NON-INVASIVE ASSESSMENT OF FIBROSIS AND INFLAMMATION IN THE WHOLE KIDNEY OF CKD PATIENTS BY DIFFUSION-WEIGHTED IMAGING WITH READOUT-SEGMENTED EPI

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Introduction

Chronic kidney disease (CKD), defined as kidney injury and/or loss of kidney function is a significant worldwide health problem with increasing medical cost as the disease worsen. CKD is associated with the apparition of renal fibrosis considered as one of the most predictive elements of its evolution. In this study, whole kidney fibrosis and inflammation was non-invasively assessed with a readout-segmented diffusion-weighted magnetic resonance imaging sequence (RESOLVE [1]) in CKD patients. An internal validation study was performed using biopsy as a gold standard.

Methods

27 transplanted CKD patients (age 54±14 years) scheduled for a renal biopsy were scanned at 3T on a MR Siemens Magnetom Trio Tim system with RESOLVE synchronized to the patient respiration using a respiratory belt. Six coronal-oblique slices of 5mm covered the kidney. The diffusion gradients were applied in 3 orthogonal directions with 10 b-values (0 to 900 seconds/mm^2). The optimized MR parameters were as follow: TR/TE = 2600/68ms, resolution = 2×2×5mm^3, GRAPPA factor = 3, number of readout segments = 5. Regions-of-interest (ROI) placement, in the upper, middle and lower pole of the kidney, was performed with OsiriX (Open source http://www.osirix-viewer.com/). For accurate positioning, image fusion between diffusion images and MOLLI T1 images as an anatomical reference (same resolution and image positioning) was used. The Apparent Diffusion Coefficient (ADC [mm^2/s]) parameter was calculated offline using MATLAB® (R2012b, MathWorks, USA). A new predictor index of ΔADC was defined as the difference of mean ADC in the renal cortex and medulla (ΔADC= <ADC $_{cortex}$> - <ADC $_{medulla}$>) and compared to the extent of renal fibrosis measured from the biopsy using Sirius red staining with morphometric analysis. Diffusion parameters were compared with histopathology as a reference using Pearson's correlation. Statistical analysis was carried out using one-way analysis of variance (ANOVA) with post-hoc Bonferroni (SPSS software, version 21.0; Chicago, Illinois, USA). A value of $p < 0.05$ was taken as statistically significant. Internal validation was performed via non-parametric Wilcoxon and Bootstrap comparing thresholds from 10-80% in steps of 10.

Results

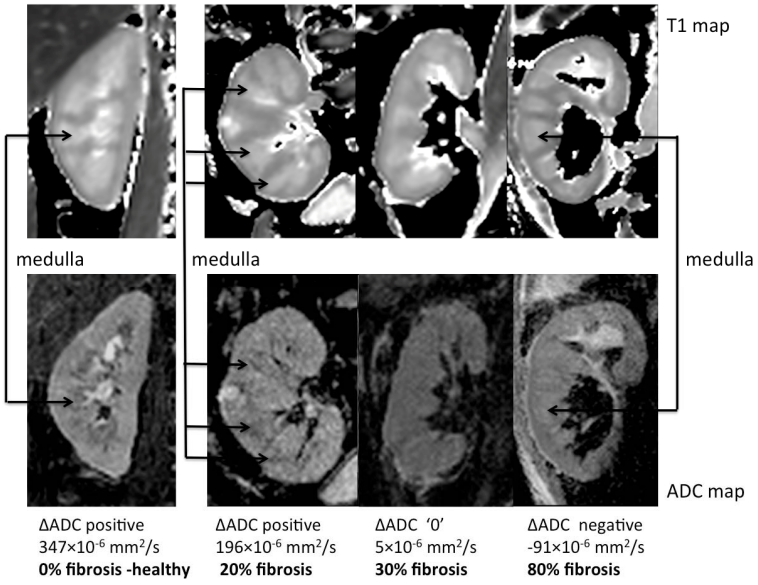

Figure 1 *The morphological MOLLI T1 map used for the positioning of the regions of interest (top row) and the ADC maps (lower row) for 3 patients showing the different ΔADC, positive, zero and negative, along with the corresponding fibrosis levels from histology.*

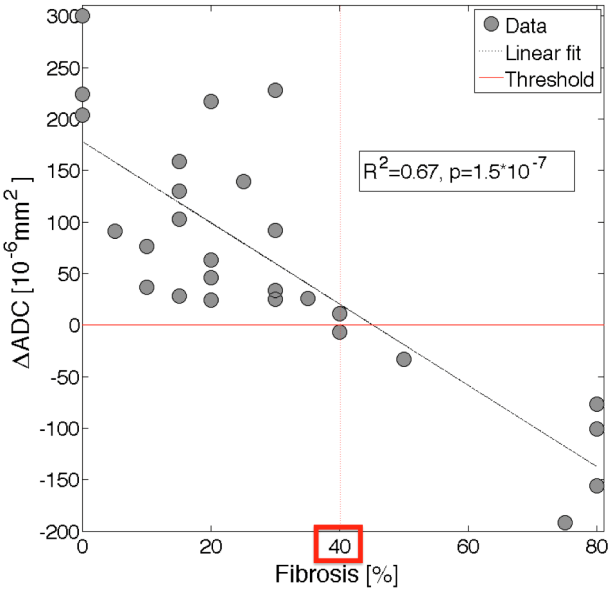

Figure 2 *Correlation of ΔADC in the patient cohort with % fibrosis from histology after routine biopsy.*

Excellent correlation was found in patients comparing ΔADC (R^2=0.70, p<0.001) to the percentages of fibrosis assessed in the biopsy specimen and moderate correlation was found comparing ΔADC (R^2=0.32, p=0.002) to the total inflammation score. A moderate correlation was also found when comparing the ADC in renal cortex with the percentages of fibrosis (r^2=0.37). However, no significant correlation was found when comparing the cortex and medulla alone with the total inflammation score (respectively r^2=0.024 and r^2=0.016) or, when comparing the ADC in the medulla with the percentage of fibrosis (r^2=0.20). A negative ΔADC value was observed for all patients harboring more than 40% interstitial fibrosis. Non-parametric Wilcoxon and 1000 bootstraps of the sample distributed for each threshold confirmed the threshold of 40% as the lowest possible detection level of fibrosis with an accuracy of 0.94, the highest among thresholds every 10%. The specificity of the 40% threshold was 100% and the sensitivity was 90%. For the calibration, the statistical c was 0.97 attesting that the prediction was close to the reality.

Discussion and Conclusions

The ΔADC improves fibrosis evaluation by comparison to ADC alone in renal transplant patients. A negative ΔADC was found in all patients with more than 40% of fibrosis suggesting the use of this index as predictor for renal fibrosis as confirmed by the results of the internal validation.

References

[1] Porter DA, Heidemann RM. High resolution diffusion-weighted imaging using readout-segmented echo-planar imaging, parallel imaging and a two-dimensional navigator-based reacquisition. Magn Reson Med. 2009;62:468-75.