Evaluation of Renal Allograft Function Early after Transplantation with Diffusion-Weighted MR Imaging - Initial Experience

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Introduction: Diffusion weighted Imaging (DWI) may be instrumental for monitoring patients early after kidney transplantation and may aid in the detection of derangements. DW-MRI yields a total "apparent diffusion coefficient" (ADC_T), which provides information on diffusion properties, but also includes contributions from concurrent micro-circulation [1]. Provided diffusion and micro-circulation contributions can be separated, DW-MRI may in addition grant information on micro-circulation, quantified with the "perfusion fraction" (F_P), and "perfusion-free" diffusion (ADC_D). No DWI study has been performed yet in human renal allografts shortly after transplantation. Previously it has been shown that DWI performed at 1.5T in transplanted kidneys with good renal function and about nine months after transplantation yields stable and reproducible parameters [2].
The goals of the current study were I) to determine if DWI measurements at 3T allow reliable determination of diffusion parameters, including perfusion contributions, in renal allografts shortly after transplantation, II) to compare these early results with the previous results obtained ~9 months after transplantation, and III) to gain first information on whether or not these parameters are altered in histologically proven acute allograft rejection.

Methods: Patients: The study comprised 15 renal transplant patients (mean age 46±11y). Mean time between transplantation and MRI was 10±4 days. Six patients received a transplant biopsy which showed acute rejection (AR) in four patients and acute tubular necrosis (ATN) in one patient. Ten patients did not demonstrate major allograft complications and were considered to have a stable transplant function, confirmed by a one-year follow-up. Serum creatinine (s-crea) levels were used to calculate creatinine clearance (GFRc) using the Cockroft-Gault formula [3].
MR Investigations: MR scans were performed on a 3T system (Trio Tim, Siemens, Germany). For DWI, a coronal diffusion–weighted echo-planar imaging sequence was applied. In order to separate micro-circulation from diffusion, ten b-values were applied between 0 and 700 sec/mm^2. Following parameters were used: 11 slices (5mm thick, 1mm gap), FOV=40×40cm^2, matrix=128x128, 6 averages, BW=2300Hz/px. Diffusion weighting gradients were applied in three orthogonal directions applying parallel imaging (GRAPPA, acceleration factor 3). Respiratory triggering was used with TR_{min}=2.8sec and TE=64msec. Minimum acquisition time was 8 min, depending on the breathing cycle.
Image Analysis: DW-MRI findings were analyzed completely blinded with respect to all clinical findings. Processing of the data was performed by I) monoexponential fitting, yielding ADC_T, which includes contributions from both, diffusion and perfusion, and II) by biexponential fitting, yielding the "perfusion fraction" (F_P), i.e. the contribution of micro-circulation of blood and movement in predefined structures such as tubular flow, and an ADC-value (ADC_D) reflecting predominantly pure diffusion.
Three ROIs were selected in both, cortex and medulla at the upper pole, midpole and lower pole on several slices. Single total ROIs were created for cortex and for medulla by merging all individual ROIs, yielding one ROI for cortex and one for medulla. In order to determine in addition to these global parameters, also focal changes, a single ROI was placed for each subject in a "suspicious region", i.e. a region on the ADC_T map that revealed deviations from normal appearance. If no visual abnormality was detectable, an "enforced" ROI had to be placed, in normal appearing tissue. This procedure does not introduce any bias because the analysis was performed blinded in all subjects.

		Time after transplantation	
		10±4days	9±4months [2]
ADC_T	cortex	228±14	217±14
	medulla	226±16	217±11
ADC_D	cortex	203±9	198±10
	medulla	199±9	198±7
F_P	cortex	18±5	19±4
	medulla	19±5	18±5

Table: ADC_T, ADC_D (x10^{-5}mm^2/sec) and F_P (%) in the 10 allografts with stable function early after transplantation and comparison with values obtained previously [2].

Results: Mean values and standard deviations of ADC_T, ADC_D and F_P values in medulla and cortex were calculated from the ten patients with stable allograft function (Table). Coefficients of variations were low for all ADC values (4-7%), while for F_P the variance was ~25%. The currently determined values for ADC_D and F_P are very similar compared to previous results obtained at a different field strength of 1.5T and in well functioning transplanted kidneys at least four months after transplantation [2]. ADC_T values are slightly higher in the current compared to the previous study, most likely because of small differences between the applied b-values, leading to different perfusion contributions.
ADC_T values of the four kidneys with acute rejection were lower in medulla and cortex than those of 8/10 recipients with good function. ADC_D values, which mostly represent pure diffusion, were relatively similar for all subjects. Allografts with acute rejection demonstrated reduced micro-circulation (F_P) in all analyzed tissues of the allograft: F_P values were lower in all four rejecting kidneys than in 9/10 (cortex) and in 8/10 (medulla and suspicious regions) kidneys with stable function (Fig). F_P in the single patient with ATN was very low, below 10%, in all investigated tissues. Significant correlations were determined between GFRc and micro-circulation contributions in cortex (R=0.52, P<0.05), medulla (R=0.52, P<0.05) and in suspicious regions (R=0.63, P<0.01).

Discussion & Conclusions: First, ADC and F_P values are similar in stable renal allografts, when assessed early and during the first year of transplantation. Second, the micro-perfusion and/or tubular flow assessed by DW-MRI is reduced in renal allografts with acute rejection. Thus, third DW-MRI has potential to obtain non-invasively information about renal allograft function.

References:
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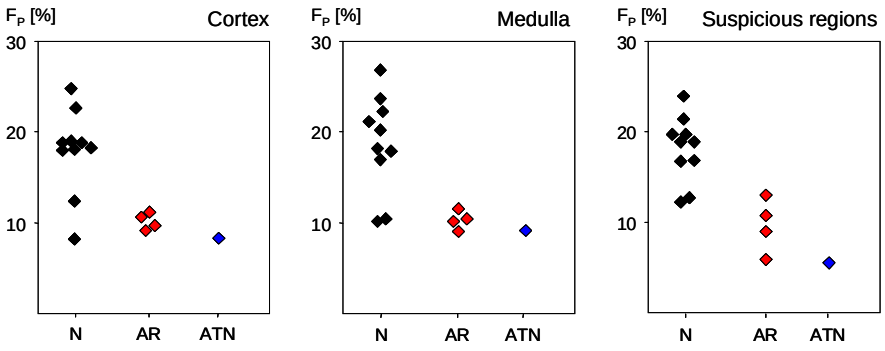

Figure: Perfusion fraction, F_P [%], in cortex, medulla and "suspicious regions" for allografts with normal function (N), with acute rejection (AR) and for the subject with ATN.