of Diffusion-weighted Magnetic Resonance Imaging in Rectal Cancer Response to Neoadjuvant Therapy. Radiol Oncol [Internet]. 2017;51(3):270–6. Available from: https://pubmed.ncbi.nlm.nih.gov/28959163
9. Ali SA, Amin DH, Abdelkhalek YI. Efficiency of whole-body 18F-FDG PET CT in detecting the cause of rising serum AFP level in post-therapeutic follow-up for HCC patients. Jpn J Radiol [Internet]. 2020;38(5):472–9. Available from: http://dx.doi.org/10.1007/s11604-020-00930-8
10. Tawfik MMH, Monib AM, Yassin A, Ali SA. Comparison between RECIST and PERCIST criteria in therapeutic response assessment in cases of lymphoma. Egypt J Radiol Nucl Med [Internet]. 2020;51(1). Available from: http://dx.doi.org/10.1186/s43055-020-00203-4
11. Ichikawa T, Erturk SM, Motosugi U, Sou H, Iino H, Araki T, et al. High-b Value Diffusion-Weighted MRI for Detecting Pancreatic Adenocarcinoma: Preliminary Results. Am J Roentgenol [Internet]. 2007;188(2):409–14. Available from: http://dx.doi.org/10.2214/ajr.05.1918
12. Qureshi PAAA, Aleem J, Mushtaq N, Noor MA, Niazi IK, Altaf MO, et al. Role of diffusion-weighted imaging in the evaluation of post-treatment tumor response in rectal carcinoma. Cureus. 2021;13(8).
13. HUANG WC, SHENG J, CHEN SY, LU JP. Differentiation between pancreatic carcinoma and mass-forming chronic pancreatitis: Usefulness of high b value diffusion-weighted imaging. J Dig Dis [Internet]. 2011;12(5):401–8. Available from: http://dx.doi.org/10.1111/j.1751-2980.2011.00517.x
14. Kartalis N, Lindholm TL, Aspelin P, Permert J, Albiin N. Diffusion-weighted magnetic resonance imaging of pancreas tumours. Eur Radiol [Internet]. 2009;19(8):1981–90. Available from: http://dx.doi.org/10.1007/s00330-009-1384-8
15. Gu J, Khong P-L, Wang S, Chan Q, Law W, Zhang J. Quantitative assessment of diffusion-weighted MR imaging in patients with primary rectal cancer: correlation with FDG-PET/CT. Mol imaging Biol [Internet]. 2010/09/25. 2011;13(5):1020–8. Available from: https://pubmed.ncbi.nlm.nih.gov/20872077
16. Curvo-Semedo L, Lambregts DMJ, Maas M, Beets GL, Caseiro-Alves F, Beets-Tan RGH. Diffusion-weighted MRI in rectal cancer: Apparent diffusion coefficient as a potential noninvasive marker of tumor aggressiveness. J Magn Reson Imaging [Internet]. 2012;35(6):1365–71. Available from: http://dx.doi.org/10.1002/jmri.23589
17. Blažić I, Maksimović R, Gajić M, Šaranović Đ. (2015). Apparent diffusion coefficient measurement covering complete tumor area better predicts rectal cancer response to neoadjuvant chemoradiotherapy. Croatian Medical Journal, 56(5), 460-469. Available from: http://

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4655931

18. Kim SH, Lee JM, Hong SH, Kim GH, Lee JY, Han JK, et al. Locally Advanced Rectal Cancer: Added Value of Diffusion-weighted MR Imaging in the Evaluation of Tumor Response to Neoadjuvant Chemo- and Radiation Therapy. Radiology [Internet]. 2009;253(1):116–25. Available from: http://dx.doi.org/10.1148/radiol.2532090027
19. Lambregts DMJ, Boellaard TN, Beets-Tan RGH. Response evaluation after neoadjuvant treatment for rectal cancer using modern MR imaging: a pictorial review. Insights Imaging [Internet]. 2019;10(1):15. Available from: https://pubmed.ncbi.nlm.nih.gov/30758688
20. van Heeswijk MM, Lambregts DMJ, Palm WM, Hendriks BMF, Maas M, Beets GL, et al. DWI for Assessment of Rectal Cancer Nodes After Chemoradiotherapy: Is the Absence of Nodes at DWI Proof of a Negative Nodal Status? Am J Roentgenol [Internet]. 2017;208(3):W79–84. Available from: http://dx.doi.org/10.2214/ajr.16.17117