Predictive value of fast and slow ADC component analysis for rectal cancer response monitoring after neo-adjuvant radiochemotherapy: initial results.

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Introduction

Radiochemotherapy (RCT) is the standard of care pre-operative treatment in primary irresectable rectal cancer. After neo-adjuvant RCT, a good pathological response is found in approximately 25% of patients. Good pathological responders have an excellent prognosis, with very low local recurrence rates and a high disease free survival (1). This questions the use of surgery in good responders because surgery is associated with substantial morbidity and even mortality (2). Retrospective studies by the group of Habr-Gama showed that omission of surgery is safe in patients with complete clinical response after neo-adjuvant RCT (3). However, to enable safe omission of surgery reliable pathological response prediction is needed. In earlier work the predictive value of diffusion weighted imaging (DWI) pathological response assessment was shown (4). Besides diffusion motion of water, a vascular component contributes to the calculated Apparent Diffusion Coefficient (ADC) (5). Low b-value based ADC values reflect perfusion (fast ADC component) while high b-value based ADC values reflect diffusion motion (slow ADC component). In this study, we show the initial results of the predictive value of the fast and slow ADC components for rectal cancer response assessment after neo-adjuvant RCT.

Patients and Methods

Eight patients with histologically proven adenocarcinoma of the rectum received neo-adjuvant RCT followed by surgical rectum resection irrespective of the response. Pre-operative therapy consisted of radiotherapy with a dose of 50 Gy in 2 Gy fractions over 5 weeks combined with oral 5-fluorouracil 2 dd 825 mg/m2 daily. MRI images were acquired before RCT and 6-8 weeks after RCT just before the surgical procedure on a 3 Tesla MRI scanner (Achieva, Philips Medical Systems, Best, The Netherlands). DWI was performed in axial plane using single shot spin echo-echo planar imaging (ssSE-EPI) sequence with b values of 0, 10, 20, 30, 40, 50, 60, 70, 80, 90, 100, 200, 400, 800, 1000 and 1200 s/mm^2 (TR: 8.0 s, TE : 71.1 ms, slice thickness: 4 mm, no slices: 45, EPI factor: 63, matrix size: 132 x 120, resolution: 2.5 x 2.5 mm^2, fat suppression: SPAIR). ADC values were calculated using, $lnS = lnA - b\,ADC$, where A is the relative amplitude and S the signal amplitude. To separate fast and slow ADC components, ADC maps were generated with b-values between 10 and 100 and with b-values between 400 and 1200, respectively. Changes in ADC between pre- and post-RCT were calculated (ΔADC).

The tumour volumes of interest (VOIs) pre- and post-RCT were defined on the pre-RCT and post-RCT b0 map. Patients were classified according their pathological response into a group of good pathological response, which consisted of pathological complete responders and patients with solitary vital tumour cells in their resection specimen and moderate responders with larger foci of tumour in the resection specimen.

Statistical analysis was performed using SPSS (SPSS 16.0: SPSS Inc.). ADC and ΔADC values between the response groups were compared using a Mann-Whitney U test. Volumes were compared using a Wilcoxon signed-rank test. For data analysis, the median ADC values of the VOIs were used. Due to our small patient group statistical significance was assessed at $p < 0.1$.

Results

Two of the 8 patients were classified as pathological good responders, one pathological complete responder and one with solitary vital tumour cells in the resection specimen.

Tumour volumes decreased significantly after RCT, mean volume pre-RCT 24.9 cc, post-RCT 3.4 cc ($p < 0.01$). This volume reduction was not significantly different between the response groups.

In the tumour, fast and slow ADC values pre- and post-RCT were not different between the response groups (figure 1a and 1b). ΔADC for the fast and the slow component was larger in the good response group than in the moderate response group ($p = 0.07$, figure 1c).

Discussion

In this study, rectal cancer response after neo-adjuvant RCT was assessed with both the fast and the slow ADC component, which reflects the perfusion and diffusion contribution in the ADC value, respectively.

In the tumour, the increase in both the slow and the fast ADC values was larger in good responders compared to moderate responders. The increase in the slow ADC values was expected due to disappearance of dense tumour tissue. The increase in fast ADC values might be attributed to more pronounced vascular changes due to inflammatory reactions on RCT in scar tissue than in remaining tumour. We can not exclude that the amount of tumor cell necrosis achieved with RCT influences both slow and fast ADC values.

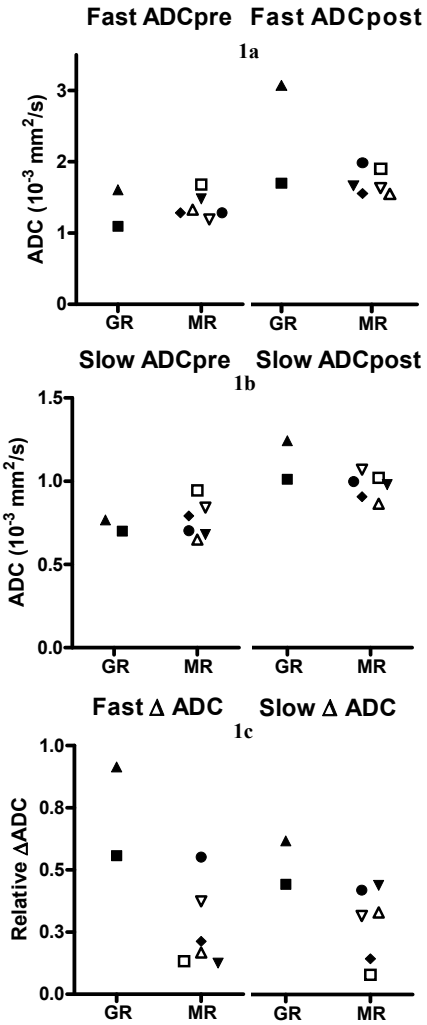

Figure 1: a) fast ADC values pre- and post RCT. b) slow ADC values pre- and post RCT. c) Relative ΔADC for fast and slow ADC values.

Conclusion

Both the change of the fast and the slow ADC component have predictive potential for pathological response after neo-adjuvant RCT. For definite conclusions inclusion of more patients is required.

References: *(1) Vecchio, IJROBP 2005 (2)* Habr-Gama, Ann Surg. 2004 *(3)* Habr-Gama, Br J Surg. 2009 *(4) Intven, ISMRM 2010 abstr # 2012 (5) Le Bihan, Radiology1988*