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Original Article

MRI tumour regression grade in locally recurrent rectal cancer

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Abstract

Background: This study aimed to investigate the agreement between magnetic resonance tumour regression grade (mrTRG) and pathological regression grade (pTRG) in patients with locally recurrent rectal cancer (LRRC). Also, the reproducibility of mrTRG was investigated.

Methods: All patients with LRRC who underwent a resection between 2010 and 2018 after treatment with induction chemotherapy and neoadjuvant chemo(re)irradiation in whom a restaging MRI was available were retrospectively selected. All MRI scans were reassessed by two independent radiologists using the mrTRG, and the pTRG was reassessed by an independent pathologist. The interobserver agreement between the radiologists as well as between the radiologists and the pathologist was assessed with the weighted kappa test. A subanalysis was performed to evaluate the influence of the interval between imaging and surgery.

Results: Out of 313 patients with LRRC treated during the study interval, 124 patients were selected. Interobserver agreement between the radiologists was fair ($k = 0.28$) using a two-tier grading system (mrTRG 1–2 *versus* mrTRG 3–5). For the lead radiologist, agreement with pTRG was moderate ($k = 0.52$; 95 per cent c.i. 0.36 to 0.68) when comparing good (mrTRG 1–2 and Mandard 1–2) and intermediate/poor responders (mrTRG 3–5 and Mandard 3–5), and the agreement was fair between the other abdominal radiologist and pTRG ($k = 0.39$; 95 per cent c.i. 0.22 to 0.56). A shorter interval (less than 7 weeks) between MRI and surgery resulted in an improved agreement ($k = 0.69$), compared with an interval more than 7 weeks ($k = 0.340$). For the lead radiologist, the positive predictive value for predicting good responders was 95 per cent (95 per cent c.i. 71 per cent to 99 per cent), whereas this was 56 per cent (95 per cent c.i. 44 per cent to 66 per cent) for the other radiologist.

Conclusion: This study showed that, in LRRC, the reproducibility of mrTRG among radiologists is limited and the agreement of mrTRG with pTRG is low. However, a shorter interval between MRI and surgery seems to improve this agreement and, if assessed by a dedicated radiologist, mrTRG could predict good responders.

Introduction

In patients with locally advanced rectal cancer (LARC), the MRI-based tumour regression grade (mrTRG), a five-tier imaging-based scoring system based on the ability to distinguish between tumour and fibrosis, has proven to be reproducible among radiologists with a good interobserver agreement[1,2]. Moreover, mrTRG has proven to be a prognostic factor for disease-free (hazard ratio (HR) 3.28; 95 per cent c.i. 1.22 to 8.80) and overall survival (HR 4.40; 95 per cent c.i. 1.65 to 11.7) in these patients, although the agreement between mrTRG and pathological tumour regression grade (pTRG) seemed suboptimal[2,3].

It is unknown whether mrTRG can be used in treatment decision-making for patients presenting with locally recurrent rectal cancer (LRRC). LRRC requires intensive neoadjuvant treatment comprising chemo(re)irradiation followed by extensive surgery[4–8]. The goal of surgery is to achieve a resection with clear resection margins, as this is the most important prognostic factor for local recurrence-free and overall survival[9–11]. Previous studies from our group showed that the addition of induction chemotherapy to the neoadjuvant treatment in patients with LRRC enhances tumour response[12,13]. In addition, it was demonstrated that pTRG is an independent predictive variable for long-term oncological outcomes in patients with LRRC[13]. Obviously, pTRG can only be obtained postoperatively, and thus does not offer the opportunity to adapt treatment strategies. In that perspective, mrTRG may be more suitable in the decision-making process, as it provides an opportunity to consider non-operative therapy in cases of clinical complete response. Therefore, this study aimed to investigate the agreement between mrTRG and pTRG in a retrospective cohort of patients with LRRC treated with

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induction chemotherapy and chemo(re)irradiation. Also, interobserver agreement between radiologists for mrTRG assessment was evaluated.

Methods

Patients

All patients with LRRC who underwent a resection in the Catharina Hospital, Eindhoven, the Netherlands, a national tertiary referral centre for LRRC, are prospectively collected in a database. All consecutive patients with LRRC who underwent a resection with curative intent between 2010 and 2018 after treatment with induction chemotherapy followed by neoadjuvant chemo(re) irradiation were retrospectively selected. Patients for whom the baseline or restaging MRI was not available for reassessment were excluded. The study was waived by the local medical ethics committee (Medical Research Ethics Committees United Nieuwegein, registration number: W19.031).

