Published in final edited form as:

Invest Radiol. 2009 September ; 44(9): 566–571. doi:10.1097/RLI.0b013e3181b4c1e8.

Comparison of 1.5 and 3T BOLD MR to study oxygenation of kidney cortex and medulla in human renovascular disease

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Abstract

Imaging of the kidney using BOLD MR presents a major opportunity to examine differences in tissue oxygenation within the cortex and medulla applicable to human disease. We sought to define the differences between regions within kidneys and to optimize selection of regions of interest for study with 1.5 and 3 Tesla systems. Studies in 38 subjects were performed under baseline conditions and after administration of furosemide intravenously to examine changes in R2* as a result of suppressing oxygen consumption related to medullary tubular solute transport. These studies were carried out in patients with atherosclerotic renal artery stenosis (n= 24 kidneys) or essential hypertension or non-stenotic kidneys (n= 39). All patients but one were treated with agents to block the renin angiotensin system (ACE inhibitors or angiotensin receptor blockers). For each kidney, three levels (upper pole, hilum, and lower pole) were examined, including three individual segments (anterior, lateral, and posterior). Low basal R2* levels in kidney cortex (12.06 ± 0.84 sec⁻¹) at 1.5 Tesla reflected robust blood flow and oxygenation and agreed closely with values obtained at 3.0 Tesla (13.62 ± 0.56 sec⁻¹, NS). Coefficients of variation ranged between 15–20% between segments and levels at both field strengths. By contrast, inner medullary R2* levels were higher at 3 T (31.66 ± 0.74 sec⁻¹) as compared to 1.5 T (22.19 ± 1.52 sec⁻¹, p<.01). Medullary R2* values fell after furosemide administration reflecting reduced deoxyhemoglobin levels associated with blocked energy-dependent transport. The fall in medullary R2* at 3.0 Tesla (-12.61 ± 0.97 sec⁻¹) was greater than observed at 1.5 T (-6.07 ± 1.38 sec⁻¹, p<.05). Cortical R2* levels remained low after furosemide and did not vary with field strength. Correlations between measurements of defined cortical and medullary ROIs within kidneys were greater at each sampling level and segment at 3.0 T as compared to 1.5 T. For patients studied with 3.0 T, furosemide administration induced a lesser fall in R2* in post-stenotic kidneys at 3.0 T (-10.61 ± 1.61 sec⁻¹) versus non-stenotic kidneys (-13.21 ± 0.72 sec⁻¹, p<.05). This difference was not evident in comparisons made at 1.5 T. The magnitude of furosemide-suppressible oxygen consumption at 3.0 T (–43 %) corresponded more closely with reported experimental differences observed during direct measurement with tissue electrodes (45–50%) than changes measured at 1.5 T. These results indicate that BOLD MR measurements at high field strength can better distinguish discrete cortical and inner medullary regions of the kidney and approximate measured differences in oxygen tension. Maneuvers that reduce oxygen consumption related to tubular solute transport allow functional evaluation of the interstitial compartment as a function of tissue oxygenation. Impaired response to alterations in oxygen consumption can be

detected at 3T more effectively than at 1.5 T and may provide real-time tools to examine developing parenchymal injury associated with impaired oxygenation.

Keywords

Blood Oxygen Level Dependent (BOLD); magnetic resonance imaging (MRI); tissue oxygenation; renal artery stenosis; kidney; hypertension

Introduction

Measurement of blood oxygen level dependent (BOLD) MR offers the potential to examine regional tissue oxygenation non-invasively based upon paramagnetic properties of deoxyhemoglobin (1). This capability is particularly important for the study of conditions within the kidney, where local differences of blood supply and energy-dependent transport produce major differences in oxygen tension between the cortex and inner medullary regions (2). How these differences translate into different propensities for tissue injury under conditions of reduced organ blood flow is difficult to study and of major clinical importance (3).

