Non-invasive determination of renal cortical, outer and inner medullary blood flow, oxygenation and diffusion in healthy volunteers using ASL, BOLD and DWI MRI

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Authors: P. Eckerbom¹, E. Cox², J. Weis¹, P. Hansell¹, I. Subasic¹, F. Palm¹, S. Francis², P. Liss¹,¹ Uppsala/SE, ²Nottingham/UK

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Aims and objectives

Due to, among other things, the risks associated with ionizing radiation, contrast media in patients with impaired renal function and the possible risk of cerebral Gadolinium deposition there is a need for non-radiative, non-invasive methods to image renal physiological parameters. Magnetic resonance imaging (MRI) can provide biomarkers for kidney function that are non-invasive and relatively fast to assess. Before use in pathological conditions, baseline renal characteristics of a healthy population must be obtained. The aim of this study was to evaluate the non-invasive MRI techniques phase contrast, arterial spin labeling (ASL), blood oxygen level dependent (BOLD) and diffusion in healthy volunteers in order to obtain normal values, to see if measurements are reliable and to see if there are differences between the genders, the pair of kidneys or regional differences between cortex, outer and inner medulla.
Methods and materials

The Institutional Review Board approved all protocols and informed written consent was obtained from every subject before being enrolled in the study. Twenty-eight healthy volunteers (13 male, 15 female) were recruited and underwent an MRI-examination using a 3T MRI-scanner (Philips, Achieva, Best, The Netherlands) to yield Phase contrast, ASL, BOLD, and diffusion sequences. Also, a T1 sequence was obtained for anatomical orientation and detail. Analyses of total renal blood flow (RBF) by phase contrast, regional RBF by ASL, oxygenation level by BOLD and water diffusion by apparent diffusion coefficient (ADC) were made on both kidneys. Kidney cortex was analyzed with one single region of interest (ROI) which encompassed most of the cortical parenchyma whereas for outer and inner medulla, measurements were done by applying a ROI in four different areas of the outer and inner medulla respectively in each kidney and the mean value of those was used in the evaluation. Analyses of obtained parameters were made bilaterally using Gyrowiew Software (Philips, Best, The Netherlands) for phase contrast, Image J (Open software, NIH, Bethesda, Maryland, USA) for ASL, Pride Software (Philips, Best, The Netherlands) for BOLD and DWI.
Results

Total renal blood flow by Phase contrast MRI.

Total renal blood flow was obtained in 26 subjects (14 females, 12 males). In two of the 28 original study subjects phase contrast measurements could not be done due to technical issues with the scanner. Total RBF in females was 467±155 ml/min in the right kidney and 453±166 ml/min in the left kidney. In males the corresponding values were 543±169 ml/min and 564±78 ml/min, respectively. No significant difference in blood flow was found between left and right kidney neither in females nor in males. The difference in total renal blood flow between males and females in our study can be related to a larger body mass/blood volume in the male group than in the female group but was not significant. Total renal blood flow was though significantly related to both body surface area (m²) and BMI, see fig 1 and 2.

The mean total renal blood flow of all measurements (females, males, left and right kidneys) was 503±138 ml/min/kidney which correlates well with previous findings (ref 1).

Regional renal blood flow by ASL

Cortical renal blood flow in females was 296±77 ml/min/100g in the right kidney and 278±68 ml/min/100g in the left kidney. The corresponding values in males were similar, 295±58 ml/min/100g and 291±61 ml/min/100g respectively. Outer medullary blood flow in females was 95±24 ml/min/100g in the right kidney and 89±15 ml/min/100g in the left kidney. The corresponding values in males were 83±26 ml/min/100g and 90±13 ml/min/100g. Inner medullary blood flow in females was 44±26 ml/min/100g in the right kidney and 38±13 ml/min/100g in the left kidney. For males these figures were 41±21 ml/min/100g and 45±24 ml/min/100g respectively.

Statistically significant inter regional differences in blood flow were found between all three studied regions, fig 3.

No significant difference in regional renal blood flow by ASL was found between left and right kidney neither in females nor in males or between the genders.