Neoadjuvant and surgical treatment

At the Catharina Hospital, Eindhoven, the Netherlands, all patients with LRRC received neoadjuvant chemo(re)irradiation. In this selected cohort, all patients received induction chemotherapy before this. Induction chemotherapy generally consisted of four cycles of CAPOX (capecitabine and oxaliplatin) or six cycles of FOLFOX (leucovorin, 5-fluorouracil, oxaliplatin). Initially, induction chemotherapy was reserved for patients with irresectable or marginally resectable disease. Gradually, the administration of induction chemotherapy became more common practice and finally became the local standard of care in 2016[13]. In radiotherapy-naïve patients, full-course radiotherapy was delivered with a cumulative dose of 50–50.4 Gy. In patients who previously received pelvic radiotherapy, radiotherapy was delivered with a cumulative dose of 30–30.6 Gy. The concomitant chemotherapy agent was capecitabine (825 mg/m^2 twice a day on radiotherapy days).

The type and extent of the surgery was left to the discretion of the treating surgical oncologist. Intraoperative electron beam radiotherapy was delivered in a dose of 10–12.5 Gy when there were no clear resection margins or when there was tumour adherence to unresectable structures.

Radiological and pathological assessment

An MRI was performed at baseline, after finishing induction chemotherapy, and 4–6 weeks after completion of neoadjuvant (chemo)radiotherapy and consisted of at least T2-weighted axial, coronal, and sagittal planes performed on a 1.5T or 3T MRI system. MRIs were performed either in the tertiary referral hospital or in the referring hospital and were reassessed by an experienced abdomen radiologist with specific expertise in LARC and LRRC. Response was scored according to the mrTRG: mrTRG 1, low signal fibrosis only, no tumour signal; mrTRG 2, more than 75 per cent fibrosis and minimal tumour signal intensity; mrTRG 3, 50 per cent tumour/fibrosis; mrTRG 4, less than 25 per cent fibrosis, predominant tumour signal; and mrTRG 5, no fibrosis[2]. The radiologist was trained using mrTRG in primary tumours in a training programme, including post-neoadjuvant treatment reporting, conducted by leader experts in this field[2]. To evaluate the reproducibility of the mrTRG in LRRC a second experienced abdomen radiologist, who was also trained, independently assessed all imaging using the mrTRG. The radiologists were blinded for the pathological assessment and the clinical outcomes.

All specimens were revised by a specialized pathologist who was blinded to the radiological assessment as well as the clinical outcomes. On the primary assessment, in general, at least one section per centimetre maximum tumour bed diameter was sampled. The pathological response grade (pTRG) was scored according to the Mandard classification: pTRG 1, complete response; pTRG 2, isolated cell nests; pTRG 3, more residual cancer cells but fibrosis still predominates; pTRG 4, residual cancer outgrowing fibrosis; and pTRG 5, absence of regressive changes[14].

Outcomes of interest

Outcomes of interest were the agreement between mrTRG and pTRG, and the interobserver radiologic agreement. In addition, a subanalysis was performed to assess the agreement between mrTRG and pTRG in patients with a long interval *versus* a short interval between MRI and surgery, based on median interval values.

Statistical analysis

Continuous data were reported as median (interquartile range; i.q.r.) and categorical data as count (percentage). The strength of agreement between mrTRG after completion of neoadjuvant treatment and the pathological response rate was assessed using the weighted *kappa* test (k value < 0.20, poor agreement; k value = 0.21–0.40, fair agreement; k value = 0.41–0.60, moderate agreement; k value = 0.61–0.80, good agreement; and k value = 0.81–1.00, very good agreement). This analysis was performed using the five categories of tumour regression, as well as using a two-tier regression scale, adapted from these standardized five-tier regression scales (Mandard 1–2 (good responders) *versus* Mandard 3–5 (intermediate/poor responders) and mrTRG 1–2 *versus* mrTRG 3–5).

The interobserver variability between the two radiologists regarding the assessment of mrTRG was analysed using the weighted *kappa* test, considering the five-tier regression scale as well as the two-tier regression scale (mrTRG 1–2 *versus* mrTRG 3–5).

Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of mrTRG with regard to the pTRG were calculated from two-by-two contingency tables using predefined categories (mrTRG 1–2 *versus* mrTRG 3–5, and pTRG 1–2 *versus* pTRG 3–5).

All statistical analyses were performed using SPSS® version 25.0 for Windows (IBM, Armonk, New York, USA).

Results

Patients

A total of 313 patients had a resection with curative intent for LRRC between 2010 and 2018, of whom 132 received induction chemotherapy followed by chemo(re)irradiation. Eight patients were excluded because no baseline or restaging MRI was available, resulting in 124 selected patients (*Fig. 1*). Demographics, tumour characteristics, and details about the treatment are shown in *Table 1*. The median (i.q.r.) interval between the end of chemoradiotherapy and surgery was 13 (11–15) weeks. Median (i.q.r.) interval between post-chemoradiotherapy MRI and surgery was 7 (5–8) weeks.

