Arterial spin labeling for quantification and monitoring of renal blood flow changes after acute kidney injury in mice – comparison with histopathology and renal function

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

[1]*Radiology, Hannover Medical School, Hannover, Germany,* [2]*Nephrology, Hannover Medical School, Hannover, Germany,* [3]*Institute of Animal Science, Hannover Medical School, Hannover, Germany*

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

Purpose: Acute kidney injury (AKI) leads to inflammation, decrease of renal perfusion, loss of renal function and progressive renal fibrosis. The purpose was to investigate whether arterial spin labeling (ASL) allows quantification and monitoring of renal perfusion impairment in a mouse model of ischemia induced AKI and to compare imaging results with invasive measurement of renal function (glomerular filtration rate, GFR) and with renal histology.

Methods: AKI was 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, fat-saturated T2-weighted turbo spin echo sequences were acquired in axial and coronal planes and kidney volumes were determined by manual segmentation. For quantification of RBF a fat-saturated flow sensitive alternating inversion recovery (FAIR) EPI ASL sequence was used: TR/TE = 10,000/16.4 ms, 13 inversion times = 30-8000 ms, matrix = 128x128, FOV = 35x35 mm^2, slice thickness = 2 mm. Motion artifacts were compensated by rigid registration of ASL-images and parameter maps of RBF were calculated. Morphological changes of renal tissue in the same animals after 4 weeks were assessed by histology and immunohistochemistry (peritubular capillaries: CD31, fibrosis: Masson-Goldner staining, α-SMA) and kidney volume loss. Furthermore, GFR was evaluated by measurement of inulin clearance. Cortical RBF measurements by MRI were compared between time points and between groups of different AKI severities and were correlated with renal function, histology and kidney volume loss. Values are given as mean±SEM.

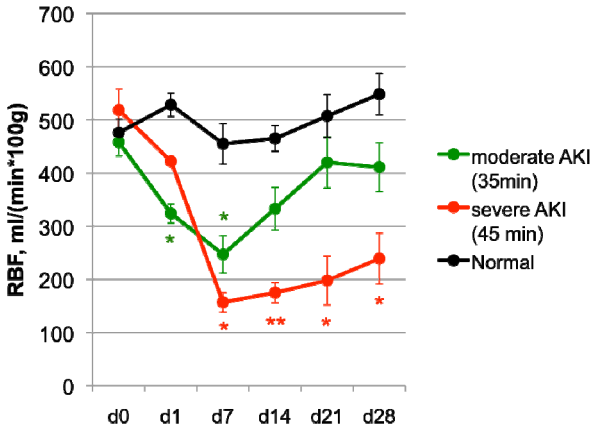

Figure 1: RBF changes at different time points after unilateral AKI. RBF after moderate (35 min, green) and severe AKI (45 min, red) and in the contralateral normal kidney (black) are shown. P-values indicate significant changes compared to baseline after Bonferroni correction. *p<0.05, **p<0.01.

Results: After moderate AKI cortical RBF at day 7 was reduced from 459±26 ml/(min*100g) to 247±36 ml/(min*100g) (**p<0.01) and returned to baseline at d28. Cortical RBF after severe AKI remained significantly reduced compared to the contralateral normal kidney and the RBF before surgery till d28 (**p<0.01). Furthermore, cortical RBF was significantly lower after severe AKI than after moderate AKI at days 14-28 (*p<0.05; Figure 1). Corresponding to renal perfusion impairment quantified by MRI, renal function and histological alterations were significantly more pronounced in animals with severe than in animals with moderate AKI. Similarly, kidney volume loss at d28 was greater after severe AKI than after moderate AKI (40±5% versus 26±6%; ***p<0.001). The percentage reduction of cortical RBF measured by MRI at day 7 significantly correlated with kidney volume loss at d28 (r=0.62, **p<0.01) indicating the predictive value of early perfusion impairment for chronic kidney damage. Example of RBF maps and morphological images of animals with moderate and severe AKI are shown in Figure 2.

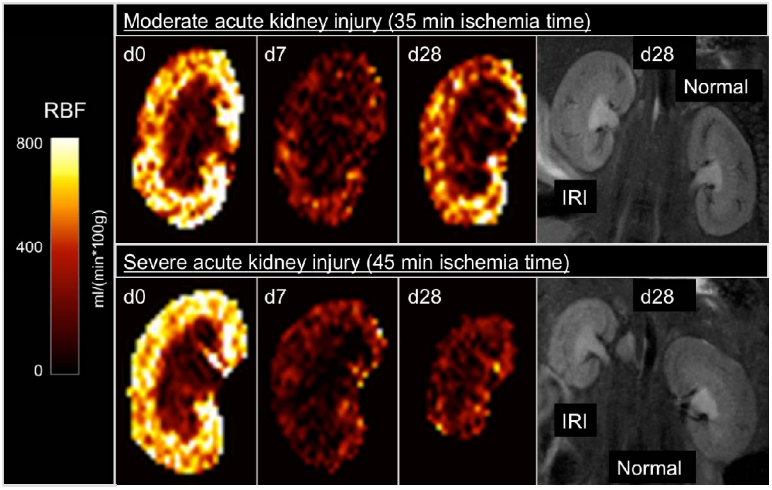

Figure 2: Examples of RBF maps and T2-weighted images after unilateral AKI. RBF changes at different time points after moderate (upper row) and severe AKI (lower row) are shown. Note that the image size as well as window level and width are similar for all RBF maps. T2-weighted images of both kidneys at day 28 (on the right) show marked kidney volume loss of the right kidney after severe AKI and minimal volume loss after moderate AKI compared to the contralateral normal kidney.

Discussion and Conclusion: ASL allows non-invasive quantification and monitoring of perfusion changes after AKI in mice. These changes correlate with impairment of kidney function and morphological kidney damage and indicate presence and severity of AKI at an early time point.