

Preliminary Evaluation of Renal BOLD MRI for Monitoring Progression in CKD Patients

M. E. Haque¹, U. Bokhary¹, S. Fettman², S. Sprague², and P. Prasad¹

¹Radiology, NorthShore University HealthSystem, Evanston, IL, United States, ²Nephrology, NorthShore University HealthSystem, Evanston, IL, United States

Introduction:

The realities of effective but limited resources heighten the need to identify and target patients at highest risk for whom aggressive medical management would have the most impact. In the clinical setting nephrologists are routinely challenged to assess the severity of chronic kidney disease (CKD) in patients and their risk for progression. Current clinical markers such as serum creatinine, kidney size, and proteinuria are not sufficient to reliably detect early CKD or predict risk of progression. Kidney biopsy can provide useful information but is invasive and poses inherent risks and can be subject to sampling errors. Hence, it is highly desirable to develop new non-invasive markers that could identify those subjects with CKD, particularly in early stages, and those that will progress to end stage renal disease.

In this preliminary study, we investigated the use of renal BOLD MRI to detect any early changes in oxygenation status in subjects with CKD. Specifically, we performed a cross-sectional study to compare intra-renal R_2^* measurements in healthy subjects, subjects with different stages of CKD and a group of anemic subjects with no renal disease. Because advanced stage of CKD is associated with anemia and since Hb levels can potentially influence BOLD MRI measurements, we included a group of subjects who have anemia but no CKD.

Material and Methods:

All procedures were performed in compliance with our institutional review board guidelines with written subject consent. A total of 19 subjects participated to-date: healthy control (n=7), anemic (n=4, Hb levels = 11.1 ± 0.69 g/dl), CKD stage 2 or 3 (n=5), and CKD stage 4 or 5 (n=3). All subjects came to the study after an overnight fast and MRI studies were performed using whole body 3.0 T Verio (Siemens Erlangen, Germany) system. BOLD imaging parameters include: Pulse Sequence= MGRE, FOV = 360 x 245mm, No. of Slice = 5, Slice thickness = 5.0mm, Matrix = 256 x 256, TR = 62ms, No. Echo = 8 equally spaced (3.09 – 32.3ms). NEX = 1. BOLD MRI data acquisitions were performed before and after administration of 20 mg of furosemide (i.v.).

Data Analysis: A T_2^* map was generated on the scanner platform and twelve ROIs were selected (six each in cortex and medulla of both kidneys) on each slice. R_2^* color maps were generated offline using Matlab (Mathwork, Natick MA). All the maps were scaled from zero to 75 s^{-1} . Note that higher R_2^* values imply relatively lower oxygenation levels. A two tailed Students t-test was performed to test for statistical significance.

Results:

Figure 1 shows representative renal R_2^* maps illustrating the changes in cortico-medullary R_2^* before and after administration of furosemide in each group.

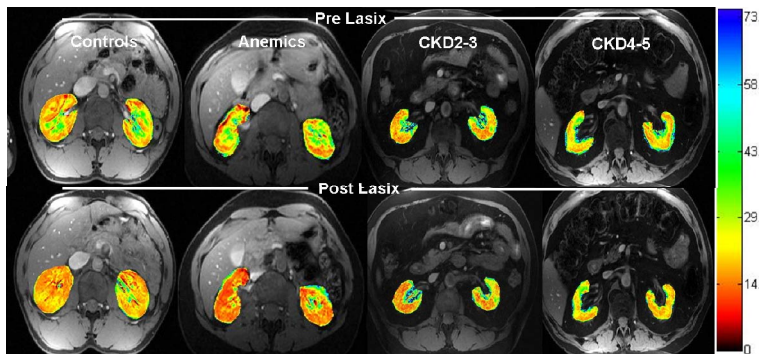
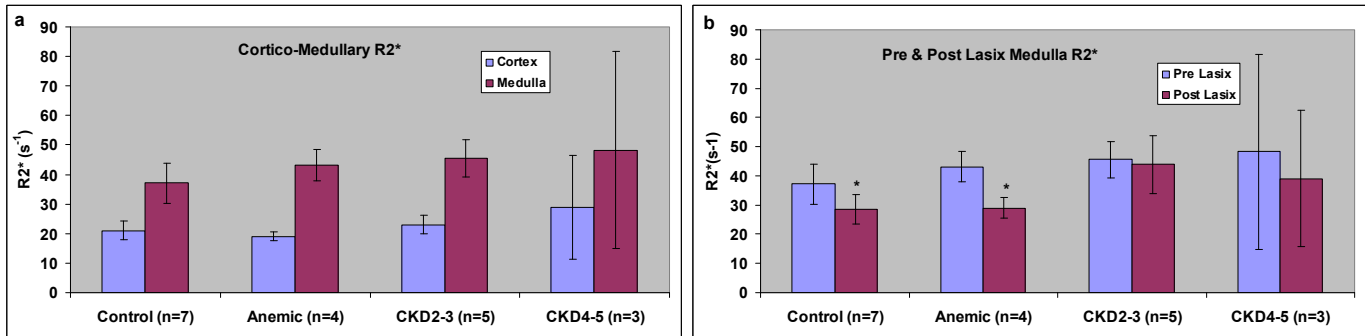


Fig 1: Representative R_2^* maps from each group. Top row is pre furosemide images from each group and the corresponding post lasix R_2^* maps are shown in the bottom row. The color bar represents the R_2^* values, red being better oxygenation whereas blue is relatively hypoxic. Note the decrease in medullary R_2^* values post-furosemide in the control and anemia groups. Also note the limited cortico-medullary contrast in patients with advanced CKD and also there is loss of renal parenchyma.

Figure 2. (a) Summarizes the cortical and medullary R_2^* values in the different groups. Note the increased levels of hypoxia with the stages of CKD. There was no significant difference between the healthy control and the anemia groups. (b) summarizes the changes in medullary R_2^* before and after administration of furosemide. Note the reduced change in R_2^* following furosemide in the subjects with CKD. Consistent with previous reports the healthy controls and anemic subjects show significant reduction in medullary R_2^* post furosemide (*P-value < 0.05). There was no change

in the cortical R_2^* values in any of the groups following furosemide (data not shown).



Discussion:

- There was no significant difference between the healthy controls and the anemic groups. This suggests the degree of change in Hb within the levels observed in CKD may not have any significant influence on the BOLD MRI measurements.
- A trend towards increasing levels of hypoxia is observed in the CKD groups, especially in the cortex.
- Subjects with CKD respond minimally to furosemide, while the control groups showed a significant decrease in medullary R_2^* i.e. 37.2 ± 6.8 to $28.7 \pm 5.0 \text{ s}^{-1}$, and 43.2 ± 5.3 to $29.0 \pm 3.5 \text{ s}^{-1}$ respectively.

In conclusion, our preliminary experience with BOLD MRI measurements in patients with CKD suggest increasing levels of hypoxia especially in the cortex and show minimal response to furosemide in terms of a change in medullary R_2^* . Further studies with larger numbers of CKD patients are warranted and currently in progress.

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