With respect of the pathology assessment in patients with a good response (Mandard 1–2), in 32 of 39 cases (82 per cent) at least one section per centimetre maximum tumour bed diameter was sampled, whereas in 5 patients (10 per cent) this could not be reassessed due to incompleteness of the report,

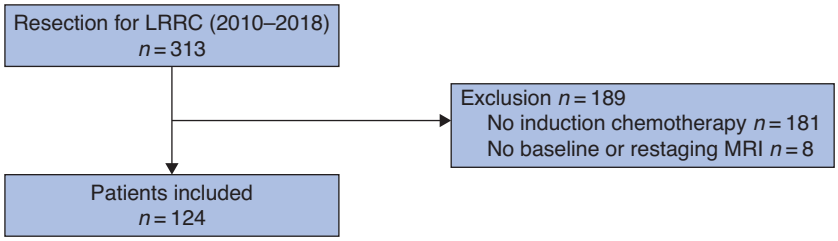

Fig. 1 Flowchart showing patient selection

LRRC, locally recurrent rectal cancer.

Table 1 Demographics and tumour characteristics

	Total (N=124) N (%)
Gender	
Female	36(29)
Male	88(71)
Age at resection (years)	
Median [IQR]	65 [58-71]
Neoadjuvant radiotherapy primary tumour	
None	31(25)
Radiotherapy	33(27)
Chemoradiotherapy	60(48)
Surgical procedure primary tumour	
Rectosigmoid resection	16(13)
LAR	63(51)
APR	45(36)
Adjuvant therapy primary tumour	
None	107(86)
Chemotherapy	15(12)
Radiotherapy	2(2)
Number local recurrence	
First	108(87)
Second/third	16(13)
Multifocality	
Yes	27(22)
No	97(78)
Number of involved compartments	
1	25(20)
2	57(46)
3	25(20)
4	17(14)
Neoadjuvant radiotherapy recurrence	
(chemo)radiotherapy	20(16)
(chemo)reirradiation	104(84)
Surgical procedure recurrence	
LAR	13(11)
APR	15(12)
Multivisceral resection	72(58)
Non-visceral resection	24(19)
Intraoperative electron beam radiotherapy	
Yes	103(83)
No	21(17)
Interval between end chemoradiotherapy and surgery (weeks)	
Median [IQR]	13 [11-15]
Interval between last MRI and surgery (weeks)	
Median [IQR]	7 [5-8]
Resection margin	
R0	80(65)
R1	41(33)
R2	3(2)
Histology*	
Adenocarcinoma	101(98)
Mucinous carcinoma	2(2)

* Not applicable for patients with a complete pathological response. i.q.r., interquartile range; LAR, low anterior resection; APR, abdominal perineal resection.

Table 2 Comparison between mrTRG and pTRG

Two-tier grading system	pTRG‡			
	Good responders (1–2)	Intermediate/poor responders (3–5)	Total	*k* value
mrTRG*				
Good responders (1–2)	18§	1	19	0.52
Intermediate/poor responders (3–5)	21	84	105	
Total	39	85¶	124	
mrTRG†				
Good responders (1–2)	25§	20	45	0.39
Intermediate/poor responders (3–5)	14	65¶	79	
Total	39	85	124	

Five-tier grading system	pTRG‡						
	1	2	3	4	5	Total	*k* value
mrTRG*							
1	4	0	0	0	0	4	0.30
2	8	6	1	0	0	15	
3	6	7	21	7	1	42	
4	3	1	14	15	3	36	
5	0	4	15	7	1	27	
Total	21	18	51	29	5	124	
mrTRG†							
1	3	4	1	0	0	8	0.25
2	11	7	12	6	1	37	
3	7	4	12	8	0	31	
4	0	0	10	6	0	16	
5	0	3	16	9	4	32	
Total	21	18	51	29	5	124	

*Lead radiologist. †Second radiologist 2. ‡pTRG graded according to Mandard. §True positive. ¶True negative. mrTRG, magnetic resonance tumour regression grade; pTRG, pathological regression grade.

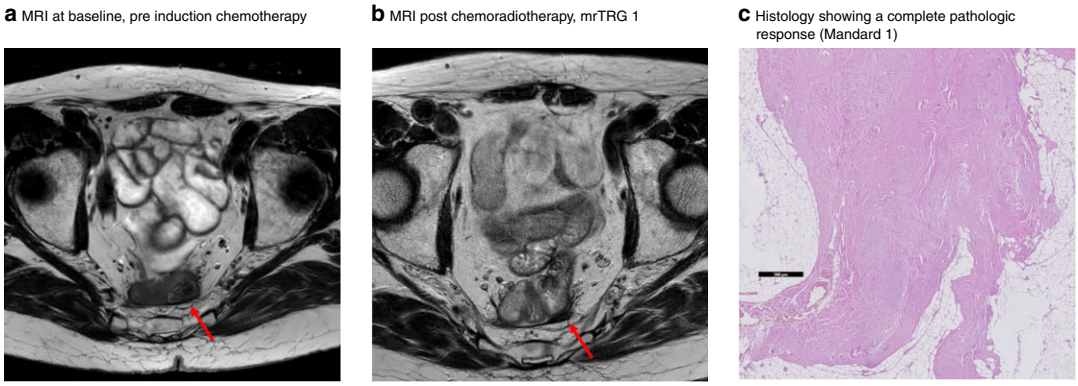

Fig. 2 MRI at baseline and after chemoradiotherapy showing a complete radiological response (mrTRG 1) and the corresponding histology imaging showing a complete response (pTRG 1). In this case, restaging was performed at less than 7 weeks. mrTRG, magnetic resonance tumour regression grade; pTRG, pathologic regression grade.