Under normal conditions, the oxygen tension in the cortex exceeds that in the medulla. Furthermore, initial studies in humans using 1.5 Tesla systems confirm the potential for BOLD MR to detect alterations within medulla and cortex in the response to nephrotoxic contrast (4;5), allograft injury (6), water loading (7) and occlusive renal arterial disease (8). These studies underscore the greater sensitivity of the medulla to be affected by changes in oxygenation as compared to cortex. Maneuvers that reduce oxygen consumption, such as inhibition of energy-dependent tubular transport of sodium in the thick ascending limb of Henle's loop with furosemide, demonstrate greater sensitivity within the medulla than cortex by at least two-fold (8). The reported magnitude of the difference between cortex and medulla has been variable, however, with differences in $R2^*$ ranging between 10.8% and 45.6% (average estimate 31%) (5;6;8–14;14–20). Exactly how regions of interest (ROI) were defined in each of these studies varied considerably between reports.

We reasoned that increasing the field strength from 1.5 to 3 Tesla would not only increase the signal strength for medullary $R2^*$ under conditions of enriched deoxyhemoglobin, but demonstrate larger $R2^*$ variation under conditions of changing oxygen consumption, thereby improving reliability and precision of these measurements. Alternatively, susceptibility artifacts related to adjacent bowel gas and image non-uniformity or shading from nonhomogeneous radiofrequency distribution may increase at 3T and negate these potential benefits. To reduce effects from image artifact and to more precisely define boundary regions, we sought to standardize definition of regions of interest (ROI) to minimize variability within the kidney and to examine regional differences related to alterations in blood flow. Observations that T2 * weighted gradient echo images sometimes depict broader zones than those observed by iodinated contrast and by in-vivo measurement (21) highlight the importance of limiting ROI to small segments in cortex and medulla (FIGURE 1). Consistent definition of the ROIs is critical to avoid partial volume artifacts between medullary and cortical zones that might occur if one attempts to include the entire medulla. Using this approach, we measured BOLD MR signals within human kidneys before and after furosemide comparing 1.5 and 3.0 Tesla systems. We undertook to compare cortical and medullary $R2^*$ signal strength and variability within several planes (upper pole, hilum, and lower pole) comparing anterior, lateral and posterior segments in kidneys of patients with and without atherosclerotic renal artery stenosis. The results of these studies confirm our hypothesis of substantial improvement in sensitivity to detect alterations in

regional oxygenation and response to suppressed oxygen consumption using 3.0 Tesla BOLD MR in humans.

Methods

Thirty-eight patients undergoing MR angiography with BOLD imaging were selected with previously identified atherosclerotic renal arterial disease or essential hypertension. Patients were included with moderate to severe renal artery stenosis, as defined by ultrasound velocities above 260 cm/sec in the affected artery, but excluding total arterial occlusion. When present and functional, the contralateral kidney was analyzed within the “non-stenotic kidney” group. Care was taken to ensure that included patients were treated with agents to block the renin-angiotensin system (angiotensin converting enzyme inhibitors (ACE inhibitors) or angiotensin receptor blockers (ARB’s)) and were not being treated with loop diuretics. Before renal MR imaging and gadolinium-enhanced MR angiography, BOLD imaging was performed at 1.5 or 3.0 Tesla field strength to measure $R2^*$ levels in medullary and cortical regions of the kidney using customized abdominal organ protocols as previously described (8;22). The records and clinical features of these subjects were reviewed with approval from the Mayo Institutional Review Boards. Studies using 3T were performed as part of a prospective treatment protocol for which all patients signed informed consent.

MRI examinations were performed either on GE Twin Speed EXCITE 1.5T systems or on GE Twin Signa EXCITE 3.0T system (GE Medical Systems, Waukesha, WI) using an 8 channel torso phased array coil. The BOLD pulse sequence used here allowed either 8 or 16 echoes. Based upon our experience, image quality was superior with 8 echoes, and the acquisition time slightly shorter. Three-plane single shot fast spin echo localizers were performed during suspended respiration followed by additional scout images (single shot fast spin echo) oriented parallel to the long axis of each kidney. These long axis scout images were then used to prescribe transverse BOLD images in a plane orthogonal to the long axis. Eight echoes were obtained for each slice location, with TE’s ranging from 2.5 ms to 30 ms. Imaging parameters for the BOLD acquisition included: TR 140 ms, flip angle 45 degrees, slice thickness 5 mm, imaging matrix 224×160–192, field of view (FOV) 32–40 cm, with 0.7–1.0 partial phase field of view (PFOV). Image matrix and TR were adjusted in patients with limited breath hold capacity, and the FOV and PFOV adjusted according to patient size. BOLD images were acquired during suspended respiration, typically with three slices through the upper pole, mid pole, and lower pole of one kidney obtained during a 20 second acquisition. Parametric images of $R2^*$ were then generated by fitting signal intensity versus TE data to an exponential function on a voxel by voxel basis.

