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Living Renal Allograft Transplantation: Diffusion-weighted MR Imaging in Longitudinal Follow-up of the Donated and the Remaining Kidney[1]

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Purpose: To determine whether diffusion-weighted (DW) magnetic resonance (MR) imaging in living renal allograft donation allows monitoring of potential changes in the nontransplanted remaining kidney of the donor because of unilateral nephrectomy and changes in the transplanted kidney before and after transplantation in donor and recipient, respectively, and whether DW MR parameters are correlated in the same kidney before and after transplantation.

Materials and Methods: The study protocol was approved by the local ethics committee; written informed consent was obtained. Thirteen healthy kidney donors and their corresponding recipients prospectively underwent DW MR imaging (multiple *b* values) in donors before donation and in donors and recipients at day 8 and months 3 and 12 after donation. Total apparent diffusion coefficient (ADC_T) values were determined; contribution of microcirculation was quantified in perfusion fraction (F_P). Longitudinal changes of diffusion parameters were compared (repeated-measures one-way analysis of variance with post hoc pairwise comparisons). Correlations were tested (linear regression).

Results: ADC_T values in nontransplanted kidney of donors increased from a preexplantation value of (188 ± 9 [standard deviation]) to (202 ± 11) × 10^{-5} mm^2/sec in medulla and from (199 ± 11) to (210 ± 13) × 10^{-5} mm^2/sec in cortex 1 week after donation ($P < .004$). Medullary, but not cortical, ADC_T values stayed increased up to 1 year. ADC_T values in allografts in recipients were stable. Compared with values obtained before transplantation in donors, the corticomedullary difference was reduced in allografts ($P < .03$). Cortical ADC_T values correlated with estimated glomerular filtration rate in recipients ($R = 0.56$, $P < .001$) but not donors. Cortical ADC_T values in the same kidney before transplantation in donors correlated with those in recipients on day 8 after transplantation ($R = 0.77$, $P = .006$). F_P did not show significant changes.

Conclusion: DW MR imaging depicts early adaptations in the remaining nontransplanted kidney of donors after nephrectomy. All diffusion parameters remained constant in allograft recipients after transplantation. This method has potential monitoring utility, although assessment of clinical relevance is needed.

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Living kidney donors have an increased long-term risk to develop higher blood pressure, proteinuria, and an accelerated loss of renal function after donation (1,2). The remaining kidney of the donor exhibits compensatory mechanisms to overcome renal mass reduction due to uninephrectomy. Compensatory hypertrophy of the remaining kidney due to uninephrectomy is associated with an increase in glomerular volume and a comparable increase in glomerular capillary volume (3). The degree of hypertrophy may have effects on the development of glomerular sclerosis (4).

Glomerular enlargement occurs in transplanted kidneys as an adaptive mechanism to an increased demand for oxygen and the increased requirement for reabsorption of solutes (5,6). Besides glomerular enlargement, up to 71% of allografts from living donors develop more than 5% interstitial fibrosis and tubular atrophy during the first 2 years after transplantation (7). However, mild fibrosis is not associated with graft survival.

Diffusion-weighted (DW) magnetic resonance (MR) imaging studies in human renal transplantation have demonstrated promise as an indicator of graft dysfunction (8–14). Analysis of DW MR imaging data yields the total apparent diffusion coefficient (ADC) (ADC_T) as a quantitative parameter. In addition to diffusion, concurrent microcirculation also contributes to signal dispersion in DW MR imaging to a certain extent, which is quantified in the perfusion fraction (F_P) (15). When DW MR imaging signal is sampled at multiple b values, the contributions from perfusion can be separated and, besides F_P, perfusion-free ADC (ADC_D) values can be obtained in addition, which are mostly determined with diffusion. DW MR imaging has been shown to be sensitive to the development of renal fibrosis (16). Physical determinants of ADC suggest that it may also be sensitive to glomerular size. We therefore performed DW MR imaging measurements in living kidney donors and their corresponding recipients before and after transplantation to determine whether DW MR imaging allows monitoring of potential changes in the nontransplanted remaining kidney of the donor because of unilateral nephrectomy and changes of the transplanted kidney before and after transplantation in the donor and recipient, respectively. A secondary aim was to determine whether the parameters from DW MR imaging are correlated in the same kidney before and after transplantation.

