Assessing Prostate Cancer Response to MR-Guided Adaptive Radiotherapy Using Apparent Diffusion Coefficient (ADC) on a 0.35T MR-Linac

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ABSTRACT

We investigated whether the apparent diffusion coefficient (ADC) from diffusion-weighted imaging (DWI) acquired at a 0.35T MR-Linac can determine prostate and intraprostatic lesion changes caused by MR-guided adaptive radiotherapy.

Four prostate cancer patients treated at a 0.35T MRIdian MR-Linac underwent DWI at this modality. DW images were denoised and used to calculate the ADC and coefficient of determination R^2 by pixel-wise mono-exponential fitting. Clinical lesion and prostate-only contours were transferred on produced ADC and R^2 maps. Pixels with $R^2 > 0.8$ were selected for ADC histogram analysis.

Lesion median ADC increased between treatment simulation and last fraction for the first 3 subjects, indicating favorable response to irradiation. The prostate-only contour demonstrated lower ADC increase for the first 2 patients and slight ADC reduction for the third one. The fourth patient showed ADC reduction for both the lesion and rest prostate, suggesting he may have not responded to radiotherapy.

Overall, DWI at a 0.35T MR-Linac may reveal ADC changes in the prostate and its malignant tumors between treatment beginning and completion. These results may differentiate responders and non-responders to adaptive radiotherapy.

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INTRODUCTION

MR-guided adaptive radiotherapy using an MR-Linac is a promising technique for treating localized prostate cancer[1]. 0.35T MRIdian MR-Linacs offer the option of diffusion-weighted imaging (DWI) in research mode. The **apparent diffusion coefficient (ADC)** obtained from DWI is considered a biomarker of prostate cancer response to radiotherapy[2], as increasing ADC values suggest alterations in cell density owing to necrosis and apoptotic-induced cell death.

We investigated whether ADC acquired at a 0.35T MR-Linac can determine prostate and intraprostatic lesion changes caused by adaptive radiotherapy performed on this treatment modality.

METHODS AND MATERIALS

Subjects: Four prostate cancer patients treated at a 0.35T MRIdian MR-Linac.

Imaging: DWI (b=100, 350, 600 s/mm^2; 1.2x1.2x3 mm^3 voxels) at the end of the planning session and last treatment fraction.

Image analysis: DW images were denoised using Local (LPCA)[3] or Marchenko-Pastur Principal Component Analysis (MPPCA)[4] in Python. The ADC and coefficient of determination R^2 were obtained by pixel-wise mono-exponential fitting of denoised trace-weighted (dTW) images.

Contour analysis: dTW images of the first and last imaging session were fused to the planning TrueFISP images (Figure 1), transferring clinical contours on respective ADC and R^2 maps. Prostate-only contours were created by excluding lesions and overlap with bladder, urethra or seminal vesicles.

ADC assessment: For each contour and treatment timepoint, pixels of ADC maps were selected if the corresponding R^2 was > 0.8 to ensure good ADC fit. ADC histograms of the lesion and prostate-only contours were produced for each timepoint. The median ADC and its absolute deviation for each contour was calculated and compared between the planning session and last treatment fraction.

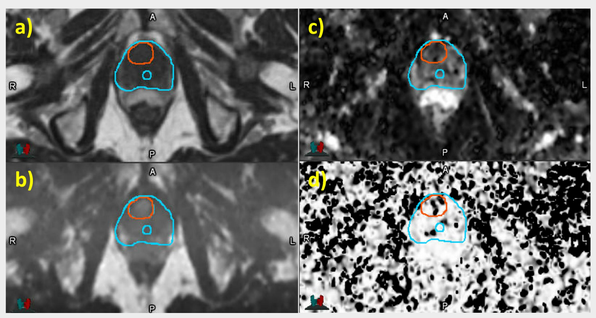

Figure 1. a) Planning TrueFISP image with the lesion (orange) and prostate-only (blue) clinical contour for patient #2. **b)** MPPCA denoised trace-weighted image of the planning session with b = 600 s/mm^2 and transferred contours. The lesion appears bright, suggesting restricted diffusion. **c)** MPPCA denoised ADC map of the planning session and **d)** its corresponding R^2 map, with lesion and prostate contours. The darkest pixels inside ADC map contours were excluded as their R^2 was low.

RESULTS

Denoising increased the signal-to-noise ratio (SNR) of trace-weighted images and of produced ADC maps, improving lesion conspicuity. Most lesions were visibly identified by their lower ADC compared to the rest of the prostate. The produced R^2 maps enabled assessments of the goodness of the ADC fit in the clinical contours (Figure 1), which are not feasible for the scanner provided ADC maps. The employed R^2 threshold allowed the selection of contour pixels with reliable ADC values for each patient.