Following the initial BOLD acquisition, furosemide (20 mg) was administered intravenously and flushed with 20 ml of saline. The BOLD measurements were repeated 15 minutes later. BOLD images were analyzed on an Advantage Windows workstation version 4.2 (GE Healthcare, London, UK) using CineTool software (GE Healthcare). This program generates a set of parametric images of $R2^*$ from the BOLD sequence data by fitting signal intensity data from each echo on a voxel by voxel basis to an exponential function describing the expected signal decay as a function of TE and solving for the unknown value of $R2^*$.

Signal-to-noise (SNR) measurements were performed on the first echo of the baseline BOLD acquisition (TE 2.5 ms, TR 140 ms) by placing ROIs in the renal cortex of the hilar slice and in the nearest adjacent air space. SNR was determined as the average renal signal intensity divided by the standard deviation of the noise measurement.

For data analysis, ROIs were traced in the cortex and medulla manually, on the 7 msec TE image or any other image yielding optimal contrast between cortex and medulla, and then

implemented at the parametric R2* image to determine average values of R2* within the ROI. Special care was taken to avoid areas of artifacts on individual slices and to ensure that each region of interest fell within identifiable medullary and cortical sections that remained within the segment upon repeat scanning after furosemide. The anterior, lateral and posterior ROIs were used for cortex and medulla on each plane of analysis (upper, hilum, and lower) (FIGURE 2). For each kidney the mean values and coefficients of variation were determined taking into account 3 cortical and 3 medullary R2* values per plane/segment, therefore providing 9 cortical and 9 medullary values per kidney.

Statistical analysis

Results were expressed using mean values and standard error of the mean (SEM). Comparison between groups studied with 1.5 and 3.0 T regarding R2* values were performed with t-tests or Wilcoxon rank sum tests as appropriate (23). Analysis of covariance (ANCOVA) was used to test for relationship between 1.5 and 3.0T groups and the response of R2* after furosemide adjusting for pre-furosemide R2*. Variability estimates between regions of interest within each plane were taken as the coefficients of variation between the anterior, lateral and posterior segments. Bivariate associations among these segments were presented as Spearman correlation coefficients. P-values <0.05 were considered statistically significant.

Results

This study included a total of 63 kidneys, of which 14 kidneys were studied with 1.5 Tesla (1.5T) BOLD MR and 49 kidneys studied with 3 Tesla (3T) BOLD MR. Both groups included kidneys affected by renal artery stenosis and non-stenotic kidneys (contralateral kidneys or kidneys of patients with essential hypertension). Age, serum creatinine and the number of kidneys for each group are summarized in TABLE 1: The degree of renal artery stenosis was estimated by Doppler peak systolic velocity above 260 cm/sec and estimated stenosis >70% (24). No kidney with total arterial occlusion as determined by an absent nephrogram with MR was included.

Variability of Cortical and Medullary R2* Values

Summarized in TABLE 2 are mean values for three locations within the kidneys studied, corresponding to the upper pole, the hilum region, and lower pole of the kidney. Cortical values were not different between 1.5 and 3.0T, but medullary R2* levels were consistently higher with 3.0 T as compared to 1.5 T at every location (e.g. hilum: 31.66 ± 1.66 /sec (3T) vs 21.19 ± 1.52 /sec (1.5T), $p < .001$; TABLE 2). Mean values agreed closely between locations, and the correlation between levels (Spearman $R = 0.716$ to 0.515) did not differ between magnet field strengths. Estimates of signal to noise ratios (SNR) were obtained using comparison between cortical ROI's and adjacent non-renal tissue. As expected, renal cortical SNR at 3T was higher than at 1.5 T (14.6 ± 1.1 vs. $7.8 \pm .8$, $p = .03$).

When considering individual segments, mean values for anterior, lateral and posterior segments obtained within each location agreed closely with one another (TABLE 3). However, internal correlations between values obtained for each kidney as predictors of other segments were higher for 3.0 T than 1.5 T for both medullary (Spearman $R = 0.491$ vs $R = 0.434$) and cortical values ($R = 0.503$ vs 0.343 , $p < .05$).