Advances in Knowledge

- The apparent diffusion coefficients (ADCs) in the nontransplanted remaining kidney in living donors increase rapidly after nephrectomy from a preexplantation value of (188 ± 9 [standard deviation]) to (202 ± 11) × 10^{-5} mm^2/sec in the medulla and from (199 ± 11) to (210 ± 13) × 10^{-5} mm^2/sec in cortex and appear to reverse slowly over time; in allograft recipients, diffusion parameters remain constant after transplantation; the corticomedullary difference decreased in allografts ($P < .03$).
- Cortical ADC values correlated with estimated glomerular filtration rate in recipients ($R = 0.56$, $P = .0005$) but not in donors.
- Cortical ADC values correlate significantly between the same kidneys in donors before nephrectomy and in recipients 8 days after transplantation ($R = 0.77$, $P = .006$).

Implication for Patient Care

- The results suggest that diffusion-weighted MR imaging may be of clinical utility for monitoring functional changes in the remaining nontransplanted kidney of donors and in transplant allografts of recipients.

Materials and Methods

Study Population

The local ethics committee approved the protocol of this prospective study. Thirteen healthy kidney donors (nine women, four men; mean age, 55 years ± 12 [standard deviation]; range, 38–72 years) and the corresponding 13 allograft recipients (four women, nine men; mean age, 50 years ± 10; range, 33–68 years) were subsequently enrolled from all available candidates between June 2007 and April 2009. The inclusion criterion was written informed consent. Four recipient-donor pairs did not consent. Exclusion criteria were ABO-incompatible transplantation (one subject); recipient younger than 18 years (2); mental retardation of the recipient (1); and standard MR exclusion criteria, such as certain metallic implants and pregnancy (none). All donors and 12 of 13 recipients completed the study; one recipient decided to withdraw consent for personal reasons. The donors and the side of kidney donation (five right and eight left) were selected according to conventional criteria for living kidney donation (17). Patient characteristics are provided in Table E1 (online).

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Abbreviations:
ADC = apparent diffusion coefficient
ADC_D = perfusion-free ADC
ADC_T = total ADC
DW = diffusion weighted
eGFR = estimated glomerular filtration rate
F_P = perfusion fraction
ROI = region of interest

Author contributions:
Guarantors of integrity of entire study, U.E., F.J.F., P.V.; study concepts/study design or data acquisition or data analysis/interpretation, all authors; manuscript drafting or manuscript revision for important intellectual content, all authors; approval of final version of submitted manuscript, all authors; literature research, U.E., H.C.T., F.J.F., P.V.; clinical studies, U.E., T.B., H.C.T., C.B., F.J.F., P.V.; statistical analysis, U.E., C.B., P.V.; and manuscript editing, U.E., H.C.T., C.B., F.J.F., P.V.

Conflicts of interest are listed at the end of this article.

Figure 1

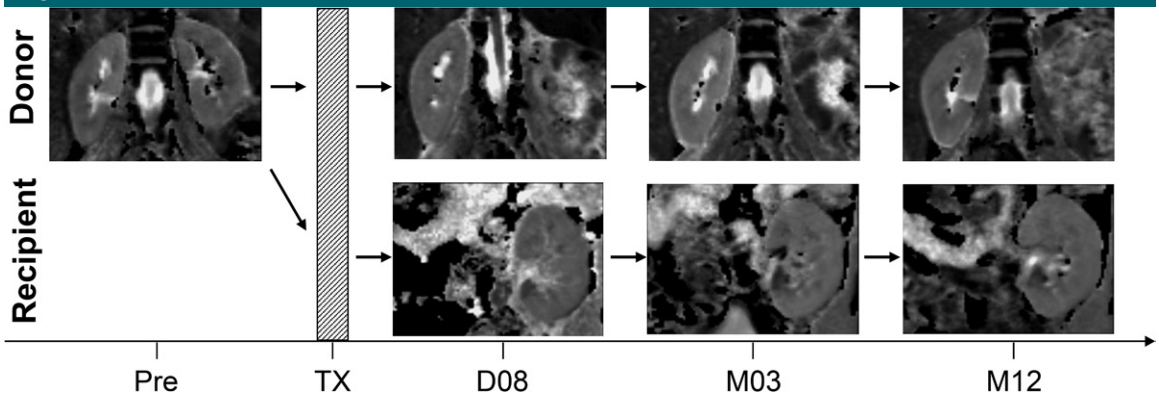

Figure 1: Schematic time schedule for the measurements in living donors and recipients with example ADC_T maps generated from DW MR images from donor 2 and corresponding recipient 2 (Table E1 [online]). *D08* = 8 days after living donation, *M03* = 3 months after living donation, *M12* = 12 months after living donation; *Pre* = before transplantation; *TX* = transplantation.