The mean cortical, outer medullary and inner medullary blood flow values of all measurements (females, males, left and right kidneys) was 289±63, 89±14 and 42±14
ml/min/100g, respectively. Our measures of mean cortical blood flow is in conformity with previous findings (ref 2,3). To the best of our knowledge, no previous studies has studied outer and inner medulla separately.

**Oxygenation level by BOLD**

Cortical oxygenation level determination by BOLD (R2*) in females was 16,5±1,2 ms⁻¹ in the right kidney and 16,1±1,8 ms⁻¹ in the left kidney. The corresponding values in males were 16,8±1,0 ms⁻¹ and 16,5±1,2 ms⁻¹ respectively. Outer medullary BOLD in females was 25,3±1,5 ms⁻¹ in the right kidney and 27,4±1,7 ms⁻¹ in the left kidney and the corresponding values in males were 26,5±2,3 ms⁻¹ and 28,4±2,9 ms⁻¹. Inner medullary BOLD in females was 33,7±5,1 ms⁻¹ in the right kidney and 37,1±3,7 ms⁻¹ in the left kidney. The corresponding values in males were 36,7±3,9 ms⁻¹ and 40±4,9 ms⁻¹.

Stastistically significant inter regional differences in oxygenation level by BOLD were found between all three studied regions, fig 4.

No significant difference in regional renal oxygenation level by BOLD was found between left and right kidney neither in females nor in males or between the genders.

The mean cortical, outer medullary and inner medullary oxygenation values of all measurements (females, males, left and right kidneys) was 16,5±1,1, 26,8±1,6 and 36,8±3,8 ms⁻¹, respectively. Our mean cortical BOLD value is in consistency with previous findings (ref 4). To the best of our knowledge, no previous studies has studied outer and inner medulla separately.

**Regional Diffusion by ADC**

The apparent water diffusion coefficient of the cortex in females was 2,06±0,33 mm² s⁻¹ in the right kidney and 2,03±0,37 mm² s⁻¹ in the left kidney. The corresponding values in males were 2,09±0,27 mm² s⁻¹ and 2,19±0,19 mm² s⁻¹ respectively. Outer medullary ADC in females was 1,82±0,35 mm² s⁻¹ in the right kidney and 1,75±0,34 mm² s⁻¹ in the left kidney. For males the corresponding values were 1,88±0,20 mm² s⁻¹ and 1,88±0,13 mm² s⁻¹ respectively. Inner medullary ADC in females was 1,63±0,43 mm² s⁻¹ in the right kidney and 1,62±0,44 mm² s⁻¹ in the left kidney. The corresponding values in males were 1,74±0,22 mm² s⁻¹ and 1,68±0,13 mm² s⁻¹.
Stastistically significant inter regional differences in water diffusion by ADC were found between all three studied regions, fig 5.

No significant difference in regional renal water diffusion was found between left and right kidney neither in females nor males or between the genders.

The mean cortical, outer medullary and inner medullary apparent water diffusion values of all measurements (females, males, left and right kidneys) was $2.09\pm0.27$, $1.83\pm0.25$ and $1.67\pm0.31 \text{ mm}^2\text{s}^{-1}$, respectively.

Our mean cortical ADC value is in relatively good consistency with previous findings (ref 5). To the best of our knowledge, no previous studies has studied outer and inner medulla separately.
Fig. 1: Total RBF vs Body surface area.

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Fig. 2: Total RBF vs BMI.

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Fig. 3: Regional RBF: Mean of dx and sin, all subjects.

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Fig. 4: Regional BOLD: Mean of dx and sin, all subjects.

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Fig. 5: Regional ADC: Mean of dx and sin, all subjects.

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Conclusion

In this study we find that non-invasive measurements of physiologically relevant renal parameters using MRI techniques phase contrast, ASL, BOLD and diffusion are reliable and able to detect significant intrarenal heterogeneity in blood flow, oxygenation and diffusion. We also find that total renal blood flow is significantly correlated to body surface area and to BMI. No significant differences regarding total RBF, regional RBF, oxygenation level or diffusion were found when comparing the right and left kidney or between the genders.
Personal information

Per Eckerbom, MD

Head of Section for Molecular and Thoracic imaging.
Centre for medical imaging
Uppsala university hospital

SE-751 85 Uppsala
Sweden

E-mail: per.eckerbom@akademiska.se
References