Differences in Medullary and Cortical values between 1.5 and 3.0 T

Absolute values for cortical and medullary R2* for all kidneys studied (mean values for all planes and all segments) are summarized in FIGURE 3. Cortical R2* did not differ between 1.5 T ($11.93 \pm .43$) and 3.0 T ($13.61 \pm .48$). Medullary R2* values were higher at 3T

(33.54 ± 1.4) as compared to those at 1.5 T ($21.89 \pm .85$) ($p < .001$). Coefficients of variation among measured cortical values averaged 14% for 1.5 T and 21% for 3.0T. Coefficients of variation for medulla were 15% for 1.5 T and 16% for 3.0 T.

At both field strengths, medullary $R2^*$ fell after furosemide, whereas no consistent change was evident in the cortical regions. Post-furosemide values at 3.0 T remained higher than those observed with 1.5 T (TABLE 3). The fall in medullary $R2^*$ after furosemide was greater at 3.0T than at 1.5 T ($-12.3 \pm .64$ vs. -5.07 ± 1.0 , $p < 0.0001$). This represented both a greater absolute and relative change (-22.9% vs -38.1% , $p < .01$) using 3 Tesla.

Stenotic vs non-stenotic Kidneys

Mean $R2^*$ values for stenotic and nonstenotic kidneys at both field strengths are summarized in TABLE 4 and FIGURE 4. Baseline cortical values for $R2^*$ did not differ between stenotic and non-stenotic kidneys at either 1.5 and 3.0T. No changes in cortical $R2^*$ were apparent after administration of furosemide at either field strength. Similarly, baseline medullary $R2^*$ did not differ between stenotic and non-stenotic kidneys at either 1.5 or 3.0T. However, absolute values were lower for both stenotic and non-stenotic kidneys at 1.5 T (TABLE 4). $R2^*$ fell after furosemide administration in both stenotic and non-stenotic kidneys. At 3T both relative (percentage) and absolute medullary changes after furosemide were reduced in the post-stenotic kidney as compared with non-stenotic kidneys ($-10.6/\text{sec}$ vs $-13.21/\text{sec}$, $p = 0.05$). Such a difference was not apparent with 1.5 T (-6.46 vs -3.67 , NS). The variability and magnitude of changes at 1.5 T were such that no difference was evident with this system.

Discussion

The results of our study delineate regional (cortex and medulla) differences in tissue oxygenation using 1.5 and 3.0 Tesla BOLD MR in hypertensive patients with and without large vessel arterial stenosis. These data underscore the functional differences in the medullary region recognized as having less blood flow and higher levels of deoxyhemoglobin as compared to the cortex (3;25). The medullary region therefore had higher $R2^*$ values when compared to cortex, consistent with its known relative hypoxia (3). This difference was magnified when examined at 3T as compared to 1.5T both in absolute and relative terms. Our results indicate that within the renal cortex little difference in $R2^*$ values before and after furosemide could be detected at either 1.5 or 3T. We interpret this to reflect a relative surfeit of blood flow that ensures well-oxygenated blood and low levels of deoxyhemoglobin. By contrast, the higher field strength allowed greater sensitivity to detect known changes in medullary $R2^*$ observed during acute changes in oxygen consumption, such as those produced by inhibiting energy-dependent solute transport (3). Comparisons of stenotic and non-stenotic kidneys at 3.0 T field strength and carefully defined regions of interest indicated that although baseline medullary $R2^*$ levels were similar in moderately stenotic and non-stenotic kidneys, furosemide-suppressible oxygen consumption (FSOC) was reduced in the post-stenotic kidneys (FIGURE 4).

Which of these estimates of cortical and medullary deoxyhemoglobin is most informative and closest to physiologic levels? Results from experimental studies in rats (26;27) and other models (25;28) using oxygen probes suggest that tissue oxygen levels fall as one moves from cortex to deep medullary regions. Often, the difference reaches 45–50% (3;28). Studies of oxygen consumption within various portions of the kidney indicate that tubular transport within thick ascending limb of Henle's loop may account for up to 65% of "suprabasal" oxygen consumption (29). Most of this segment is located within the medullary region. Time-studies suggest that intravenous furosemide reaches near maximal inhibition of tubular chloride transport in the thick ascending limb within 10 minutes and changes little thereafter

(29). Our results suggest that inhibition of medullary tubular solute transport reduces medullary $R2^*$ values by nearly 40% in non-stenotic kidneys (FIGURE 4). These observations support the view that differences observed with the 3T between cortex and medulla, and particularly the larger changes observed as furosemide-suppressible oxygen consumption (FSOC) using the 3T system were consistent with expected physiologic changes.