MR examinations were performed in donors within 3 weeks (mean, 8 days ± 7) of donation (before explantation), and in donors and recipients at approximately 8 days (donors, mean of 8 days ± 3; recipients, mean of 9 days ± 3), 3 months (donors, mean of 103 days ± 24; recipients, mean of 99 days ± 12), and 12 months (donors, mean of 358 days ± 18; recipients, mean of 356 days ± 14) after living donation (Fig 1). In one recipient, the measurement at day 8 could not be performed for medical reasons unrelated to the kidney status. Thus, overall, 87 MR examinations were performed. The subjects were told to eat and drink moderately before the MR examination; however, they were told to do so without exact control of their hydration status, because of the anticipated small effect on diffusion results (8).

At the day of each MR examination, serum creatinine concentrations were measured, and the estimated glomerular filtration rate (eGFR) was calculated by employing the Modification of Diet in Renal Disease formula (18). The graft recipients underwent a standardized initial quadruple immunosuppressive protocol consisting of basiliximab (Simalect; Novartis, Bern, Switzerland), prednisolone, cyclosporine (Sandimmun Neoral; Novartis) or tacrolimus (Prograf; Astellas Pharma, Wallisellen, Switzerland), and mucophenolate mofetil (Cellcept; Roche, Reinach, Switzerland) or mucophenolic acid (Myfortic; Novartis). After 12 months, all recipients were receiving a triple immunosuppression regimen with cyclosporine (eight subjects), tacrolimus (two subjects), everolimus (Certican; Novartis) (two subjects), or sirolimus (Rapamune; Pfizer, Zurich, Switzerland) (one subject) in combination with prednisone or prednisolone and mucophenolate mofetil, mucophenolic acid, or azathioprine (Imurek; Pro Concepta Zug, Baar, Switzerland). Clinical follow-up of transplant recipients and donors was performed regularly in the outpatient clinic of the Nephrology Department according to local clinical standards. However, the results were used in our study only for determining the general clinical status of the patients and were not correlated with diffusion parameters.

MR Imaging

MR imaging was performed with a 3-T MR imaging unit (Tim Trio; Siemens, Erlangen, Germany) by using a combination of a spine coil and a phased-array body coil with six elements.

For morphologic evaluation, a coronal T2-weighted half-Fourier acquisition single-shot turbo spin-echo sequence was performed, and axial and coronal T1-weighted fast low-angle shot gradient-echo imaging was performed. The image acquisition details are provided in the Table.

For DW MR imaging, a coronal DW multisection single-shot echo-planar imaging sequence was applied. To separate microcirculation from diffusion contributions, 10 *b* values were applied. Diffusion gradients were applied in three orthogonal directions and were subsequently averaged. Respiratory triggering was used to reduce motion artifacts. Section positioning was identical to that of the coronal T1-weighted sequence. Minimum acquisition time was 4 minutes 30 seconds, depending on the breathing cycle.

Data Processing

Processing of the DW MR imaging data was performed by using a homebuilt interactive data language program (IDL; RSI, Boulder, Colo).

DW MR imaging findings were analyzed by a trained technician, a nonauthor with more than 10 years of experience, who was blinded to any clinical findings to eliminate bias. Processing of the DW MR imaging data was performed on a pixel-by-pixel basis in two different ways, as previously described (9). In brief, the method was as follows: *(a)* An ADC_T value was calculated from all *b* values by using a monoexponential fitting model, and, thus, it includes contributions from both diffusion and perfusion. *(b)* The acquisition of multiple *b* values allows for separating diffusion

Imaging Parameters

Sequence	Imaging Plane	TR/TE (msec)	Flip Angle (degrees)	Voxel Size (mm^3)	*b* Value (sec/mm^2)	Bandwidth (Hz/pixel)	Matrix	No. of Sections	No. of Acquisitions
T2W half Fourier	Coronal	2000/89	150	1.25 × 1.25 × 5.0	NA	490	320 × 288	21	1
T1W FLASH	Coronal	93/3.17	70	1.25 × 1.25 × 5.0	NA	320	320 × 256	21	1
T1W FLASH	Transverse	100/3.17	70	1.09 × 1.09 × 5.0	NA	320	320 × 166	22	1
DW single-shot echo planar imaging	Coronal	1 RC/52	90	2.3 × 2.3 × 7.0	10, 20, 40, 70, 100, 150, 250, 400, 550, 700	2300	128 × 128	11	4

Note.—FLASH = fast low-angle shot, half Fourier = half-Fourier acquisition single-shot turbo spin-echo sequence, NA = not applicable, RC = respiratory cycle, TE = echo time, T1W = T1 weighted, T2W = T2 weighted, TR = repetition time.

and "microperfusion" contributions to the signal decay. This was performed in a second analysis with biexponential fitting of the same data, yielding the F_P, which represents the contribution of microcirculation of blood and movement in predefined structures, such as tubular flow to the signal decay, and ADC_D. This calculation of F_P and ADC_D values has been described previously in more detail (9,15). The findings for ADC_T and for ADC_D were similar. Therefore, only ADC_T values are presented in detail. The corresponding ADC_D results are presented in Tables E2 and E3 (online) and Figures E1–E3 (online). Maps for the different diffusion parameters were created.