The median ADC was selected for evaluating treatment effects because ADC histograms from contours of individual patients (example Figure 2) generally demonstrated skewed distributions.

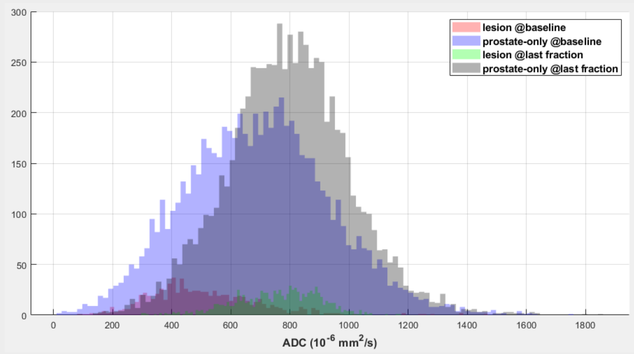

Figure 2. Histograms of ADC values for pixels with $R^2 > 0.8$ in the lesion and prostate-only contours of example patient #2 at the two imaging timepoints.

Obtained median ADC values for the lesion and prostate-only contours of each studied patient are displayed on Figure 3. Median ADC was lower for the intraprostatic lesion than the rest of the prostate, signifying adequate lesion detection on ADC maps, for patients 1-3.

Lesion median ADC increased between treatment simulation and last fraction for the first 3 subjects, by 28%, 60%, and 14%, respectively, indicating favorable response to irradiation. However, the Quantitative imaging biomarkers alliance (QIBA) criterion of 27.7% for detecting a true change between baseline and follow-up measurement with 95% confidence interval[5], was only satisfied for patients 1 and 2.

ADC in the prostate-only contour also increased after treatment for the first 2 patients (by 5% and 15%, respectively) but decreased by 6% for the third one. The fourth patient demonstrated ADC reduction for both the lesion (13%) and rest prostate (5%), suggesting he may have not responded to radiotherapy. Since all observed prostate ADC changes were below the QIBA threshold, they may have been due to measurement imprecision.

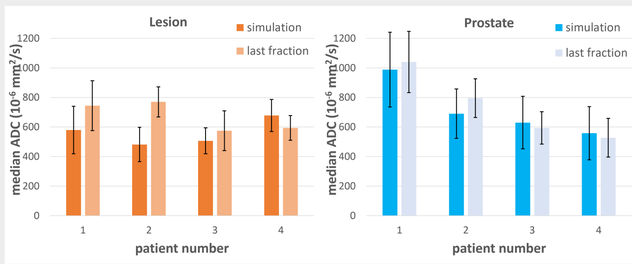

Figure 3. Median ADC for the intraprostatic lesion (**left**) and prostate-only contours (**right**) of every patient in each DWI session. Error bars represent median absolute deviation.

DISCUSSION

Prostate DWI implementation on a 0.35T MRIdian MR-Linac is novel and offers the advantage of data acquisition during the same imaging session and with the same modality employed for treatment planning and delivery. As opposed to the standard clinical workflow of DWI acquisition at an MR scanner of higher field strength, our approach reduced registration errors between DW and planning TrueFISP series since the patient remained in the same position.

The challenge of low signal-to-noise ratio (SNR) of DW images on the low field MR-Linac was addressed by successfully applying denoising algorithms developed for brain DWI. An additional methodological improvement was the calculation of the coefficient of determination R^2 that provided a quality measure of the mono-exponential fit which produced the ADC values. An R^2 threshold enabled selection of contour pixels with reliable ADC fit.

Our work suggests that intraprostatic lesions may be identified on 0.35T ADC maps, potentially eliminating the need for an additional MR examination for DWI acquisition in future. While the whole prostate is usually assessed, our separate evaluation of ADC changes on intraprostatic lesions and the rest of the prostate revealed stronger irradiation effects for the lesions. Half of the studied patients showed a significant ADC increase with MR-guided adaptive radiotherapy for the lesion, indicating treatment response. In contrast, ADC changes in prostate areas excluding the lesion were not significant according to the QIBA criterion[5].

The different ADC trends and amounts of change observed for individual patients suggest a potential to identify responders and non-responders. This differentiation could inform subsequent treatment options and improve clinical outcomes.

CONCLUSIONS

DWI at a 0.35T MR-Linac may reveal ADC changes in the prostate and its malignant tumors between treatment beginning and completion. These results may differentiate responders and non-responders to adaptive radiotherapy.

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