Several previous studies using 1.5T, including our own, report less striking baseline differences between cortex and medulla (5;6;9;14). Our previous mean $R2^*$ with 1.5 T was 22.2 /sec in cortex and 24.3 /sec in medulla (8). Measurement of FSOC demonstrates consistently reduced medullary $R2^*$ levels(18), as we observed before (8). Our results in the present study were intended to more precisely define smaller regions of interest within cortex and medulla. A significant pitfall in describing larger regions of interest based upon BOLD source images is the imprecise separation between outer cortex and inner medulla, with a “border zone” of outer-medulla/inner-cortex that may not be sharply defined (21) (FIGURE 1). A further hazard is that repeat imaging after furosemide may be associated with slight shifts in tissue location that induce inadvertent partial volume artifact between medulla and cortex. Our efforts here were to standardize smaller regions clearly within outer cortex and clearly in deep medulla that would not likely drift into a different zone during repeat measurement. As noted in TABLE 2, both cortical and medullary regions as defined in this fashion were reproducible and consistent between different sampling sites using this method (both between upper pole, hilum and lower pole planes, and between anterior, lateral, and posterior segments within planes). The role of partial volume artifact induced by larger cortical ROI was confirmed by comparing the present measurements to those obtained during the previous study. Using this method to define ROIs, differences between regional $R2^*$ levels were more consistently observed (at both 1.5 and 3T alike), than in most previous human studies.

Measurement of $R2^*$ responses related to FSOC confirmed the value of this approach. The fact that cortical values remained nearly constant as expected, suggested that the smaller ROI's in fact remained localized to the cortex on re-measurement. Most importantly, medullary $R2^*$ levels fell more consistently than observed in previous studies and at both 1.5 and 3 T field strengths. Imaging abdominal organs using 3T can be affected by artifacts from adjacent structures. Occasionally, gas in the colon or small bowel generated significant artifact and limited accurate measurement of $R2^*$. Swapping phase and frequency direction of BOLD acquisition sometimes helped, but often simply moved the artifacts to a different location. In our experience, gas artifacts have been variable using 3T, but not to the extent of negating the benefits of higher magnetic field strength for BOLD imaging. We believe that limiting analysis to localized, stable segments in cortex and medulla represents an improvement in analytical technique.

Conducting BOLD MR studies at 3.0T provided additional advantages over 1.5 T when comparing stenotic and non-stenotic kidneys. As noted above, the absolute and relative differences between medulla and cortex were larger at 3.0T, consistent with higher level detection of the paramagnetic effects of deoxyhemoglobin per se. An additional feature related to measurement of FSOC at 3T was the ability to detect reduced change in medullary $R2^*$ values in post-stenotic kidneys that was not evident using the 1.5 T unit (FIGURE 4).

The reduction in FSOC in post-stenotic kidneys may have several explanations. We believe that blunted responses to furosemide represented a marker of kidney tubulo-interstitial injury that resulted in reduced energy-dependent tubular transport. Previous studies from our institution and others indicate that the post-stenotic kidney often has reduced blood flow and glomerular filtration (30;31). Measurements of FSOC in kidneys that are non-functional

beyond complete arterial occlusion demonstrate minimal responsiveness (8;22). Similar changes with reduced medullary $R2^*$ signal are evident in kidney allografts with active interstitial inflammation (6) or during acute ureteral obstruction due to stones (9). We suspect that kidneys that remain functional beyond partial atherosclerotic occlusive lesions as observed here have partial impairment of FSOC as part of gradually progressive interstitial injury. Studies in an animal model of atherosclerosis and renal artery stenosis indeed demonstrate tubular dysfunction distal to the occlusive lesion (32). An additional mechanism may reflect reduced FSOC in stenotic kidneys on the basis of reduced pharmacologic activity, e.g. reduced arterial delivery of furosemide, reduced filtration and luminal activity and transport of the drug. These mechanisms are not mutually exclusive and further studies to define the basis for alterations in medullary $R2^*$ signals in health and disease are needed.