Up to three ellipsoid regions of interest (ROIs), one in the upper, one in the middle, and one in the lower pole, were positioned in both cortex and medulla on a maximum of five sections covering large parts of the kidneys. The ROIs were placed simultaneously on a coregistered morphologic image with good corticomedullary contrast and on corresponding DW images by a technician. In donors, the mean individual ROI size was 0.25 $cm^3 \pm 0.08$ and 0.28 $cm^3 \pm 0.12$ for the medulla and cortex, respectively, and in recipients, the mean individual ROI size was 0.27 $cm^3 \pm 0.08$ and 0.30 $cm^3 \pm 0.11$ for the medulla and cortex, respectively. The parameters of the up to 15 individual ROIs in the medulla and cortex (mean, 11.2 ± 2.1 and 11.2 ± 1.8, respectively) were averaged to create separate total ROIs, one ROI for the medulla and one for the cortex that represented overall medullary or cortical diffusion properties. While we might have missed focal changes by using this procedure, we did not hypothesize that focal changes might occur in the transplanted kidney or in the remaining nontransplanted kidney. The corticomedullary difference of ADC (ΔADC_T and ΔADC_D) was calculated for each subject by subtracting the ADC value of the averaged ROI in medulla from the value of the ROI in cortex.

Statistical Analysis

A sample size of 12 allograft donors and their corresponding recipients was selected on the basis of a power analysis by using previous DW MR imaging results in transplanted and native kidneys (8,9). The standard deviations in these articles (8,9) were in the range of 5% (approximately 10×10^{-5} mm^2/sec) for ADCs and 22% for F_P. The use of these numbers yields a longitudinal change in ADC of the transplanted kidney or the remaining kidney of less than 6% (eg, a change from [200 to 212] $\times 10^{-5}$ mm^2/sec) and a change in F_P of approximately 20% that could be detected at a significance level of .05 and a statistical power of 80%. These calculated differences for ADC can be presumed reasonable in view of previous results, while the effect size might be slightly high for detecting changes for F_P because of the relatively high variance.

Shapiro-Wilk tests were performed to evaluate for normality. ADC and F_P values were found to be normally distributed. Repeated-measures one-way analysis of variance was conducted. Post hoc pairwise comparisons were performed to compare the parameters at different times. The tests were performed with Bonferroni corrections, which resulted in a multiplication of the uncorrected *P* value by six. Two-tailed paired Student *t* tests were used to compare ADC and F_P values of the remaining kidney in donors with those of the subsequently donated kidney and to compare cortical with medullary values. Pearson correlation coefficient analysis was performed to determine correlations between diffusion parameters and eGFR and between diffusion values in kidneys before explantation and after implantation. A *P* value of less than .05 was assumed to represent a significant difference.

Statistical analyses were performed with statistical software (SPSS, version 18.0.0; SPSS, Chicago, Ill) and spreadsheet software (Excel 2007; Microsoft, Redmond, Wash). Power analysis was performed by using other software (Piface) (19).

Results

All donors and recipients had stable renal function after month 12. No donor or recipient developed significant proteinuria (> 0.5 g per day).

