Diffusion-weighted MRI and ADC value: their role in detection of metastatic lymph nodes in patients with primary rectal cancer

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Authors: A. Ferrari¹, F. Schirru¹, G. F. Satta¹, A. Restivo¹, F. Scintu¹, L. Zorcolo¹, M. Cerci¹, J. Suri², L. Saba¹, L. Zorcolo/IT, Pocatello, CA/US
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Purpose

Introduction

Rectal cancer is a malignant tumour that originates from the rectal mucosa epithelium. Typically it is the result of malignant degeneration of polyps, which represent pre-cancerous lesion in about 80% of cases. The rectum is the most common site of colorectal cancer being affected in 35-40% of cases [1].

It is the third most frequently diagnosed cancer in men and the second among women, with 1.4 million cases in 2012. The incidence of sporadic rectal cancer increases with age, especially after 45-50 years. The mortality rate is less than the incidence. In 2012 were estimated 694'000 deaths (8.5% of all deaths from cancer) [2].

The stage evaluation in pre-surgery management is now essential for the most appropriate therapeutic choice, both for "early" neoplasms (Tis, T1, T2) and for locally advanced tumours. Furthermore the study after neoadjuvant chemo-radiotherapy is also now essential to evaluate therapy response, and after surgical treatment to evaluate the presence of local recurrence.

The most important tumour features that influence treatment decisions are: the parietal infiltration depth, the involvement of the mesorectal space and the mesorectal fascia, the possible involvement of regional lymph nodes [3].

The therapeutic approach to rectal cancer is primarily surgical, with curative or palliative purpose, and should be early: should not spend more than 4 weeks from diagnosis.

In recent years, in locally advanced disease (stages # T3-T4), surgery is associated with a chemo-radiotherapy neoadjuvant treatment, which led to a significant increase in survival and to a decrease of local recurrences [4].

Preoperative chemoradiotherapy has allowed a statistically significant reduction of local recurrence (from 27 to 11%), with pathological complete response rates of about 10% and a major possibility to preserve the sphincter [5,6]. In addition, the percentage of conservative interventions, rather than demolition interventions, and post-operative mortality has fallen from 10 to 2% [7, 8]

The importance of lymph node staging

The nodal stage seriously influences the prognosis of rectal cancer and its treatment.
The presence of lymph node metastases is a negative prognostic factor for both the 5-year survival and for local recurrence.

A study by Gunderson et al. [9] showed that the 5-year survival for tumours with N0 is 73%, 65% in those with N1 and 52% in N2. The survival of the N categories is further influenced by the T-stage, decreasing with the increasing infiltration.

In the same study, the percentage of patients who developed local recurrence at 5 years after diagnosis is 9% for N0 tumours, 10% for N1 and 14% for N2, while those who develop distant metastases are 20% for N0 tumours, 29% for N1 and 42% for N2.

For N+ tumours it is recommended preoperative radiotherapy followed by surgery with TME (tumour mesorectal excision): this protocol led to a decrease in local recurrence [4, 5, 10].

It is well known that the ERUS (endorectal ultrasound), CT and MRI are not sufficiently accurate in the staging of lymph node status in rectal cancer with sensitivity and specificity ranging respectively from 55% to 67% and from 74% to 78% [11], and with slightly better performance for the RM after chemo-radiotherapy [12, 13].

The characteristics that should arouse suspicion in magnetic resonance imaging are the size, but above all the morphology, of the lymph node and the inhomogeneous signal [14].

In the effort to improve diagnostic accuracy, the research has moved to lymphotropic contrast media and especially on imaging Diffusion-weighted (DWI).

The aim of our study is to demonstrate the diagnostic value of DWI and ADC value in the detection of metastatic lymph nodes in patients with primary rectal cancer.
Methods and materials

This retrospective study took into account 20 patients who performed an MRI exam of the rectum for local primitive tumour staging in the period between January 2016 and July 2016.

