Diffusion Weighted MRI as a predictive tool for effect of radiotherapy in locally advanced cervical cancer

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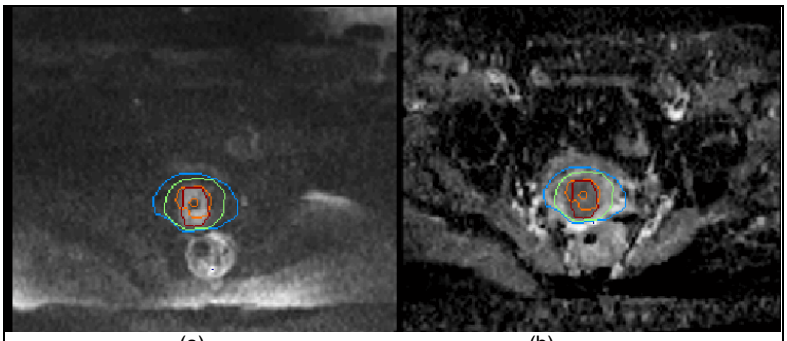
Purpose

Diffusion Weighted MRI (DW-MRI) is used for diagnostic cancer imaging and may have value for monitoring of tumor response to antineoplastic treatment such as radiotherapy (RT). In this study, Diffusion Weighted MRI was evaluated as a non-invasive biomarker for prediction of local failure in RT of locally advanced cervical cancer.

Methods

Fifty two patients were treated with 45-50Gy whole pelvis external beam RT (EBRT) and 2 fractions of brachytherapy (BT). Patients underwent MRI examination 3 times during treatment with the BT applicator in situ: 1) a preplanning MRI (BT0) one week prior to first BT, 2) at time of first BT and 3) at time of second BT (BT2) one week after first BT. Dose-planning for BT was based on T2-weighted MRI following the GEC-ESTRO guidelines[1] (Figure 1). DW-MRI (b=0, 600, 1.000 s/mm^2) was included in all three MRIs using a 1.5T MRI (Magnetom Symphony, Siemens Erlangen, Germany). Median follow-up time from start of treatment was 714 days (min/max: 167/1412 days). Blinded visual assessment of signal intensities on DW-MRI, b=1.000 s/mm^2 at time of BT0 was evaluated for hyper-intensity at tumor site and was found in 22/52 patients (table 1). Images of Apparent Diffusion Coefficients (ADC maps) were calculated for the 22 patients with hyper-intense signal on DW-MRI for b=1.000 s/mm^2 at time of BT0 and BT2. K-means clustering (using ADC-map and DW-MRI, b=1.000 s/mm^2, as input) was used for automatic, user independent contouring of the region of hyper-intensity on DW-MRI, b=1.000 s/mm^2 and hypo-intensity on ADC (DWI ROI)[2]. The relationship between local failure and ADC, change in ADC and volumes was investigated.



(a) (b)

Figure 1: (a) DWI, b=1.000 s/mm^2 and (b) ADC for dose-planning with GEC-ESTRO contours: IRCTV (blue), HRCTV (green) and GTV (orange), DWI ROI (red).

Results

There was a significant correlation between non-responders (Fischer's exact test p=0.021) and presence of hyper-intense signal on DW-MR images at b=1.000 s/mm^2 at time of BT0 (Table 1). The lower ADC for DWI ROI in responders compared to non-responders was not significant at BT0 (Students t-test p=0.21) (Table 2). There was no significant change in ADC for both responders and non-responders from BT0 to BT2 (Students t-test p = 0.44). There was a significant decrease in the volume of the DWI ROI for both responders (p = 0.016) and non-responders (p = 0.003), but the mean DWI ROI volume at time of BT2 was significantly larger (Students t-test p=0.006) for non-responders than for responders.

Table 1	Responders	Non-responders
Hyper-intense signal@BT0	14	8
No hyper-intense signal@BT0	21	1
Non-evaluable (bad image quality)	8	0

Table 2	DWI ROI, BT0		DWI ROI, BT2	
	ADC [mean ± sd 10^{-3} mm^2/s]	Volume [mean ± sd cm^3]	ADC [mean ± sd 10^{-3} mm^2/s]	Volume [mean ± sd cm^3]
Responders	1.21 ± 0.19	5.06 ± 4.72	1.20 ± 0.21	1.51 ± 1.36
non-responders	1.31 ± 0.24	7.54 ± 5.02	1.31 ± 0.25	4.12 ± 3.12

Discussion

The presence of remaining hyper-intense tumor signal at highly diffusion sensitive images (b = 1.000 s/mm^2) at time of BT seems to be a strong indicator for increased risk of persistent local disease or local recurrence. However, the qualitative and subjective nature of the visual evaluation of hyper-intense signal at DW-MR images is an issue that should be addressed in future work. At this time of treatment the ADC appears stable before and after the BT fraction and it was not possible to use the ADC to differentiate between responders and non-responders before nor after the RT fraction. The study shows that the tumor delineated by the DWI ROI decreases during treatment although the ADC value did not change. Since high-intensities on high b-value images is only visible in part of the patients, the study also raises the question of how to draw ROIs used for ADC comparison to measure effect of therapy on the patients with no hyper-intense signal. If ROIs are drawn based on for instance T2W images, the resulting ADC values will be sensitive to RT effects in normal as well as tumor tissue, thereby risking comparing RT effects in tissues with varying amounts of normal tissue. Guidelines for drawing ROIs, when using DW-MRI for measuring the effect of therapy, should be made before the use of ADC values for monitoring therapy can have any value.

Conclusion

This study indicates that DW-MRI may be of value for monitoring RT-treatment and predicting local failure already during treatment although the ADC value could not be used for predicting outcome. The volume of hyper-intense signal on diffusion sensitive images decreases for both responders and for non-responders but is significantly smaller for responders than for non-responders at BT2.

1. Haie-Meder C et al. Recommendations from Gynaecological (GYN) GEC-ESTRO Working Group (I): concepts and terms in 3D image based 3D treatment planning in cervix cancer brachytherapy with emphasis on MRI assessment of GTV and CTV. Radiother Oncol 2005;74(3):235-245.
2. Haack S et al B0-correction and k-means clustering for accurate and automatic identification of regions with reduced Apparent Diffusion Coefficient (ADC) in advanced cervical cancer at the time of brachytherapy, ISMRM 2012 #4133.