T2 mapping and diffusion weighted imaging for quantification of acute and chronic renal pathology following acute kidney injury in mice – comparison with histopathology

Katja Hueper[1], Martin Meier[2], Marcel Gutberlet[1], Song Rong[3], Xia Lu[4], Hermann Haller[3], Frank Wacker[1], Dagmar Hartung[1], and Faikah Gueler[3]

[1]*Radiology, Hannover Medical School, Hannover, Germany,* [2]*Institute of Animal Science, Hannover Medical School, Hannover, Germany,* [3]*Nephrology, Hannover Medical School, Hannover, Germany,* [4]*Zunyi Medical College, Wuhan, China*

Target audience: Radiologists and physicist with an interest in experimental imaging studies in small animal models and functional MRI of the kidney.

Purpose: Acute kidney injury (AKI) is associated with inflammation, loss of renal function and progressive renal fibrosis. The purpose was to investigate whether T2 mapping and diffusion weighted imaging (DWI) allow quantification and monitoring of acute and chronic changes after ischemia induced AKI in mice and to compare imaging results with histology.

Methods: Different severities of AKI were induced in C57Bl/6 mice by transient unilateral clamping of the right renal pedicle for 35 min (n=10, moderate AKI) or 45 min (n=7, severe AKI). MRI was performed in fully anesthetized animals prior to surgery and at different time points after surgery (d1, d7, d14, d21, d28) using a 7 Tesla scanner (Bruker, Pharmascan). Respiratory triggered multi-echo turbo spin echo (TR = 2000 ms, TE = 11, 22, 33 ms, matrix = 256x256, FOV = 35x35 mm^2, slice thickness = 2 mm) and fat-saturated respiratory triggered echoplanar diffusion-weighted sequences (TR/TE = 4000/22 ms, 7 b-values = 0-700 s/mm^2, matrix = 128x128, FOV 35x35 mm^2, slice thickness = 2 mm) were acquired. Parameter maps of T2 and apparent diffusion coefficients (ADC) were calculated using a monoexponential fit. Renal T2 and ADC values were determined in cortex, outer medulla and inner medulla. In the same animals kidney damage after 4 weeks was assessed by histology and immunohistochemistry (fibrosis: Masson-Goldner staining, α-SMA, inflammation: F4/80 as marker of macrophage infiltration) and by the kidney volume loss. T2 and ADC values of different anatomical layers were compared with the contralateral normal kidney and between groups of moderate and severe AKI and were correlated with kidney volume loss and histology. Values are given as mean±SEM.

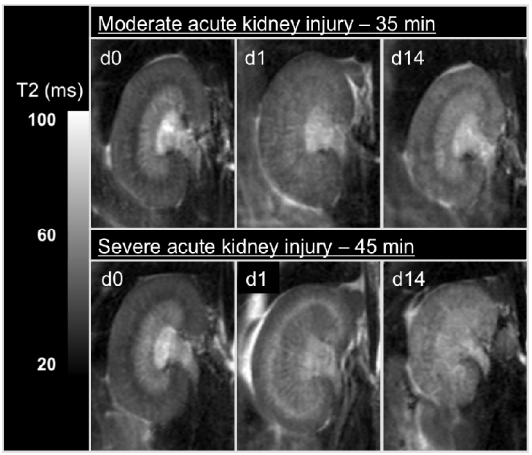

Figure 1: T2 maps at different time points after moderate AKI (upper row) and after severe AKI (lower row). Note that the image size as well as window level and width are similar for all images.

Results: After AKI increase of T2 was most pronounced in the outer medulla (Figure 1). At day 1 after surgery, T2 values were 26±6% higher after severe AKI (**p<0.01) and 13±7% higher after moderate AKI compared to the contralateral normal kidney. Maximum T2 values were reached 7 days after surgery with an increase of 32±7% (**p<0.01) after severe and 27±4% after moderate AKI (***p<0.001, Figure 2A). In animals with severe AKI T2 increase in the outer medulla was significantly higher when compared to moderate AKI at day 7-14 (*p<0.05). At day 7, T2 values significantly correlated with kidney volume loss at day 28 (r=0.69, **p<0.01). Medullary ADC after severe AKI was reduced from 1.59±0.06*10^{-3} mm^2/s to 1.28±0.05*10^{-3} mm^2/s (**p<0,01) at day 1 after surgery and restriction of diffusion compared to the contralateral normal kidney persisted till day 28 (**p<0.01). ADC changes after moderate AKI were less pronounced (Figure 2B). Consistent with changes of MRI parameters, the severity of histological changes (fibrosis, inflammatory cell infiltration) in the same animals at day 28 was significantly higher after severe than after moderate AKI. Similarly, kidney volume loss at day 28 was more pronounced after severe than after moderate AKI (40±5% vs. 26±6%, ***p<0.001).

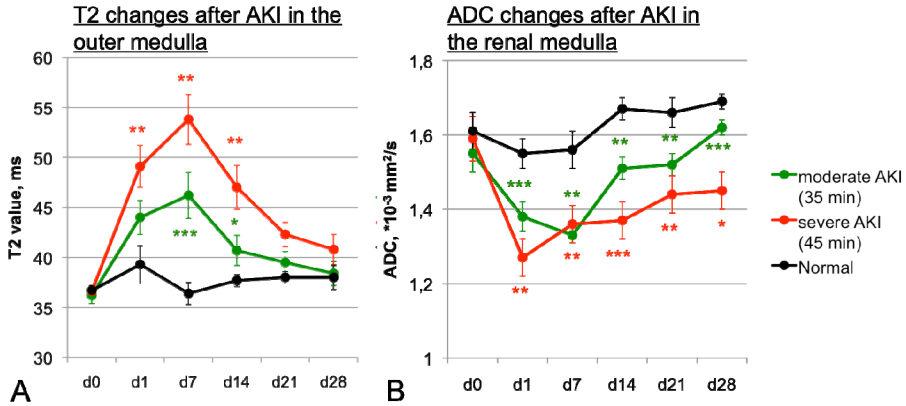

Figure 2: T2 and ADC changes at different time points after unilateral AKI. T2 values in the outer medulla (A) and ADC values in the renal medulla (B) are shown after moderate (35 min ischemia time, green) and severe AKI (45 min ischemia time, red) and in the contralateral normal kidney (black). P-values indicate significant changes compared to the normal kidney. *p<0.05, **p<0.01, ***p<0.001.

Discussion and Conclusion: T2 mapping and DWI allow non-invasive quantification and monitoring of presence and severity of acute (edema, inflammatory cell infiltration) and chronic (fibrosis, kidney volume loss) changes after AKI in mice. The magnitude of acute changes of T2 and ADC indicates the severity of chronic kidney damage.