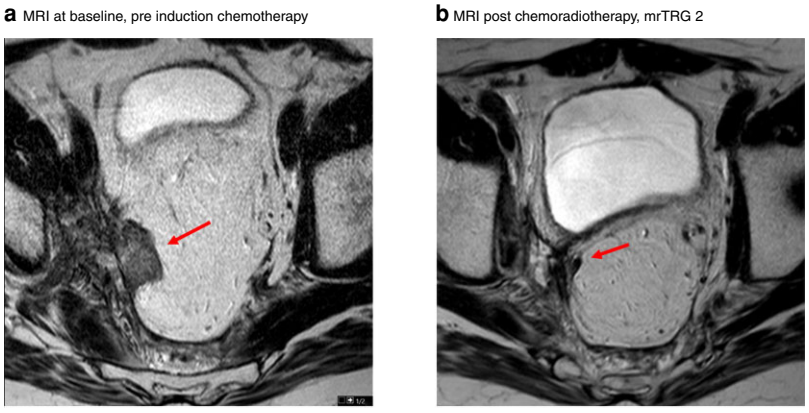

Fig. 3 MRI at baseline and after chemoradiotherapy showing a near complete radiological response (mrTRG 2). In this case, restaging was performed at less than 7 weeks. mrTRG, magnetic resonance tumour regression grade.

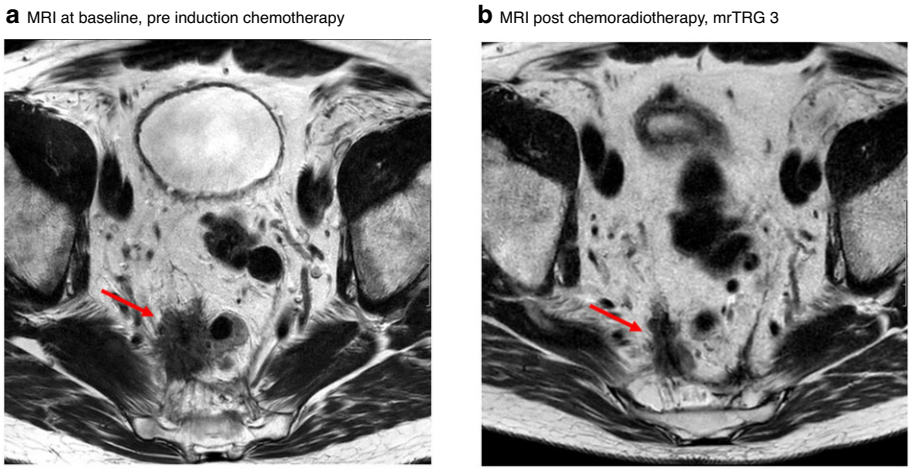

Fig. 4 MRI at baseline and after chemoradiotherapy showing a moderate radiological response (mrTRG 3). In this case, restaging was performed at more than 7 weeks. mrTRG, magnetic resonance tumour regression grade.

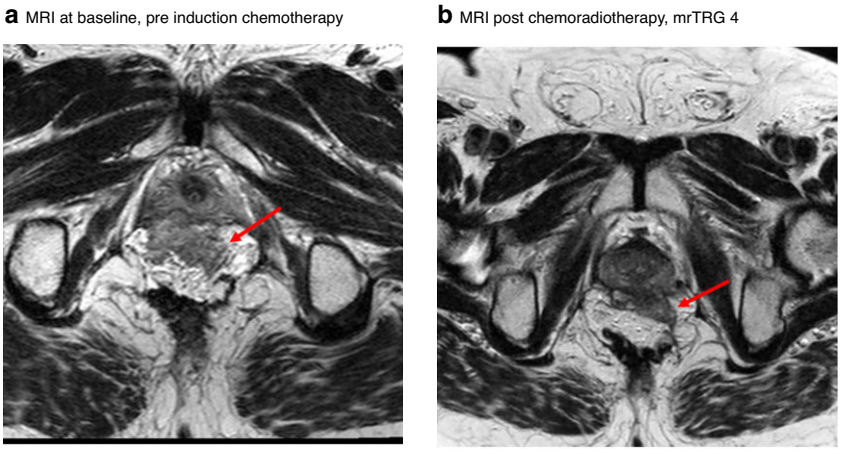

Fig. 5 MRI at baseline and after chemoradiotherapy showing a slight radiological response (mrTRG 4). In this case, restaging was performed at more than 7 weeks. mrTRG, magnetic resonance tumour regression grade.