Limitations in this study reflect the differences in specific patients and sample size analyzed using the methods reported here. While the absolute medullary $R2^*$ levels and relative change after furosemide using the 3T system were different in all patients with hypertension with and without renal artery stenosis, we cannot exclude the possibility that differences between stenotic and non-stenotic kidneys partly reflected differences in the patients studied rather than intrinsic differences in magnet field strength. The larger numbers of patients studied with 3T using these methods may have improved detection limits of some of these differences. We were gratified to observe that analytic strategies to more sharply localize cortical and medullary regions of interest improved the resolution of functional differences between local areas of the kidney at both field strengths.

Taken together, these studies extend the potential for BOLD MR to be applied as a functional tool to examine disease states in the kidney. Our results underscore the need to precisely define stable and consistent ROI's within cortex and medulla that avoid volume averaging artifacts. They further demonstrate substantially higher relative and absolute $R2^*$ signals in the ischemic regions of the kidney, consistent with demonstrated areas of locally reduced tissue oxygen. Most importantly, these preliminary studies using 3T BOLD MR indicate changes in $R2^*$ after inhibition of transport-related tubular oxygen consumption reach a quantitative level approximating established suprabasal oxygen consumption related to tubular transport in the medulla. Changes observed with 1.5 T were consistently below this magnitude. These data support application of BOLD MR imaging using 3T with precisely defined ROI's as a functional measure of regional tissue oxygenation and changes in oxygen consumption for further study of human renovascular disease.

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Figure 1. (A, Left) BOLD image at Hilum level of non-stenotic right kidney at baseline (before furosemide) obtained in a subject with atherosclerotic renovascular disease imaged at 3T. (B) Iodinated contrast image from CT angiogram of the same kidney defining the cortical and medullary regions clearly. Note that the cortical regions delineated by CT are narrower than regions defined by the T2 signal with MR. The bright segments with MR reflect higher T2 signals (hence lower levels of $R2^*$, defined as $1/T2^*$) that extend into outer medulla. These figures underscore the need to define carefully limited cortical and deep medullary regions of interest (ROIs) to examine regional differences reproducibly (see text).

Figure 2.

Schematic illustration of three levels (Upper, Hilum, Lower) routinely sampled for BOLD MR in this project, with demarcation of three segments sampled in each plane. Care was taken to apply the region of interest (ROI) in each case to a limited area that would reliably fall in the same region of repeat examination and would avoid volume averaging artifacts between cortex and medulla as seen in FIGURE 1 (see text).

Figure 3.

Furosemide-induced changes in BOLD MR: Comparison of $R2^*$ at 1.5 and 3.0 T: Mean $R2^*$ values for cortex and medulla at baseline and after intravenous furosemide to inhibit solute transport. The change in medullary $R2^*$ after furosemide represents a fall in deoxyhemoglobin (i.e. furosemide-suppressible oxygen consumption (FSOC)). By contrast, no differences were apparent in $R2^*$ between 1.5 and 3T in cortex and no consistent change was observed after furosemide.

Figure 4.

Changes in Medullary R2* values after intravenous furosemide in subjects with functioning kidneys identified with and without renal arterial stenosis. Both absolute values (TABLE 4) and changes in R2* were less with 1.5 T as compared to 3.0 Tesla ($p < .01$). For the patients studied with 3.0 T, medullary R2* fell to a lesser extent in stenotic kidneys as compared with non-stenotic kidneys ($p < .05$).

TABLE 1

Demographic characteristics of subjects undergoing Blood Oxygen Level Dependent (BOLD) MR at 1.5 and 3.0 Tesla

Magnet Strength	1.5 T	3T
Gender F/M	5F/4M	15F/14M
Mean age	76 (59–85)	66.2 (33–84)
Number of analyzed kidneys	14	49
Number of stenotic kidneys	7	17
Number of non stenotic kidneys	7	32
Serum creatinine : mean (min-max)	1.6 (0.8–3.9)	1.04 (0.5–2.6)

Note: Each stenotic kidney was evaluated from a separate patient.