Figure 2

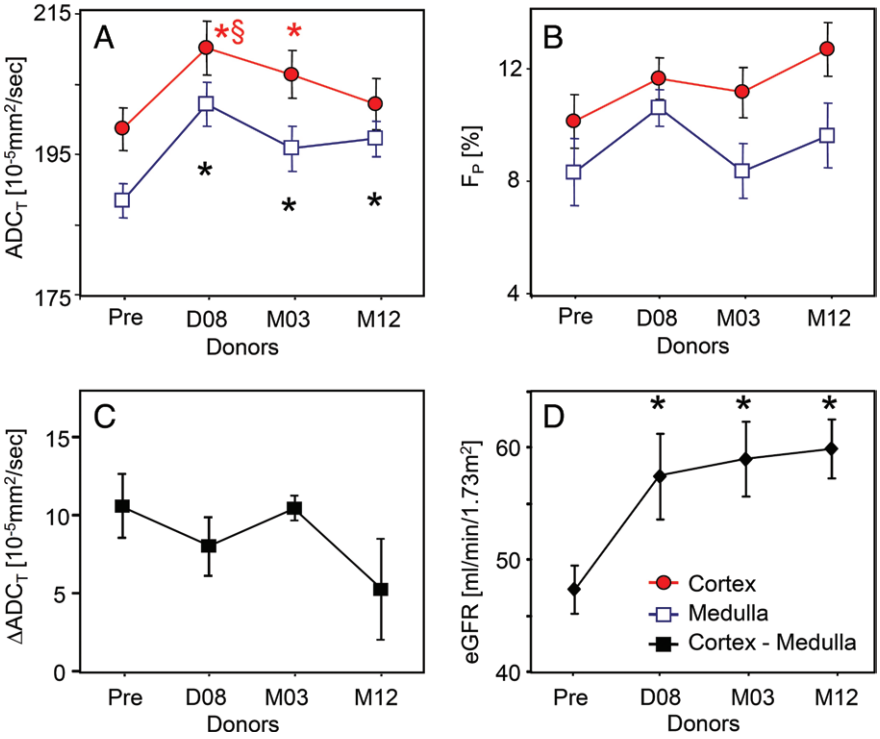

Figure 2: Graphs show times of functional DW MR imaging parameters and eGFR of the native nontransplanted kidneys before and after uninephrectomy in donors. *A,* ADC$_T$. *B,* F_P. *C,* Corticomedullary ΔADC$_T$. *D,* eGFR. Values are plotted versus image times before transplantation *(Pre)* and 8 days *(D08)*, 3 months *(M03)*, and 12 months *(M12)* after explantation. Significant changes (including corrections for multiple comparisons) are indicated: * = Comparison versus before transplantation, § = comparison versus 12 months after explantation. Error bars = standard error of the mean.

The morphologic evaluation of the T2-weighted half-Fourier acquisition single-shot turbo spin-echo and T1-weighted fast low-angle shot images showed no major complication of the allografts in the recipients and of the remaining kidneys in the donors (data not shown).

All DW MR imaging measurements of the 12 allograft recipients and 13 donors were included in the analysis. An example for the longitudinal time course with ADC$_T$ maps of the donor and corresponding recipient (donor 2 and recipient 2, Table E1 [online]) is shown in Figure 1.

Longitudinal Evaluation in Donors

After explantation of one native kidney ADC$_T$ increased significantly in the remaining nontransplanted kidney of all but one donor at day 8 and remained high at month 3 (Fig 2, *A*). From before explantation to day 8, ADC$_T$ increased from (188 ± 9) to (202 ± 11) × 10^{-5} mm^2/sec (P = .0012) in the medulla and from (199 ± 11) to (210 ± 13) × 10^{-5} mm^2/sec (P = .0036) in the cortex. ADC$_T$ declined back toward baseline in the cortex ([202 ± 13] × 10^{-5} mm^2/sec, P = .035 compared with the value at day 8) at month 12, while it remained significantly increased in the medulla ([197 ± 9] × 10^{-5} mm^2/sec, P = .037 compared with the value before transplantation), demonstrating only a trend toward declined values. The corticomedullary difference of ADC$_T$ (ΔADC$_T$), which is clearly present before transplantation, persisted until month 3 and then vanished at month 12 (Fig 2, *C*), although this decrease was not significant after correction for multiple comparisons. The decrease was significant for ΔADC$_D$ at month 12 (P = .028 compared with the value before transplantation), as detailed in Fig E1, *B* (online). F_P increased slightly, albeit not significantly, with time after transplantation (Fig 2, *B*). The eGFR per kidney (ie, dividing the nominal value by two before explantation) increased significantly from before explantation to day 8 (P < .02, compared with day 8 and months 3 and 12) and was constant thereafter until month 12 in the donors (Fig 2, *D*).

Longitudinal Evaluation in Recipients

During 1 year, all determined parameters remained remarkably stable in allograft recipients (Fig 3). No significant change was determined among day 8, month 3, and month 12. Also, when we compared the corresponding values in the donors obtained before explantation (before transplantation in donors [Fig 3]) with the values obtained in the same kidneys after transplantation, no significant difference was determined for ADC$_T$ and F_P.

The corticomedullary difference of ADC$_T$ (ΔADC$_T$) decreased significantly after transplantation (Fig 3, *C*) (P < .03, compared with months 3 and 12). The decrease was also significant for ΔADC$_D$ at month 12 (P = .035, compared with that before transplantation in Fig E1, *B* [online]). The eGFR remained stable in the recipients after transplantation; the comparison with the corresponding pretransplantation eGFR values in donors showed a trend toward higher posttransplantation values (Fig 3, *D*).

