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Original article

Proton Magnetic Resonance Spectroscopy: Ex vivo study to investigate its prognostic role in colorectal cancer

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ABSTRACT

Background: Proton Magnetic Resonance Spectroscopy (1H MRS) is used for clinical diagnosis in some tumours. The aim of this study is to explore ex vivo the potential of 1H MRS in identifying malignancy through metabolic markers in the perspective of its application in all cases of difficult diagnosis and after neoadjuvant treatment.
Methods: Spectroscopy was performed ex vivo on 29 colorectal specimens. All patients were staged with imaging, underwent radical surgery and then followed-up. Spectral quantification analysis of components expressed in colorectal tumours and in healthy mucosa were evaluated. The MRS-tumour marker (MRS-tm) was calculated for each case. The U-test was used to compare MRS-tm in tumours and in healthy mucosa. In order to select a cut-off for MRS-tm in the tumour and healthy mucosa and to distinguish patients who were disease-free or with recurrence-progression, we performed the ROC curve analysis.
Results: In the 24 subjects without neoadjuvant treatment, it was found that MRS-tm is able to discriminate healthy and neoplastic tissue and can discriminate patients with risk of recurrence/progression
Conclusion: Our data seem to show that 1H MRS may be successfully applied in vivo non-invasively to differentiate tumours from healthy mucosa and could also distinguish patients with different prognoses.

1. Introduction

In clinical practice, 1H MRS is mainly applied to the diagnosis and histological classification of tumours of the brain and occasionally for tumour of the breast, prostate, thyroid, neck squamous cell carcinomas and melanomas [1–6].

In colorectal cancer, the application of 1H MRS in vivo could increase the diagnostic accuracy, especially after neoadjuvant treatment. In these cases, the diagnosis with biopsy and imaging is not accurate, and patients with clinical complete response (c-CR) or minimal residual tumour are difficult to identify [7,8]. This strongly influences the treatment and facilitates the abandonment of conservative treatments (sphincter preserving surgery, transanal endoscopic microsurgery (TEM)/traditional local excision) and the non-operative strategy (Watch & Wait).

In colorectal cancer, the MRS was used primarily on biopsies or serum [5,6,9,10] and allowed the identification of the metabolic profile of the tumour and to define the levels of its aggressiveness [11].

There is no research that has used the 1H MRS for surgical specimens with colorectal cancer.

The application of 1H MRS in vivo, complicated by the low signal/noise ratio, tumour volume, peristaltic movement of the colon and the presence of intraluminal air was only experimented on in two papers on advanced and distal rectal cancer using MRI 3 Tesla (T) and 1.5 T.

In the present paper, we propose a quantitative approach with 1H-MRS ex-vivo using a preclinical scanner (4.7 T) on surgical specimens with colorectal cancer. By applying 1H MRS on the specimen, we studied tumour tissue and healthy mucosa.

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The quantitative approach proposed may be useful to in vivo application of 1H MRS, particularly in the perspective of its application in all cases of difficult diagnosis, endoscopic or with imaging, or in rectal cancer after neoadjuvant treatment, especially in patients with clinical complete response (c-CR).

Another objective of this research is to evaluate if the neoplastic metabolites can have prognostic significance and then can identify patients with increased risk of recurrence-progression of disease.

2. Materials and methods

From January 2010 to February 2011, 157 cases of colorectal cancer were observed and treated at the First Division of General Surgery of the University of Verona. At the Section of Anatomy, 29 surgically removed specimens (21 from male patients and nine from females) were analysed using 1H MRS. Study protocol was approved by the departmental ethics committee. All subjects provided informed consent prior to the spectroscopy.

The patients' age was 69 ± 13 years. There were 22 cases of colon cancer, two of rectal cancer and five of rectal cancer that had completed neoadjuvant treatment and were operated on 8 weeks after CRT. Preoperative CRT consisted of 4500 cGy (180 cGy × 25) to the whole pelvis with a 540 cGy boost (180 cGy × 3) to the mesorectum, to a total dose of 50.4 Gy and Capecitabine 1650 mg/m^2 chronomodulated.

In 11 cases, right hemicolectomy was performed, in four cases left hemicolectomy, in five cases sigma resection, in seven cases low anterior resection (LAR) and in two cases abdomino-perineal resection (APR). The primary tumour was excised radically in all cases (R0). The metastases were not excised because they were defined as unresectable.

