DIFFUSION WEIGHTED MRI FOR RADIOTHERAPY TREATMENT OF LOCALLY ADVANCED CERVICAL CANCER – TREATMENT RESPONSE ASSESSMENT USING DIFFERENT SEGMENTATION METHODS

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PURPOSE

Diffusion weighted imaging (DWI) and the calculated Apparent Diffusion Coefficient (ADC) values may have value for monitoring tumor response to radiotherapy (RT) treatment. An important step for clinical use of quantitative DWI is the automatic segmentation of tumor tissue, but the choice of segmentation method may strongly influence the observed distribution of ADC values. This study 1) evaluates different segmentation methods, and 2) the change of tumor ADCs during RT treatment depending on segmentation method.

MATERIALS AND METHODS

Twelve patients with locally advanced cervical cancer underwent an MRI examination three times during their RT treatment: 1) prior to RT treatment 2) during the external beam (EB) RT and 3) one week before first brachytherapy (BT) RT but examined with applicator in place. DWI-MRI (b = 150, 600, 1000 s/mm^2) was included in all three MRIs using a 3T scanner (Philips Achieva 3T-X, Best, The Netherlands). ADC values for the segmented volumes were calculated using all b-values . A ROI was placed surrounding the entire torso for determination of the noise defined as the standard deviation (SD). Secondly a ROI was placed to contain the cervix, lower uterus, entire tumor and the surrounding tissue. Only voxels inside this ROI were included in the following three segmentation methods: 1) threshold on the b=1000 s/mm^2 as compared to image noise[1]. Pixels with intensity >4xSD identified as tumor tissue, 2) k-means clustering using b = 1000, 600 s/mm^2 and ADC map mm^2/s as input and 3) region-growing method[2] based on the b=1000 s/mm^2 image. Histogram analysis of ADC values was performed comparing the tumor pixels for each timepoint (Fig. 2). The mean ADC and the kurtosis of the ADC histogram (distinct from diffusion kurtosis[3]) were compared across time points and segmentation methods. The kurtosis (k) describes the steepness of the distribution function where a kurtosis = 3 corresponds to a normal Gaussian distribution. The assessment of treatment response is expressed as the percent change in ADC using the formula %ΔADC = $[(ADC_{RT} − ADC_{pre})/ADC_{pre}]$ x 100]. The results were statistically evaluated using oneway Anova (three timepoints) or Students t-test (two timepoints).

Fig. 1 ADC map with delineated tumor

Fig. 2 Histogram analysis (4SD method used) for one RT patient (PRE-RT (green), EBRT (red) and BT0 (blue)).

RESULTS

There was a significant change in mean ADC during treatment for both the 4SD and the clustering method (p = 0.007 and p = 0.019 respectively), but not for the region-growing method (p = 0.107), table 1. The segmented volume also changed significantly during RT for 4SD and clustering (p = 0.023 and p = 0.003 respectively) but not for region-growing (p = 0.25). There was a significant change in kurtosis from PRE-RT to EBRT for the 4SD and clustering method (Students t-test p = 0.005 and p = 0.005 respectively), table 1.
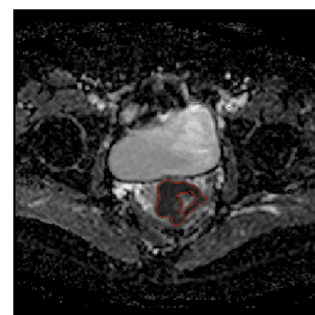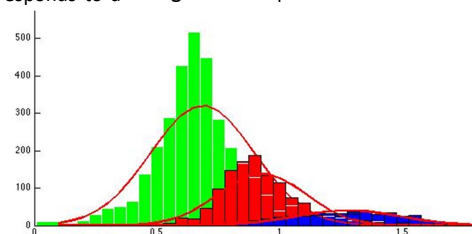
	PRE-RT			During EBRT				Time of BT			
	Volume Mean+/-SD [cm^3]	ADC 10-3 mm^2/s mean+/-SD	k	Volume Mean+/-SD [cm^3]	ADC 10-3 mm^2/s mean+/-SD	k	%ΔADC PRERT/ EBRT	Volume Mean+/-SD [cm^3]	ADC 10-3 mm^2/s mean+/-SD	k	%ΔADC PRERT/ BT
Signal > 4xSD	28.6±22.2	0.94±0.2	6.5±1.1	19.3±11.2	1.09±0.1	4.3±0.9	18.2±14.3	7.4± 8.0	1.19±0.1	3.7±1.7	35.8±22.4
Clustering	25.7±15.5	0.94±0.2	6.5±1.4	16.0±7.4	1.12±0.2	4.4±2.0	22.5±20.1	6.5± 6.9	1.23±0.2	3.3±1.2	42.5±29.4
Regiongrowing	20.0±17.4	0.94±0.2	5.3±1.3	14.1±8.5	1.11±0.2	6.2±4.6	21.7±20.0	10.6± 8.3	1.08±0.1	4.1±1.9	25.4±25.8

Table 1 Volumes, ADC and kurtosis (k) for the different segmented volumes for the different timepoints of treatment.

DISCUSSION

Both the 4SD method and the clustering method detected significant changes in ADC during treatment, and both methods could be used for stable segmentation of hyper-intense signal in DW-images at b=1000 s/mm^2. The region-growing method failed probably because the signal-to-noise became poorer at time of BT resulting in a larger segmented volume at time of BT as compared to the other two methods. This is explained by the region-growing method being more sensitive to signal-to-noise variations and also depending on a proper seed-point. The increase in ADC during treatment could express change of tissue structure as the RT causes edema and fibrouses. The change of kurtosis distribution during therapy might express the change of tumor cellular structure from a homogeneous tumor tissue at time of PRE-RT to a more heterogeneous structure during RT including edema, necrotic cells and tumor cells.

CONCLUSION

Objective methods for segmenting the hyper-intense tumor signal when evaluating changes in ADC during treatment are pertinent for the quantitative use of DWI for individualized RT planning and treatment. This 3T study demonstrated the feasibility of objective segmentation using both a high b-value threshold and a k-means clustering approach. Significant biologically feasible correlations between RT treatment and mean ADC and kurtosis were found. As many studies emphasize, it is important to reach consensus on the proper diffusion acquisition scheme including the appropriate choice of b-values. But it is equally important to find an objective and optimal method for segmenting the hyper-intense tumor signal when changes in ADC during treatment should be evaluated. Further studies will reveal which objective segmentation techniques will provide the best correlation between DWI measures and RT treatment response.

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