Correlations of Diffusion Parameters with eGFR

The initial increase of cortical and medullary ADC$_T$ values in the remaining nontransplanted kidney in donors after explantation was accompanied by an increase of eGFR values (Fig 2). However, no significant correlation was observed between ADC$_T$ values and eGFR and between F_P values and eGFR in donors.

Figure 3

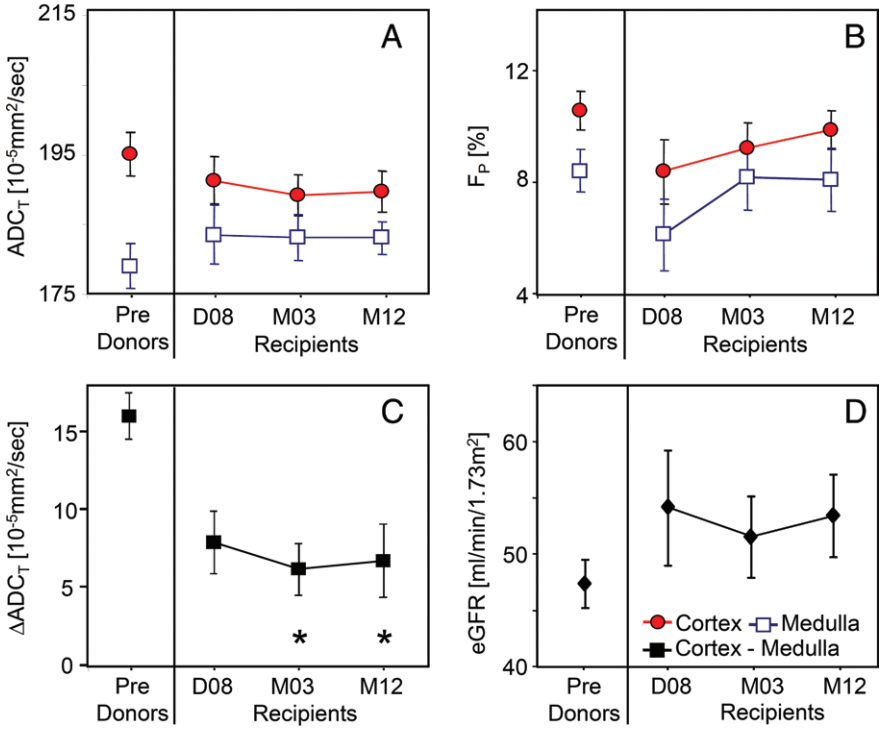

Figure 3: Graphs show times of functional MR parameters and eGFR of the same transplanted kidneys obtained before transplantation *(Pre)* for the subsequently donated kidney from the donor and on day 8 *(D08)* and at month 3 *(M03)* and month 12 *(M12)* after explantation in the corresponding recipient. *A*, ADC_T. *B*, F_P. *C*, ΔADC_T. *D*, eGFR values. * = Significant changes (including corrections for multiple comparisons) in comparison versus before transplantation. Error bars = standard error of the mean.

Figure 4

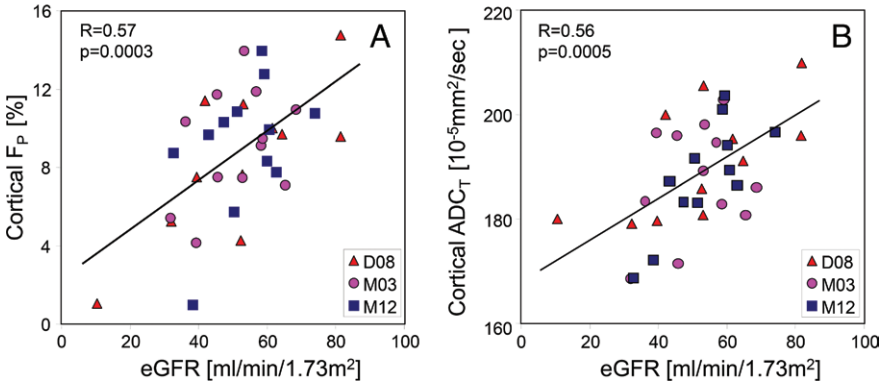

Figure 4: Graphs show relationship between eGFR and, *A*, F_P and, *B*, ADC_T in the cortex of transplanted kidneys. With increasing eGFR, cortical F_P and ADC_T increased in transplanted kidneys. *D08* = day 8, *M03* = month 3, *M12* = month 12.