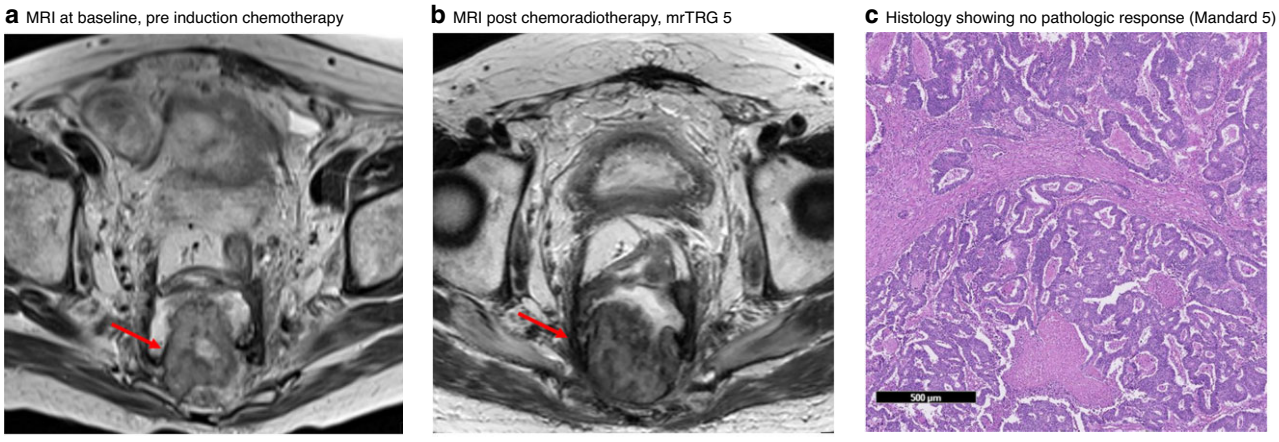

Fig. 6. MRI at baseline and after chemoradiotherapy showing no radiological response (mrTRG 5) and the corresponding histology imaging showing no regressive changes (pTRG 5). In this case, restaging was performed at less than 7 weeks. mrTRG, magnetic resonance tumour regression grade; pTRG, pathologic regression grade.

Table 3 Agreement between radiologists

	mTRG*					
	1	2	3	4	5	Total
mrTRG†						
1	2	2	0	0	0	4
2	3	7	5	0	0	15
3	3	19	11	5	4	42
4	0	6	14	9	7	36
5	0	3	1	2	21	27
Total	8	37	31	16	32	124

*Second radiologist. †Lead radiologist. mrTRG, magnetic resonance tumour regression grade.

and in two patients less than one section per centimetre tumour diameter was sampled.

Agreement mrTRG–pTRG

There was a fair level of agreement ($k = 0.30$; 95 per cent c.i. 0.20 to 0.40) between the lead radiologist and the pathologist when using the five-tier grading system, and a moderate level of agreement ($k = 0.52$; 95 per cent c.i. 0.36 to 0.68) when comparing good (mrTRG 1–2 and Mandard 1–2) and intermediate/poor responders (mrTRG 3–5 and Mandard 3–5). *Table 2* shows the agreement between the radiologists and the pTRG using the two-tier grading system, and the five-tier grading system. *Figures 2–6* show MRI imaging of cases in which the mrTRG assessment corresponded with the pTRG. *Figures 2* and *6* also show the corresponding histology images.

Using the two-tier grading system, assessment of the agreement between pTRG and mrTRG in patients with a long interval between MRI and surgery (more than 7 weeks, $n = 61$) resulted in a fair agreement ($k = 0.34$, 95 per cent c.i. 0.12 to 0.56), whereas the agreement was good in patients with a short interval (7 weeks or less; $n = 63$; $k = 0.69$, 95 per cent c.i. 0.49 to 0.90). The five-tier system resulted in k values of 0.26 and 0.32 for long and short intervals respectively, and therefore seems less suitable for clinical use.

When using the two-tier grading system, the lead radiologist underestimated the presence of residual tumour in 1 per cent of cases, correctly assessed the residual tumour in 82 per cent, and overestimated the presence of residual tumour in 17 per cent of cases.

The agreement between the other abdomen radiologist and the pTRG was fair ($k = 0.25$; 95 per cent c.i. 0.14 to 0.35) using the five-tier grading, as well as when using the two-tier grading system ($k = 0.39$; 95 per cent c.i. 0.22 to 0.56) (*Table 2*).

Interobserver agreement

The mrTRG scores for both radiologists are shown in *Table 3*. The interobserver agreement between the two radiologists was moderate when using the five-tier regression scale ($k = 0.44$; 95 per cent c.i. 0.34 to 0.54) and fair when using the adjusted regression scale comparing good responders (mrTRG 1-2) with intermediate/poor responders (mrTRG 3–5, $k = 0.28$; 95 per cent c.i. 0.12 to 0.44).