Of these, 11 patients were excluded from the study for the following reasons:

- 5 patients made neoadjuvant chemotherapy and radiotherapy;
- 6 patients did not carry out surgery.

So 9 patients (7 males and 2 females; average age 70 years, ranging from 52-86 years) were analysed in this study.

MR imaging

All MRI examinations were performed with an MRI of 1.5T (Philips Achieva; Philips Healthcare Amsterdam, Holland) with body phased-array coil. The examinations were completed with intravenous administration of paramagnetic contrast Medium (Gadovist 1.0 mmol/ml, Bayer, dosing 0.1 ml/kg body weight).

The MRI protocol included Turbo Spin Echo (TSE) T2-weighted and Spin Echo (SE) T1-weighted sequences, with and without suppression of the fat signal.

The scout sequences were acquired on axial, sagittal and coronal plans, and used in order to obtain sagittal T2-W sequences. The images in the sagittal had been used for obtain oblique axial images. The images in the oblique axial and oblique coronal plane (T1-weighted and T2-weighted) were obtained, respectively, according to an orthogonal plane and a parallel plane to the long axis of the rectum.

The post-contrast examination had been completed with volumetric gradient echo T1 Fat Sat sequence (Thrive).

Oblique axial diffusion sequences (DWI) were obtained with Single Shot Echo Planar with free breathing. Parameters, such as thickness and gap layer, were maintained equal to the parameters of the T2 sequences. The b values used were b = 50, b = 600 and b = 1000.

The total examination time was approximately about 25 minutes.
Quantitative analysis

Regional lymph nodes were evaluated in the axial T2 sequences by an expert radiologist and two residents.

The ADC value was calculated with OsiriX software (Pixmeo SARL) with plugins ADCmap (Programming: Brian Hargreaves, Kyung Sung, Qiu Deqiang.). The ROIs were been positioned in the central portion of lymph nodes with a diameter ≥ 2 mm, in order to avoid signal interference from nearby structures or partial volume effects.

The ADC value was measured by operators in each node.
Standard reference

To facilitate a proper pairing of the ADC value and histological report, the nodes were categorized into 4 groups according to the surgical report: peritumoral, perirectal, pericolic and around inferior mesenteric artery.

The histopathological report indicated the number of the nodes collected and the number of pathological nodes for each group. When all the collected lymph nodes were positive, they were considered positive also in the MR image; the same was done when all the collected lymph nodes were negative. In the case of mixed results, the lymph nodes are considered suspicious according to size criteria and inhomogeneity of the T2 signal.

Statistic analysis

To obtain an optimum cut-off value for discriminating pathological and non-pathological nodes was performed a ROC curve analysis, applied to the average values of the ADC.

The areas under the ROC curve (AUC) and the confidence intervals of 95% were calculated to determine the statistical significance of the ADC value. All statistical analyses were performed using SPSS software (IBM Corp., Armonk, NY, USA). A P value less than 0.05 was considered statistically significant.
### Images for this section:

<table>
<thead>
<tr>
<th>Parameters</th>
<th>T2W</th>
<th>DWI</th>
</tr>
</thead>
<tbody>
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<td>Repetition Time (TR)</td>
<td>3635 ms</td>
<td>5400 ms</td>
</tr>
<tr>
<td>Echo Time (TE)</td>
<td>90 ms</td>
<td>93 ms</td>
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<tr>
<td>Slice thickness (mm)</td>
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<td>3.5 mm</td>
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<td>Interslice gap</td>
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<td>Matrix</td>
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<tr>
<td>NSA</td>
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</tr>
<tr>
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<td>295 x 262 mm</td>
</tr>
<tr>
<td>Acquisition time</td>
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<td>3 min 52 s</td>
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<tr>
<td>Slice number</td>
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</tr>
</tbody>
</table>

**Fig. 1:** Tab. 1: MR sequences

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![Fig. 1: Tab. 1: MR sequences](image1)

**Fig. 2**

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![Fig. 2](image2)
Results

Population study

All patients went to surgery:

- 8 patients underwent a rectal-colonic anterior resection,
- 1 patient underwent an abdominal-perineal resection.