In recipients, the constancy of ADC_T values and F_P corresponded to eGFR, which also remained stable during 1 year. ADC_T values in cortex (P = .0005) and F_P values in cortex (P = .0003) and in medulla (P = .048) correlated positively and significantly with eGFR in recipients (Fig 4). ΔADC_T values did not correlate significantly with eGFR.

Comparison of Diffusion Values in Kidneys before and after Transplantation

Interestingly, cortical ADC_T values obtained before transplantation in donors correlated significantly with those obtained in the same kidney in recipients on day 8 after transplantation (R = 0.77, P = .006) (Fig 5), while medullary ADC_T values and F_P did not correlate significantly between donors and recipients. Correlations between values in kidneys of donors and recipients at later times (months 3 and 12) were not significant.

Pretransplantation DW MR Imaging Results in Donors

A secondary finding in donors was that ADC_T in cortex and F_P in cortex and medulla were found to correlate significantly between the two native kidneys (ie, the subsequently donated and the remaining nontransplanted kidney) (cortical ADC_T, R = 0.65, P = .016; cortical F_P, R = 0.72, P = .005; medullary F_P, R = 0.79, P = .0012). Surprisingly, mean ADC_T in medulla was significantly higher in the remaining kidney ([188 ± 9] × 10^{-5} mm²/sec vs [180 ± 10] × 10^{-5} mm²/sec, P = .021), as exemplified in the pretransplantation values in Figures 2, *A*, and 3, *A*. Other parameters were not significantly different between the subsequently donated and the remaining kidney. Comparisons of parameters between right and left kidneys did not yield any significant differences.

The mean pretransplantation ADC_T and F_P values of living donors were found to be significantly higher in the cortex than in the medulla (eg, ADC_T, [197 ± 9] × 10^{-5} mm²/sec vs [184 ± 7] × 10^{-5} mm²/sec, with P < .0001; F_P, 11% ± 3 vs 9% ± 4, with P = .011, for the mean of the subsequently donated and the remaining kidney, respectively), while the mean differences between the cortex and the medulla were lower in transplanted kidneys (eg, ADC_T, [189 ± 9] × 10^{-5} mm²/sec vs [183 ± 7] × 10^{-5} mm²/sec, with P = .023; F_P, 9% ± 2 vs 7% ± 2, with P = .007, for the mean of day 8 and months 3 and 12).

Discussion

The results of this longitudinal DW MR imaging study on living renal allograft donors and corresponding recipients show a rapid increase of ADCs in the remaining nontransplanted kidney in living donors after nephrectomy, which appears to reverse slowly over time. In allograft recipients, all determined diffusion parameters remained remarkably constant after transplantation.

In donors, glomerular and also tubular enlargement after uninephrectomy and transplantation are known to represent an early compensatory adaptation mechanism to achieve an adequate renal function (3,6). This renal hypertrophy combined with glomerular hyperfiltration may result in less restricted diffusion and thus be at least partly reflected by the initial increase of ADC values. The subsequent slow decrease of ADC values can be explained either by a reversal of the glomerular hyperfiltration or by the development of interstitial fibrosis or glomerular sclerosis after transplantation, which was found to have an opposite effect on the ADC (16), thus counteracting the initial ADC increase. Glomerular sclerosis in remnant kidneys after nephrectomy has been described frequently in animal models (3,4,20,21) as a consequence of glomerular enlargement (22,23). Glomerular fibrosis is prevalent in the outer cortex (24), which could explain that the ADC values in the cortex decrease more than in the medulla, thus reducing the corticomedullary difference. The gradually decreasing ADC values may herald lower renal function in donors (1) and, thus, may be of clinical relevance. Similarly, the steepness of the initial ADC increase may be of clinical relevance. However, additional long-term studies are required to test this hypothesis.

Hypertrophy is also a well known adaptation process (3,5,6,23) in transplanted kidneys and may be followed by development of interstitial fibrosis and glomerular sclerosis (7,23,25). Thus, an early increase in ADC values comparable to that of the remnant kidney in donors would have been anticipated for the allograft. However, longitudinal ADC values in recipients were stable during the 1st postoperative year. ADC changes and differences do not solely reflect glomerular or tubular size adaptation. Other factors such as cold ischemia time, nephrotoxicity of immunosuppressive therapy, or the occurrence of unrecognized rejection can induce functional changes in the transplant and, as a consequence, can affect ADC values: Especially, the use of calcineurin inhibitors as immunosuppressants is responsible for a partly reversible, long-term intense arteriolar vasoconstriction and, hence, a reduction of glomerular filtration rate that counteracts a possible glomerular hyperfiltration after renal transplantation (26). The result that the diffusion parameters in allografts are relatively stable over time corresponds to findings in previous DW MR imaging studies in unrelated stable renal allografts at a mean of 10 days ± 4, 9 months, and almost 3 years after transplantation, where quite constant values were obtained (8,9,27).