The tumour stages were: T1N0M0 (two cases), T2N0M0 (four cases), T3N0M0 (nine cases), T3N0M1 (liver) (one case), T3N1M0 (three cases), T3N2M0 (one case), T3N2M1 (liver) (one case), T4N0M0 (one case), T4N2M0 (one case) and T4N2M1 (liver + lung) (one case). The stages of rectal cancer after neoadjuvant treatment were: yp-T0N0M0 (one case), yp-T1N0M0 (two cases), T2N0M0-yp (two cases).

BMI, CEA, SUVmax (maximum standardized uptake value), histology (WHO), grading, perineural infiltration, lymphocytic

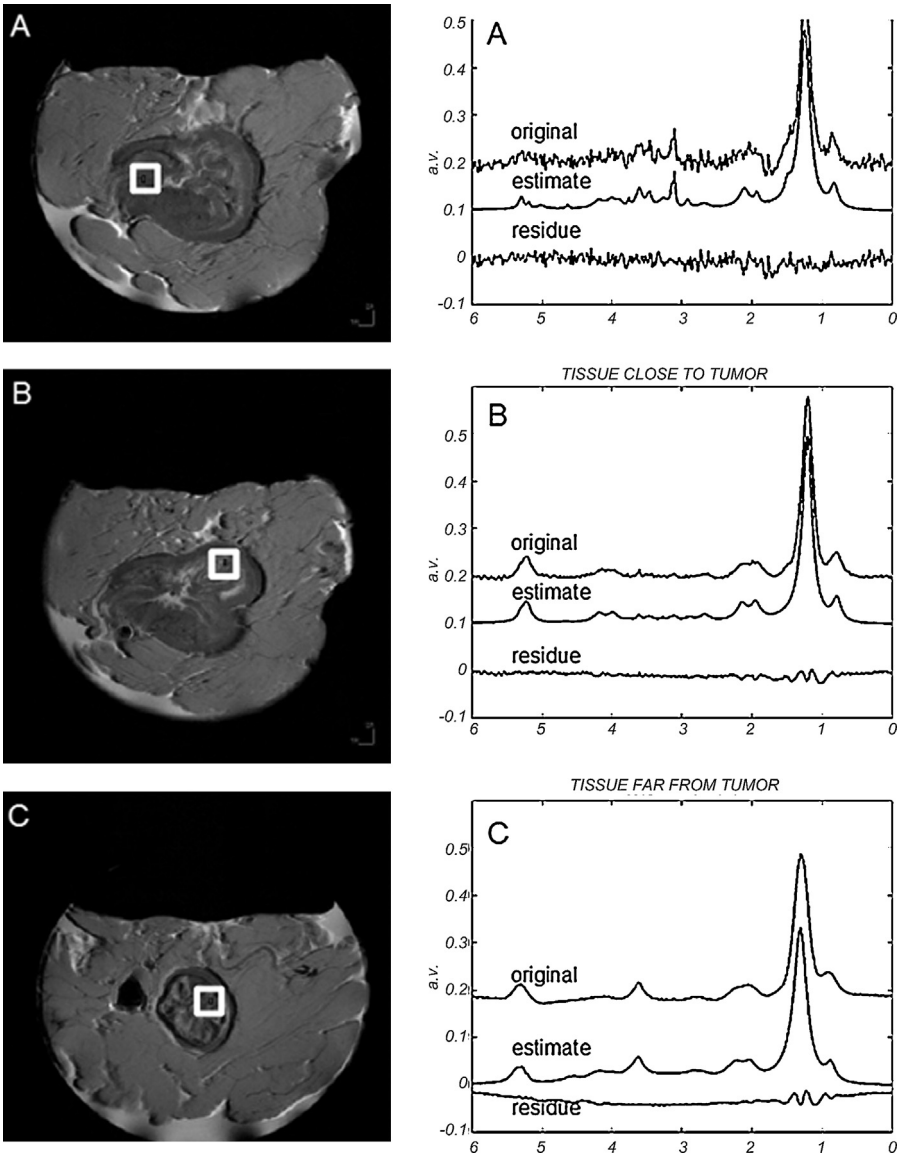

Fig. 1. On the right side, the original 1H MRS signal, its estimation by jMRUI and the obtained residual are show respectively for tumour (A), healthy mucosa close from the tumour (B) and far from the tumor (C), whose voxels for 1H MRS measurements are displayed on the left side.