Diffusion weighted magnetic resonance imaging for pathological response prediction after neo-adjuvant radiochemotherapy for locally advanced rectal cancer.

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Introduction

Radiochemotherapy (RCT) followed by total mesorectal excision (TME) is the standard treatment in locally advanced rectal cancer (LARC). The pathological response after surgery is correlated with the outcome. The better the pathological response, the better the outcome with 5 year local recurrence risk of 3% and 5-year overall survival of 88% in pathological complete responders (pCR). This low local recurrence risk questions the additional value of surgery in good responders because surgery is associated with substantial morbidity and even mortality (1). In clinical good responders after RCT, organ-sparing might be beneficial. However, this approach remains controversial because of the known dissociation between clinically and pathologically assessed responses. To improve response assessment diffusion-weighted MR imaging (DW-MRI) that reflects microanatomy is increasingly used in oncology (2). The aim of this study was to assess the predictive potential of DW-MRI for the selection of favorable pathological responders after RCT for LARC to provide a reliable selection of patients eligible for organ-sparing treatment.

Patients and Methods

Forty-four patients with LARC received standard of care neo-adjuvant RCT that was followed 6-10 week later by surgical rectum resection irrespective of the response. MR images were acquired 1-2 weeks before RCT and 1-2 weeks before surgery on a 3 Tesla MRI scanner (Achieva, Philips Medical Systems, Best, The Netherlands). All scans were performed in the radiotherapy treatment position without specific bowel preparation. The MRI protocol consisted of transverse T1w-, sagittal and transverse T2w- and transverse DW-MRI. DW-MRI consisted of a single-shot Spin-Echo Echo Planar Imaging (ssSE-EPI, TR/TE: 7600ms/63ms; EPI factor: 63), with spectral attenuated inversion-recovery (SPAIR) fat suppression and isotropic diffusion weighting in 3 directions with b-values: 0, 200, 800 s/mm2. Images were acquired with a 132 x 120 matrix, a slice thickness of 4 mm and a slice gap of 0 mm, the number of averages was 3. The total examination time was approximately 25 minutes with a DW-MRI sequence of 4.08 minutes. ADC values were calculated using all b-values with, $lnS = lnA - b\,ADC$, where A is the relative amplitude and S the signal amplitude (figure 1). On the b0 DW-images, a volume of interest (VOI) consisting of tissue suspicious for tumor was defined before and after therapy. Necrotic areas and fluid rectal content were excluded from the VOI based on the image with a b-value of 800 s/mm^2. Changes in ADC between pre- and post-RCT VOI were calculated (ΔADC). Patients were classified according their pathological tumor regression grade into a group of good pathological response (GR), which consisted of pCR and patients with solitary vital tumour cells and moderate responders with larger foci of tumor. Statistical analyses were performed using GraphPad Prism 5.00 (Graphpad Software Inc, USA) and SPSS 16.0.1. (2007, SPSS Inc., USA). Since the Kolmogorov-Smirnov tests showed distributions with non-normally distributed ADC values in some VOIs, ADC values are referred as median values in the VOI. ADC and ΔADC values between the response groups were compared using a Mann-Whitney U test. Significance was assigned at $p \leq 0.05$.

	pre-RCT ADC		relative ΔADC	
Diagnostic Value	pCR : non-pCR	GR : MR	pCR : non-pCR	GR : MR
cut-off	1.07*10^{-3} mm^2/s	1.07*10^{-3} mm^2/s	48% increase	43% increase
Accuracy	80%	86%	93%	95%
Sensitivity	80%	89%	80%	89%
Specificity	79%	86%	95%	97%
PPV	33%	62%	67%	89%
NPV	97%	97%	97%	97%

Table 1:Predictive values.

Results

The GR group consisted of nine patients (20%) with five patients with pCR. Both the pre-RCT ADC values and relative ΔADC were predictive for the pathological response. Pre- RCT ADC values showed a positive predictive value (PPV) of 33% for pCR and 62% for GR using a cut-off value of 1.07*10^{-3} mm^2/s (figure 2). For ΔADC the optimal threshold for predicting pCR was 48% and for GR 43% increase of ADC. Applying these thresholds, a PPV of 67% and 89% were found for pCR and GR, respectively (figure 3).

Discussion

Our results showed that DW-MRI is a reliable tool for the selection of favorable pathological responders after RCT for LARC. This predictive potential was also shown by others, but various predictive values were reported (3-8). These diverse results could be due to lack of standardized pathology and differences in timing of imaging protocols and surgery. Also differences in DW-MRI such as the choice of b-values and the magnetic field strength may affect the results. However the effect of these variations is unknown due to lack of reproducibility studies. Before implementation of DW-MRI for selection of good treatment responders for an organ-sparing treatment also the repeatability of the measurements needs to be known to distinguish therapy related response from measurement variations.

Conclusion

Both low pre-RCT ADC values and high relative ΔADC correspond with pathological good response in LARC. DW-MRI could be used in a protocol to select good responders after RCT for an organ-sparing treatment.

References: *(1) Vecchio, IJROBP 2005 (2) Padhani, Neoplasia 2009 (3) Dzik-Jurasz, Lancet 2002 (4) DeVries, IJROBP 2003 (5) Kim, Radiology 2009 (6) Sun, Radiology 2010 (7) Kim, Eur Radiol 2010 (8) Lambrecht, IJROBP 2011*

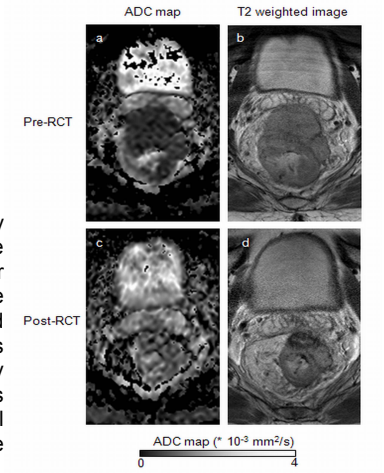

Figure 1: ADC maps T2w MRI images of a patient with locally advanced rectal cancer before and after RCT.

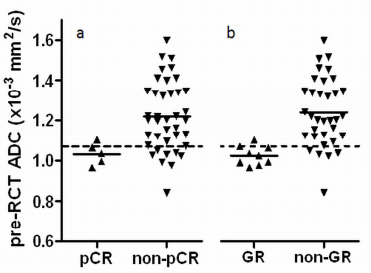

Figure 2: The pre-RCT ADC values in the pCR and non-pCR groups (a) and the good and moderate response groups (b). The horizontal solid lines represent the response group median ADC value. The horizontal dotted line indicates the optimal cutoff value.

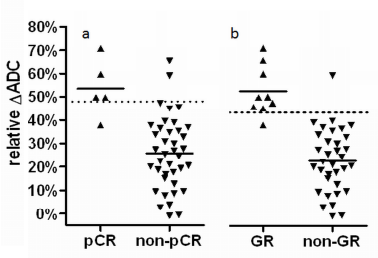

Figure 3: The relative ΔADC in the pCR and non-pCR groups (a) and the good and moderate response groups (b). The horizontal solid lines represent the response group median ΔADC value. The horizontal dotted line indicates the optimal cutoff value.