The lower corticomedullary difference of ADC values in allografts compared with native kidneys may correspond to the similarly small difference at month 12 in the remaining kidney of donors and may be due to glomerular fibrosis primarily in the outer cortex in transplants (7). This smaller corticomedullary difference was also previously detected in transplanted kidneys (9).

In contrast to ADC, the perfusion contribution of F_P did not change significantly in donors after transplantation and demonstrated only a trend toward higher cortical values. F_P also did not change significantly in allograft recipients. In view of the hyperfiltration and correspondingly increased blood flow in allografts (24,28), the absence of an increase of F_P is largely surprising. In part, this can be explained by the relatively large variations of estimated F_P values. Nevertheless we trust the present results, because F_P values correlated between the subsequently donated and the remaining kidney. F_P is probably determined, in addition, by other factors, such as the time of medication intake. It should be noted that the values for F_P are lower than previously reported (9). This apparent discrepancy can be explained primarily by shorter echo times used in the present study compared with those used in previous articles (8,9,27), as has been demonstrated recently (29). Lower F_P may, in addition, result from improved signal stability (lower spurious inclusion of signals from other tissue, such as from the pelvis) and by slight processing differences.

Velosa et al (30) noted that the donated kidney is exposed to a variety of insults, including the trauma of surgical removal and reimplantation, variable periods of warm and cold ischemia, or the influence of nephrotoxic agents. However, the significant correlations of cortical ADC values between the same kidney in the donor and in the recipient before and at day 8 after transplantation indicate an important effect of the original kidney status on diffusion parameters, counterbalancing at least some of these insults. Transplanted kidneys may adapt with time to the metabolic and hemodynamic characteristics of the recipient (6,31), a phenomenon explaining possibly the disappearance of correlations of diffusion parameters between the kidney in the donor and the recipient after longer times.

Figure 5

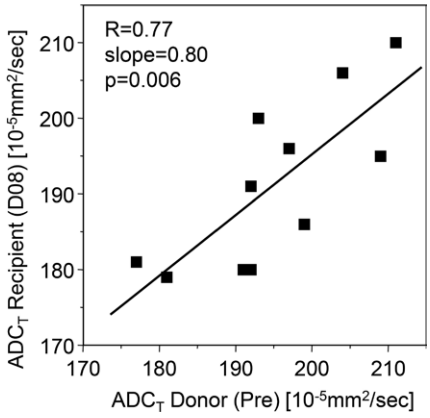

Figure 5: Graph shows comparison of cortical ADC_T in the same kidney before transplantation *(Pre)* in donors and on day 8 *(D08)* after transplantation in recipients, with a significant positive correlation.

Our results for eGFR are in agreement with findings in a previous study (30) in which the researchers demonstrated an increase in glomerular filtration rate within 1 week after transplantation and stability thereafter, traditionally explained by a compensatory hypertrophy. Correlations between diffusion parameters and eGFR confirm previous findings in native kidneys (32) and in transplanted kidneys, where exactly the same correlations were found between diffusion parameters and serum creatinine level as a measure for renal function (9). These results suggest again that the parameters are determined in part by eGFR. Additional studies are required to determine whether DW MR imaging measurements provide information beyond eGFR.

The finding that the diffusion parameters were correlated before transplantation between the subsequently donated and the remaining kidney was anticipated. However, the significant ADC difference between the remaining and the donated kidneys was unexpected. The difference may be caused by common clinical preselection criteria on the side of nephrectomy, such as vessel length. However, currently we do not have a conclusive explanation for this finding, which may also be spurious. Methodological bias, especially bias from systematic differences between right and left kidneys, was not confirmed as an explanation.

There were several limitations to our study. First, the variability of F_p estimation is still quite large, which may reduce the clinical utility of this parameter. In the current study, only respiratory triggering was used, but no respiratory-cardiac double triggering, which has been shown to reduce the variability of the diffusion parameters in kidneys (33,34). Second, no histopathologic correlations were available to better understand and substantiate the interpretation of the detected DW MR imaging findings. Third, the sample size was relatively small.

In conclusion, the present investigation demonstrates that DW MR imaging has the capability to help detect early adaptations in the remaining nontransplanted kidney of donors after nephrectomy. All determined diffusion parameters remained constant in allograft recipients after transplantation. Our results suggest that there is a potential monitoring utility of the method. However, the assessment of the potential clinical relevance of functional MR imaging in renal transplantation deserves further clinical studies.

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