Sensitivity, specificity, PPV, and NPV

Overall, sensitivity was 46 per cent (95 per cent c.i. 30 per cent to 63 per cent), specificity was 99 per cent (95 per cent c.i. 94 per cent to 100 per cent), PPV was 95 per cent (95 per cent c.i. 71 per cent to 99 per cent), and NPV was 80 per cent (95 per cent c.i. 75 per cent to 84 per cent) for the lead radiologist for predicting a good response (Mandard 1–2).

For the other abdomen radiologist, sensitivity was 64 per cent (95 per cent c.i. 47 per cent to 79 per cent), specificity was 76 per cent (95 per cent c.i. 66 per cent to 85per cent), PPV was 56 per cent (95 per cent c.i. 44 per cent to 66 per cent), and NPV was 82 per cent (95 per cent c.i. 75 per cent to 88 per cent) for predicting a good response (Mandard 1–2).

Discussion

This retrospective study aimed to investigate the correlation between the mrTRG and pTRG in patients with LRRC after treatment with induction chemotherapy and chemo(re) irradiation. A fair to moderate agreement between mrTRG and pTRG was observed, suggesting that the predictive value for pTRG is limited. Moreover, the interobserver agreement between the two radiologists was fair to moderate, indicating low reproducibility. However, there was a good agreement between the radiological assessment and pathology when the interval between MRI and surgery is short (≤7 weeks), and when assessed by the lead radiologist, mrTRG can safely predict good responders (PPV 95 per cent).

Radiological evaluation of LRRC is often difficult due to postoperative changes in anatomy, previous radiotherapy, and the presence of fistula and/or abscesses. This hampers not only the initial assessment, but also makes evaluation of the mrTRG score more difficult. Despite those difficulties, the agreement between mrTRG and pTRG in this study ($k = 0.30$ and $k = 0.25$ for the lead radiologist and the other abdomen radiologist respectively) was comparable to the literature on LARC ($k = 0.24$)[3].

Surgery for LRRC generally involves resection of multiple organs as well as soft tissue, bony, and vascular resections, resulting in complex procedures and the necessity of reconstructive surgery. This is associated with a high postoperative morbidity rate and an impaired quality of life[10,15,16]. Recently, it was reported that patients with LRRC with a pathological complete response have excellent long-term survival[13]. Preoperative prediction of the pathological response potentially provides an opportunity to adopt a non-operative treatment strategy in patients with a clinical complete response, which may be very valuable in the light of the complexity and impact on quality of life of LRRC surgery. To select patients with a clinical complete response, a high PPV is especially important, as a false-positive prediction can lead to undertreatment with possible disastrous consequences. In the present study, the mrTRG had a PPV for a good response of 95 per cent when assessed by the lead radiologist; underestimation of the presence of residual tumour occurred in only one patient. This suggest that the mrTRG score has the potential to predict good responders.

However, in the present study overstaging was, as in LARC, much more frequent; in 17 per cent of patients the presence of residual tumour was overestimated when using mrTRG[17]. In LARC, endoscopy and a digital exam may aid in assessing the response[18]. However, in LRRC, these diagnostic modalities are usually not sufficient due to the location and/or extent of the tumour and decisions therefore have to be made solely based on the assessment of the MRI. An MR grading system incorporating T2-weighted as well as diffusion-weighted imaging (DWI) might be able to reduce overstaging and consequently improve the selection of complete responders. Although DWI has a greater vulnerability to susceptibility artefacts and careful interpretation of T2 shine-through effect is required, it has proven to improve

the sensitivity of the mrTRG score without decreasing the specificity in restaging LARC[19–21]. Such a combined grading system has recently been proposed in patients with LARC and could be the focus of future research in LRRC[22].

The interval between MRI and surgery may also play an important role in over- and under-staging. As shown in this study, the agreement between mrTRG and pTRG was superior in cases with an interval of 7 weeks or less compared with the agreement in cases with an interval of more than 7 weeks. This is consistent with previous studies that showed, in LARC, that a shorter interval between MRI and surgery resulted in a stronger association between mrTRG and pTRG[23]. The length of interval may particularly play a role in mrTRG 3 cases. In these cases, a long interval may provide an opportunity for a continuation of response, or, although rare, progression of disease. Ideally, mrTRG should therefore be assessed shortly before surgery.

The interobserver variability between radiologists was moderate when using the five-tier grading, which is comparable to what was found in a study performed by 35 radiologists assessing the mrTRG in patients with LARC[1]. However, when using the two-tier regression scale, the agreement was only fair. This indicates suboptimal reproducibility of the mrTRG.

