MRI-based Mapping of Intra-renal Oxygenation in Human Subjects

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Medullary hypoxia is an inevitable accompaniment of effect urinary concentration: High oxygen-demand and lower medullary blood flow.
Motivation

• **Current status of AKI management**
  high mortality with only supportive therapies

• **Impaired oxygen delivery in AKI**
  altered organ micro-circulation in sepsis AKI
  spatial & temporal heterogeneities of capillary flow

• **Reduced efficiency for sodium transport in AKI**
  0.8 ml of $\text{O}_2$/mmol (control) vs. 1.9 ml $\text{O}_2$/mmol (AKI)

• **Medullary hypoxia: a hallmark of renal pathogenesis**
  morphological & structural lesions:
  - tubular necrosis; intra-renal collagen; interstitial fibrosis

• **Limited tools to quantify renal hypoxia**
  micro-electrode, optic oxygen sensor
  invasive, point of interest, not applicable to human
Role of MRI in Kidney Research

- anatomy/morphology/function
- T1/T2/T1ρ; pH/MT; Perfusion; Water Diffusion; Contrast-Enhanced; Multi-Nuclide (Na, $^{13}$C);

Stefan Haneder, et al., ISMRM 2012
BOLD and Renal BOLD

Air
90% O2 / 10% CO2

Ogawa et al, PNAS 1990.

Baseline Post-furosemide Post-Angiotensin II Post-L-NAME Post-nor epinephrine

AKI CKD Diabetes Hypertension Transplant

Prasad, 2006
Quantitative BOLD (qBOLD)

- Renal BOLD only provides a semi-quantitative, relative and indirect indicator of intra-renal oxygenation;
- Renal $R2^*$ is not specific to renal tissue oxygenation; and does not reflect disease severity.

\[ DBV = \ln \left( \frac{S_{\text{extrapolated}}(0)}{S_{\text{measured}}(0)} \right) \]

$DBV$: deoxyhemoglobin-containing blood volume
$OEF$: oxygen extraction fraction

$R2^* \approx DBV \times OEF$

Yablonskiy & Haacke, MRM 1994
He & Yablonskiy, MRM 2007, 2008
Renal qBOLD: Technique

Siemens Clinical 3T MR Scanner; Spatial Resolution: 1.44x1.44x6 mm³
Breath-hold of ~20 seconds; Total time: 4 - 8 minutes

renal parenchyma tissue

\[ S_t(t) = \exp\left(-R_2^t \cdot t - DBV \cdot f_c(t/t_c)\right) \]

intravascular blood (distribution of cylinders)

\[ \bar{S}(t) = S(0) \cdot F_s(t) \cdot \{(1 - DBV) \cdot S_t + \lambda' \cdot DBV \cdot S_b\} \]

macroscopic field inhomogeneities

fraction of intravascular blood

He & Yablonskiy, MRM 2007
He et al, MRM, submitted
Renal qBOLD: Model

- Oxygen saturation: 86.2% (cortex) vs. 45.0% (inner medulla)
- Blood volumes: 20.6% (cortex) vs. 3.1% (inner medulla)
Renal qBOLD: Baseline

OEF

T2* W

OEF

T2* W
Renal qBOLD: Spatial Heterogeneity

OEF, inf -6 mm

OEF, center

OEF, sup +6 mm
## Renal qBOLD on Healthy Subjects

<table>
<thead>
<tr>
<th>Study</th>
<th>Slice Orientation</th>
<th>Oxygenation (%, Cortical)</th>
<th>Oxygenation (%, Medulla)</th>
<th>Oxygenation (%, OM)</th>
<th>R₂*(Cortical) (sec⁻¹)</th>
<th>R₂*(Medulla) (sec⁻¹)</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>Axial</td>
<td>78.3±8.2</td>
<td>54.1±14.6</td>
<td>63.8±6.7</td>
<td>17.1±9.0</td>
<td>34.6±9.1</td>
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<tr>
<td>2</td>
<td>Axial</td>
<td>81.0±5.6</td>
<td>52.3±17.7</td>
<td>62.2±11.7</td>
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<td>38.8±11.6</td>
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<td>3</td>
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<td>80.6±8.9</td>
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<tr>
<td></td>
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<td>81.8±9.9</td>
<td>48.4±22.0</td>
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<td>82.1±8.8</td>
<td>58.4±19.7</td>
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<td>47.0±17.1</td>
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<td>68.8±12.9</td>
<td>16.1±2.9</td>
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<td>Mean</td>
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<td>83.8±3.0</td>
<td>50.8±4.7</td>
<td>63.6±6.6</td>
<td>17.0±1.5</td>
<td>32.6±4.9</td>
</tr>
</tbody>
</table>

pO₂ ~ 53 mm Hg  
pO₂ ~ 27 mm Hg  
pO₂ ~ 35 mm Hg
Renal qBOLD: Acute Water Intake

OEF
Water Restriction

OEF
Water-Diuresis

T2* W
Renal qBOLD of PKD Patient

T2* weighted

OEF

None-cyst cortical lesion shows elevated OEF, thus tumor hypoxia.
Single Kidney RVO₂

- **T2-Weighted R2 (1/sec)**
  - T2: 127 ms
- **OEF:** 17%
- **RBF:** 570 ml/min
- **RVO₂:** 480 μmol/min

- **T1-Weighted**
- **Phase-Contrast**
  - Renal Artery
  - Renal Vein

Graph showing TE (ms) vs. signal intensity with a linear relationship.
Intra-renal Oxygenation in AKI: Specific Aims

**Aim 1:** To develop & optimize renal qBOLD approach for robust quantification of intra-renal oxygen and whole kidney oxygen consumption in human subjects.

*Intra-renal oxygenation and global RVO2 can be robustly quantified in human subjects in the baseline state and under renal functional challenges.*

**Aim 2:** To determine the pattern of distribution of intra-renal oxygenation in patients with and without sepsis induced-AKI using qBOLD MRI, and to compare these readouts to clinical markers of renal dysfunction.

*Patients with AKI will have decreased intra-renal oxygenation and higher global renal oxygen consumption than patients without AKI; and that this phenotype will correlate with clinical markers of dysfunction.*
Summary & Discussion

- MRI-based renal qBOLD based technique provides non-invasive and absolute quantification of intra-renal oxygenation in human subject;
- Renal qBOLD technique also provides a global kidney oxygen metabolism;
- Non-invasive investigation of intra-renal oxygenation enables the monitoring the renal hypoxia status in AKI patients; It may help to resolve the interplay between AKI to CKD.
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- MR Research Center at UPMC
Renal qBOLD: Animal Model

(a) T1 W  (b) OEF, air  (c) OEF, 100% O2