**Timecourse of BOLD response in normal rat kidney following vasomodulator administration using standard 1.5T clinical hardware.**

Neil Peter Jerome¹, Jessica K R Boult¹, Matthew Orton¹, James D'Arcy¹, David J Collins¹, Dow-Mu Koh⁲, and Simon P Robinson¹

¹CRUK-EPSRC Cancer Imaging Centre, The Institute of Cancer Research, Sutton, Surrey, United Kingdom, ²Department of Radiology, Royal Marsden Hospital, Sutton, Surrey, United Kingdom

**Introduction**

Clinical MRI scanners are being increasingly exploited for pre-clinical studies, a reflection of significant hardware advances available on such platforms, and enhanced clinical relevance. Use of the human-optimised system for small animal work naturally has limitations in resolution, but the use of parallel imaging with existing coils can attempt to bridge the gap from simple volumetric to more functional studies. The introduction of a small-loop extremity coil, in parallel with a head/neck array allows greater sensitivity to signals arising from small rodents, and allows detection of BOLD changes following administration of vasomodulators such as hydralazine, furosemide and angiotensin II. We demonstrate sensitivity to these challenges in images acquired using standard 1.5T clinical hardware, and the use of this setup to follow the timecourse of the BOLD response.

**Experimental**

Female Sprague-Dawley rats (n=3) were anaesthetised and a lateral tail vein cannulated with a heparinised 27G butterfly catheter for intravenous administration of agents. MRI was performed on a 1.5T Siemens Avanto scanner, in three sessions at least one week apart. For MR imaging, each animal was secured supine, using an insulating vacuum beanbag to retain body heat and to prevent excessive movement, centered on a small-loop TMJ coil and centered within the multi-element head RX coil. Elements of the head/neck array were used in parallel with the small-loop coil during all acquisitions. BOLD scans were acquired with multiple gradient echo sequence, with echo times 5, 10, 20, 30, and 40ms, fat suppression, and parallel imaging factor 2; voxel size was 0.6x0.6 mm in-plane, 5mm slice thickness. A 128x128 matrix was acquired and interpolated to 256x256. Flip angle was 25, with 12 averages, for a scan time of 4 minutes 30 seconds. The BOLD scan was conducted at baseline, and then repeated three times immediately following administration of either hydralazine (5 mg/kg) and furosemide (5 mg/kg), administered as a bolus, or angiotensin II infused at 0.5 µg/min/kg. Images were processed using proprietary software (ADEPT, The Institute of Cancer Research, UK), with ROIs drawn for whole kidney, using anatomic T₂-weighted scans as reference. Scans where significant (through-plane) partial voluming was observed for the kidney were not analysed. Fitting for T₂* used Markov Chain Monte Carlo (MCMC) Bayesian statistical approach [1], with no filtering or smoothing of data.

**Results**

A typical image, and the corresponding T₂* map, are shown in Figure 1; acceptable resolution was achieved with an appreciable slice thickness, although through-plane voluming precluded segmentation of cortex and medulla; at the longest echo time of 40 ms, the signal approached the noise floor. The median values of T₂* are given in Table 1; baseline values for each challenge were not significantly different (p > 0.25, unpaired t-test). Each of the agents caused a measurable and significant change in T₂*, the timecourse of which is shown in Figure 2. Hydralazine caused a decrease in T₂* that became significant after the first post-bolus scan and continued to decrease. Administration of furosemide caused an increase in T₂* that was significant for all time points; at 7 and 11 minutes following the bolus, the T₂* appeared to level off at approximately 48 ms. Angiotensin II decreased T₂* at both first time point, but immediately plateaued, with the T₂* 11 minutes after injection being significantly greater than that at 7 minutes (p = 0.016, Wilcoxon signed rank sum test).

![Figure 1: Typical GRE (TE 20 ms) image and T₂* map acquired using parallel combination of TMJ and head coils. In-plane resolution 0.6x0.6 mm, slice thickness 5mm.](image)

Table 1: Average values (ms, mean ± std. error) for median T₂* of whole kidney in successive scans. * indicates p < 0.05 against baseline value, and † indicates p < 0.05 against previous time point (Wilcoxon).

<table>
<thead>
<tr>
<th>t (mins)</th>
<th>Hyd</th>
<th>Fuo</th>
<th>Ang</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>37.7 ± 2.0</td>
<td>36.7 ± 2.3*</td>
<td>34.5 ± 1.5**</td>
</tr>
<tr>
<td>2.25</td>
<td>36.7 ± 2.3*</td>
<td>44.7 ± 2.4**</td>
<td>48.5 ± 2.8**</td>
</tr>
<tr>
<td>6.85</td>
<td>34.5 ± 2.4</td>
<td>29.8 ± 1.9**</td>
<td>29.4 ± 1.1*</td>
</tr>
<tr>
<td>11.4</td>
<td>30.2 ± 1.4**</td>
<td>47.8 ± 3.0*</td>
<td>30.7 ± 1.1**</td>
</tr>
</tbody>
</table>

![Figure 2: Timecourse of whole kidney median T₂* (n=6) following administration of (black) hydralazine bolus, (blue) furosemide bolus and (red) angiotensin II infusion. Data shown are mean ± s.e.](image)

**Discussion**

We demonstrate here the ability to successfully image small animals using a parallel arrangement of vendor coils; sufficient signal arises from the combination of extremity and head coils to conduct multiple gradient-echo images within a reasonable timeframe to monitor renal T₂* response to vasomodulation. The effect of hydralazine bolus was a clear decrease in T₂* that continued even over the experimental timecourse, consistent with the well-described vasodilatory action of this drug. In contrast, furosemide and angiotensin II challenges appear more difficult to interpret, perhaps due to a more complex mechanism of action. Furosemide is a potent loop diuretic that inhibits reabsorption in the thick ascending loop of Henlé, causing a decrease in renal blood volume which is reflected by this change in T₂* [2]. Angiotensin II is a naturally-occurring hormone and has a complex role within the renal renin-angiotensin system (RAS) [3], and the T₂* decrease observed may be due to a combination of actions including reactive vasoconstriction.

**Conclusion**

This study clearly demonstrates the use of a conventional clinical imaging platform for pre-clinical BOLD MR imaging of renal physiology, and the longitudinal T₂* response to vasomodulation within the medulla and cortex. Combined with other intrinsic MR imaging biomarkers, this approach will enable a deeper interrogation and understanding of the homeostatic response to vasomodulation, with the potential to be extrapolated to sequential investigations of renal disease and pathophysiology.

**References**


**Acknowledgements**

We acknowledge the support received for the CRUK and EPSRC Cancer Imaging Centre in association with the MRC and Department of Health (England) (grants C1060/A10334 and C16412/A6269) and NHS funding to the NIHR Biomedical Research Centre.