The level of agreement between the lead radiologist and the pTRG, and the other abdomen radiologist and the pTRG differed; the agreement was moderate for the lead radiologist, whereas this was fair for the other abdominal radiologist. Although both are experienced abdominal radiologists, the lead radiologist has specific expertise in LARC and LRRC and is the main radiologist responsible for the weekly LARC/LRRC multidisciplinary team (MDT) meeting. The presence of an MDT is crucial in the treatment of patients with colorectal cancer, as it improves their outcome[24]. Moreover, MDT discussion improves the accuracy of MRI in staging rectal cancer[25–27]. It is reasonable to assume that more intensive involvement of the radiologist in the LARC/LRRC MDT improved the accuracy of the restaging assessments. For example, through participation in the MDT, the radiologist receives feedback from the discussion of the pathology of postoperative patients, strengthening the learning curve. This may explain the difference in agreement, in favour of the lead radiologist. Additionally, refining the definitions of the categories of tumour regression, especially in mucinous and fibrotic tumours, may contribute to improving the radiologist's performance.

This study has several limitations. mrTRG was only assessed by two radiologists. Ideally, this assessment would have been performed by a larger group. However, LRRC is rare and surgical treatment is centralized in only a small number of tertiary referral centres, and even in these centres the radiological expertise is usually limited to one or two radiologists. In addition, the interval between the MRI and surgery was long, which may have negatively influenced the agreement. Moreover, although pathological assessment is the 'gold standard' for determining response, and Mandard provides a high accuracy in predicting prognosis, variable reproducibility has been reported[28,29]. The strength of this study is that it is the first study assessing mrTRG in patients with LRRC. Moreover, the size of this homogenous cohort of patients with LRRC is unique with a large series of patients analysed.

According to the present results, mrTRG can predict a good response after neoadjuvant treatment with chemotherapy and chemoradiotherapy for LRRC when assessed by an experienced, dedicated, and trained radiologist. However, the reproducibility of mrTRG between radiologists is limited and the agreement between mrTRG and pTRG is low in cases with a long interval between MRI and surgery. Therefore, mrTRG cannot simply be used as a predictor for pTRG, and treatment decision-making during the MDT cannot yet be based on the mrTRG. Further studies are needed to evaluate the optimal timing of the MRI, the prognostic value of mrTRG, and the value of mrTRG in combination with other imaging modalities such as PET/CT in LRRC.

Disclosure. The authors declare no conflict of interest.

Data availability

The data generated and analysed during the present study are available from the corresponding author on reasonable request.

References

1. Siddiqui MRS, Gormly KL, Bhoday J, Balyansikova S, Battersby NJ, Chand M *et al.* Interobserver agreement of radiologists assessing the response of rectal cancers to preoperative chemoradiation using the MRI tumour regression grading (mrTRG). *Clin Radiol* 2016;**71**:854–862
2. Patel UB, Taylor F, Blomqvist L, George C, Evans H, Tekkis P *et al.* Magnetic resonance imaging-detected tumor response for locally advanced rectal cancer predicts survival outcomes: MERCURY experience. *J Clin Oncol* 2011;**29**:3753–3760
3. Sclafani F, Brown G, Cunningham D, Wotherspoon A, Mendes LST, Balyasnikova S *et al.* Comparison between MRI and pathology in the assessment of tumour regression grade in rectal cancer. *Br J Cancer* 2017;**117**:1478–1485
4. Bosman SJ, Holman FA, Nieuwenhuijzen GAP, Martijn H, Creemers GJ, Rutten HJT. Feasibility of reirradiation in the treatment of locally recurrent rectal cancer. *Br J Surg* 2014;**101**:1280–1289
5. van der Meij W, Rombouts AJM, Rutten H, Bremers AJA, De Wilt JHW. Treatment of locally recurrent rectal carcinoma in previously (chemo)irradiated patients: a review. *Dis Colon Rectum* 2016;**59**:148–156
6. Nielsen MB, Laurberg S, Holm T. Current management of locally recurrent rectal cancer. *Color Dis* 2011;**13**:732–742
7. Vermaas M, Ferenschild F, Verhoef C, Nuyttens J, Wiggers T, Marinelli A *et al.* Pre-operative radiotherapy improves outcome of multimodality treatment in recurrent rectal cancer. *Ann Surg Oncol* 2006;**11**:S108
8. Glynne-Jones R, Wyrwicz L, Tiret E, Brown G, Rö C, Cervantes A *et al.* Rectal cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol.* 2017;**28**(Suppl 4):iv22–iv40
9. Alberda WJ, Verhoef C, Schipper MEI, Nuyttens JJ, Rothbarth J, De Wilt JHW *et al.* The importance of a minimal tumor-free resection margin in locally recurrent rectal cancer. *Dis Colon Rectum* 2015;**58**:677–685
10. Nielsen M, Rasmussen P, Pedersen B, Hagemann-Madsen R, Lindegaard J, Laurberg S. Early and late outcomes of surgery for locally recurrent rectal cancer: a prospective 10-year study in the total mesorectal excision era. *Ann Surg Oncol* 2015;**22**:2677–2684
11. Westberg K, Palmer G, Hjern F, Johansson H, Holm T, Martling A. Management and prognosis of locally recurrent rectal cancer – a national population-based study. *Eur J Surg Oncol* 2018;**44**:100–107
12. van Zoggel DMGI, Bosman SJ, Kusters M, Nieuwenhuijzen GAP, Cnossen JS, Creemers GJ *et al.* Preliminary results of a cohort study of induction chemotherapy-based treatment for locally recurrent rectal cancer. *Br J Surg* 2018;**105**:447–452

