Using dynamic contrast-enhanced MR-CEST urography for detecting changes in kidney function following urinary tract obstruction

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Introduction: Urinary tract obstructions (UTOs) are blockages in the urinary tract that impede normal urine flow, causing urinary retention and increased retrograde pressure[1]. Because the extent of recovery of renal function depends on severity and duration of obstruction, early diagnosis and intervention are crucial for preventing irreversible kidney damage[1]. While effective in characterizing the upper tract, ultrasonography and traditional CT are limited in quantifying kidney function[2]. Renal scintigraphy can be applied for assessment of differential kidney function but its anatomical resolution is poor[2]. In contrast, iopamidol-enhanced chemical exchange saturation transfer (CEST) MRI has been shown to provide functional information by generating spatially localized renal pH maps and time-activity curves [3,4,5]. In this study, we explore the potential of dynamic contrast-enhanced MR-CEST urography in mice with UUO.

METHODS: For the in vivo study, the right ureter of six mice was obstructed via suture ligation and animals imaged at day 1 (3 mice) and 2 (3 mice) post-obstruction on a 11.7 T Bruker MRI scanner. A total of 204 CEST images, including twelve M_0 images and 96 sets of saturated images at 4.3 and 5.5 ppm were collected with: B_1 = 3.6 μT, t_{sat} = 3sec, TE/TR = 3.49/5125 msec, matrix: 64x64, slice thickness: 1.5 mm, RARE factor: 32. Iopamidol was injected via tail-vein catheter. Renal time-course enhancement curves were measured as a percentage change in the post-injection CEST- signal at 4.3 ppm relative to the average pre-injection signal. For pH mapping, saturation transfer ratio (ST_{Ratio}) at 4.3 and 5.5 ppm was quantified from three averaged images collected at the peak enhancement time. Averaged pre-injection maps were then subtracted from the post-injection images to remove endogenous signals. Renal pH values were obtained using a calibration curve as described previously[3].

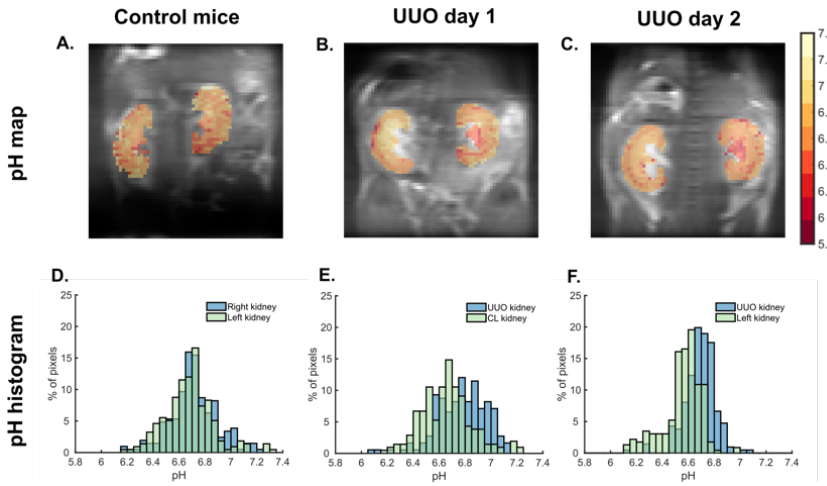

Figure 1: pH maps and pH histograms measured in (A, D) a control mouse, (B, E) UUO mice at day 1 and (C, F) day 2 after obstruction.

Results: For the healthy mice, the dynamic CEST curves of both kidneys were nearly identical and displayed rapid excretion. The representative renal pH map and histogram displayed similar acidity for both kidneys (pH 6.71 ± 0.06 and 6.68 ± 0.08, **Fig. 1**). In UUO mice, the time-activity curve for the obstructed kidneys displayed prolonged contrast excretion and decreased ST_{ratio} values. These time-activity curves showed clear differences between the healthy and UUO kidneys which reflects the uptake and excretion of iopamidol differences. At one day after UUO, there was an increase in pH values in the obstructed kidney, especially in the inner and outer medulla, compared with the contralateral (pH 6.77 ± 0.05 and 6.66 ± 0.05 in the UUO and CL kidney, respectively). The same trend could be observed at day 2 after obstruction (pH 6.69 ± 0.05 and 6.56 ± 0.04 in the UUO and CL kidney, respectively). Box-plot analysis for all six UUO mice revealed increased pH values in the UUO kidneys compared with the native kidney.

Discussion: We have applied DCE-MR CEST urography to a murine model of obstructive nephropathy and non-invasively assessed kidney function over 2 days after UUO. Our results demonstrate that a dynamic CEST acquisition combined with a single injection of iopamidol allows simultaneous measurements of both renal perfusion and pH, as opposed to the conventional diagnostics, which provide only one type of metric to characterize kidney function. As early as one day after UUO, we observed both increased pH values, which are likely due to tubular defects in urinary acidification and retention of iopamidol in the renal parenchyma of the UUO kidney, which suggests a decline in renal function. Overall, these results suggest that CEST imaging might be particularly useful for monitoring progression of renal injury caused by UTOs. We believe that our dynamic CEST MRI protocol is promising for early assessment of upper UTOs and could be translated to patients with obstructive nephropathy.

CONCLUSION: Our findings indicate that DCE-MR-CEST urography can detect changes in renal filtration and pH homeostasis and distinguish between obstructed and unobstructed kidney as early as one day after UUO.

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