The average length of the tumour was 52 mm (range between 25 mm and 120 mm).

The tumours were located:

- 6 in the lower rectum (between 30 and 81 mm from the anal margin),
- 2 in the medium rectum (between 80 mm and 120 mm from the anal verge)
- 1 in the upper rectum (between 120 mm and 160 mm from the anal margin).

Histopathological staging results are summarized in Table 2.

![Table 2](image)

Fig. 3: Tab 2

References: Department of Radiology, AOU - Cagliari/IT

A total of 68 lymph nodes were considered (36 metastatic and 32 not-metastatic) in the statistical calculation. On closer analysis 11 lymph nodes with necrosis characteristics were excluded, thus only 57 (25 positive and 32 negative) were considered in a further statistical calculation.

Quantitative analysis
In a first statistical analysis which included all the 68 lymph nodes, the ADC value of the two groups of lymph nodes, positive and negative, did not show a statistically significant association (ROC n° 1; AUC 0.55, p = 0.46) (Tab 3).

Fig. 4: Tab 3

References: Department of Radiology, AOU - Cagliari/IT

Excluding necrotic lymph nodes, characterized by high ADC values (1.57 +/- 0.47 x 10^-3 mm2/s) and considering only 57 lymph nodes (including 25 positive and 32 negative) is observed an important significance statistics (ROC No. 2; AUC 0.715; p = 0.002) (Tab 4).

Fig. 5: Tab 4

References: Department of Radiology, AOU - Cagliari/IT
The average value of metastatic lymph nodes (0.75 +/- 0.29 x 10^{-3} mm^2/s) was indeed significantly lower than non-metastatic (1.08 +/- 0.26 x 10^{-3} mm^2/s).

The thresholds of sensitivity and specificity were then generated for different values of the ADC.

By choosing an ADC value of 0.95 x 10^{-3} mm^2/s as cut-off to distinguish pathological from healthy lymph nodes, a sensitivity value of 76% and a specificity value of 68.7% is obtained.

Although the results in the literature on the usefulness of ADC value in identifying metastatic lymph nodes are mixed (Table 5), the results in our study are consistent with those obtained by Cho et al.

![Table 5](image)

**Fig. 6:** Tab 5  
**References:** Department of Radiology, AOU - Cagliari/IT
Images for this section:

Fig. 3: Tab 2

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Fig. 4: Tab 3

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**Fig. 5:** Tab 4

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<table>
<thead>
<tr>
<th>Anno</th>
<th>N°</th>
<th>ROI</th>
<th>AUC</th>
<th>ADC metast.</th>
<th>ADC non metast.</th>
<th>p-value</th>
<th>Cut-off</th>
<th>Se (%)</th>
<th>Sp (%)</th>
<th>PPV (%)</th>
<th>PPN (%)</th>
<th>Acc (%)</th>
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<td>0,78</td>
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<tr>
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<td>2013</td>
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<td>18</td>
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<tr>
<td>Cerny et al.</td>
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<td>1,06 ± 0,18</td>
<td>1,37 ± 0,32</td>
<td>0,0012</td>
<td>-</td>
<td>-</td>
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<td>Qiu et al.</td>
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<td>1,11 ± 0,89</td>
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<td>Lambregts et al.</td>
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<td>1,25</td>
<td>53</td>
<td>82</td>
<td>35</td>
<td>91</td>
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</tr>
</tbody>
</table>

**Fig. 6:** Tab 5

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Conclusion

Although T2W nodes characteristic is still the gold standard in defining the N Stage of a tumor, ADC value could be useful in differentiating between benign and metastatic pelvic lymph nodes in patients with rectal carcinoma, especially in doubtful nodes.
References