13. Voogt ELK, van Zoggel DMGI, Kusters M, Nieuwenhuijzen GAP, Bloemen JG, Peulen HMU *et al.* Improved outcomes for responders after treatment with induction chemotherapy and chemo(re)irradiation for locally recurrent rectal cancer. *Ann Surg Oncol* 2020;**27**:3503–3513
14. Mandard AM, Dalibard F, Mandard JC, Marnay J, Henry-Amar M, Petiot JF *et al.* Pathologic assessment of tumor regression after preoperative chemoradiotherapy of esophageal carcinoma. Clinicopathologic correlations. *Cancer* 1994 ;**73**:2680–2686
15. Glyn T, Frizelle F. Quality of life outcomes in patients undergoing surgery for locally recurrent rectal cancer. *Semin Colon Rectal Surg* 2020;**31**:100767
16. Esnaola NF, Cantor SB, Johnson ML, Mirza AN, Miller AR, Curley SA *et al.* Pain and quality of life after treatment in patients with locally recurrent rectal cancer. *J Clin Oncol* 2002;**20**:4361–4367
17. Lambregts DMJ, Boellaard TN, Beets-Tan RGH. Response evaluation after neoadjuvant treatment for rectal cancer using modern MR imaging: a pictorial review. *Insights Imaging* 2019;**10**:15
18. Habr-Gama A, Perez RO, Wynn G, Marks J, Kessler H, Gama-Rodrigues J. Complete clinical response after neoadjuvant chemoradiation therapy for distal rectal cancer: characterization of clinical and endoscopic findings for standardization. *Dis Colon Rectum* 2010;**53**:1692–1698
19. Lambregts DMJ, Vandecaveye V, Barbaro B, Bakers FCH, Lambrecht M, Maas M *et al.* Diffusion-weighted MRI for selection of complete responders after chemoradiation for locally advanced rectal cancer: a multicenter study. *Ann Surg Oncol* 2011;**18**:2224–2231
20. 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* 2009;**253**:116–125
21. Chandramohan A, Siddiqi UM, Mittal R, Eapen A, Jesudason MR, Ram TS *et al.* Diffusion weighted imaging improves diagnostic ability of MRI for determining complete response to neoadjuvant therapy in locally advanced rectal cancer. *Eur J Radiol Open* 2020;**7**:100223
22. Lee MA, Cho SH, Seo AN, Kim HJ, Shin KM, Kim SH *et al.* Modified 3-point MRI-based tumor regression grade incorporating DWI for locally advanced rectal cancer. *Am J Roentgenol* 2017;**209**: 1247–1255
23. West MA, Dimitrov BD, Moyses HE, Kemp GJ, Loughney L, White D *et al.* Timing of surgery following neoadjuvant chemoradiotherapy in locally advanced rectal cancer – a comparison of magnetic resonance imaging at two time points and histopathological responses. *Eur J Surg Oncol* 2016;**42**: 1350–1358
24. Munro A, Brown M, Niblock P, Steele R, Carey F. Do multidisciplinary team (MDT) processes influence survival in patients with colorectal cancer? A population-based experience. *BMC Cancer* 2015;**15**:686
25. Yu L, Wang L, Tan Y, Hu H, Shen L, Zheng S *et al.* Accuracy of magnetic resonance imaging in staging rectal cancer with multidisciplinary team: a single-center experience. *J Cancer* 2019;**10**:6594–6598
26. Ye YJ, Shen ZL, Sun XT, Wang ZF, Shen DH, Liu HJ *et al.* Impact of multidisciplinary team working on the management of colorectal cancer. *Chin Med J* 2012;**125**:172–177
27. Swellengrebel HAM, Peters EG, Cats A, Visser O, Blaauwgeers HGT, Verwaal VJ *et al.* Multidisciplinary discussion and management of rectal cancer: a population-based study. *World J Surg* 2011;**35**:2125–2133
28. Lindebjerg J, Hansborg N, Ploen J, Rafaelsen S, Jorgensen JCR, Jakobsen A. Factors influencing reproducibility of tumour regression grading after high-dose chemoradiation of locally advanced rectal cancer. *Histopathology* 2011;**59**:18–21
29. Chetty R, Gill P, Govender D, Bateman A, Chang HJ, Deshpande V *et al.* International study group on rectal cancer regression grading: interobserver variability with commonly used regression grading systems. *Hum Pathol* 2012;**43**:1917–1923