TABLE 2

BOLD MR R2* values (Mean±SEM) for each plane (upper pole, hilum, lower pole) and for 1.5 and 3 Tesla Systems

Type of MRI	1.5T			3T		
	Upper pole	Hilum	Lower pole	Upper pole	Hilum	Lower pole
Mean R2* ± SEM						
Cortex baseline	12.19 ± 0.4	12.06 ± 0.84	11.53 ± 0.33	13.39 ± 0.51	13.62 ± 0.56	13.6 ± 0.44
Cortex post furosemide	12.39 ± 0.59	12.31 ± 0.5	12.93 ± 0.48	13.01 ± 0.51	13.66 ± 0.44	14.27 ± 0.43
Medulla baseline	22.09 ± 0.92	22.19 ± 1.52	21.41 ± 0.79	33.69 ± 1.05	31.66 ± 0.74	31.68 ± 0.99
Medulla post furosemide	18.26 ± 1.24 **	16.11 ± 1.08 **	16.11 ± 0.98 **	20.44 ± 1.1 **	19.05 ± 0.82 **	20.64 ± 1.21 **
Medullary response to furosemide	-3.83 ± 1.29	-6.07 ± 1.38	-5.3 ± 1.22	-13.26 ± 1.03 #	-12.61 ± 0.97 #	-11.04 ± 1.19 #

** p<.001 vs baseline

p<.01 vs changes observed at 1.5 T.

TABLE 3
R2* values (Mean±SEM) per segment (anterior, lateral, posterior) and for 1.5 and 3 T BOLD MRI.

Type of MRI	1.5T			3T		
	Anterior	Lateral	Posterior	Anterior	Lateral	Posterior
Mean R2* ±SEM						
Cortex Baseline	11.36 ± 0.48	12.5 ± 0.87	11.92 ± 0.33	13.23 ± 0.45	13.6 ± 0.51	13.76 ± 0.54
Cortex post furosemide	12.39 ± 0.3	12.04 ± 0.58	13.2 ± 0.81	13.29 ± 0.44	13.89 ± 0.43	13.7 ± 0.5
Cortical response to furosemide	1.03 ± 0.56	-0.46 ± 0.47	1.28 ± 0.87	0.23 ± 0.31	0.3 ± 0.32	-0.06 ± 1.05
Medulla Baseline	21.86 ± 1.01	21.82 ± 1.34	22 ± 1.09	32.08 ± 1.02	31.51 ± 0.77	33.44 ± 0.82
Medulla post furosemide	16.79 ± 0.87 **	14.76 ± 0.67 **	17.17 ± 1.18 **	20 ± 0.99 **	18.03 ± 0.74 **	20.72 ± 1.05 **
Medullary response to furosemide	-5.07 ± 1.18	-7.06 ± 1.2	-4.83 ± 1.28	-12.09 ± 1.06 #	-13.48 ± 0.71 #	-12.72 ± 0.75 #

** p<.001 vs baseline

p<.01 vs changes observed at 1.5 T.

TABLE 4
R2* values (Mean±SEM) for stenotic and non stenotic kidneys with 1.5 and 3 T BOLD MRI

Type of MRI	1.5 T				3T			
	SK (n=7)		NSK (n=7)		SK (n=17)		NSK (n=32)	
	Mean R2*	SEM	Mean R2*	SEM	Mean R2*	SEM	Mean R2*	SEM
Cortex Baseline	11.61	0.76	12.24	0.44	13.46	0.81	13.58	0.59
Cortex post furosemide	12.17	0.45	12.92	0.41	13.88	0.8	13.52	0.46
Cortical response to furosemide	0.56	0.48	0.68	0.69	0.43	0.34	-0.06	0.26
Medulla Baseline	21.57	1.57	22.22	0.81	33.15 ##	1.76	31.92	0.69
Medulla post furosemide	15.11 &	0.87	18.55 \$	1.2	22.55 * &	1.56	18.71 \$	0.72
Medullary response to furosemide	-6.46	1.25	-3.67	1.47	-10.6 # **	1.16	-13.21	0.72

* p=.0075 vs 1.5 T

\$ p< .0001 vs baseline

& p< .0001 vs baseline

p=.0486 vs 1.5 T

p< .0001 vs 1.5 T

** p=.05 vs NSK

SK = Stenotic kidneys; NSK = Non stenotic kidneys