MRI qBOLD Based Evaluation of Renal Oxidative Metabolism

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Background

High oxygen-demand and lower medullary blood flow often renders the kidney functions in hypoxic milieu (highly susceptible to ischemic insult)
Motivation

- Current status of AKI management
  - ~2/3 of critically ill patients develop AKI
  - ~50% of sepsis patient develop AKI
  - ~20% AKI mortality ( ~5% without AKI)
  - supportive therapy: hemodynamic management
  - unknown link between hemodynamic parameters and improved renal function

- Medullary hypoxia is a hallmark of AKI pathogenesis
  - Micro-vascular perfusion defects induced intra-renal oxygenation deficiency in AKI
  - Sepsis induces heterogeneity of micro-vascular flow pattern, leading to impairment of oxygen delivery and tissue hypoxia

- Global renal oxygen consumption (RVO2) is correlated with kidney function (GFR)
  linear, slope depends on efficiency
Current Status

- **Micro-electrode, optic oxygen sensor**
  - invasive, point of interest, …
  - oxygenation of tissue, or all blood
  - not applicable to human in-vivo study

- **Non-invasive MR BOLD (T2*/R2*)**
  - semi-quantitative and relative; $R2^* \leftrightarrow$ oxygenation
  - not specific; renal $R2^* \leftrightarrow$ disease severity

- **Global RVO2**
  - catheter at renal draining vein (RBF, SO2)

*MRI-based renal qBOLD techniques can be used to sensitively, reliably and non-invasively track and quantify the regional and global renal oxygen content and oxygen metabolism in AKI patients.*
Quantitative BOLD (qBOLD): Theory

\[ S_{meso}(t) = \text{Exp}[-DBV \cdot f(t/t_c)] \]

\[ R2' = \frac{4\pi}{3} \cdot DBV \cdot \gamma \cdot \Delta \chi_0 \cdot Hct \cdot (1-Y) \cdot B_0 \]

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

DBV: deoxyhemoglobin-containing blood volume
Y: blood oxygenation level

Yablonskiy & Haacke, MRM 1994
Brain qBOLD: Application & Validation

isoﬂurane

alpha chloralose

He and Yablonskiy, MRM, 2007, 2008
MR qBOLD fMRI

He & Yablonskiy, Proc. ISMRM, 2010
Measurement of CMRO2

MR qBOLD on Disease Model

Tumor

T1W

Radiation Necrosis

T1W

Stroke Model

Baseline

Unilateral Carotid Occlusion
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: Acute Water Intake

OEF

Water Restriction

OEF

Water-Diuresis
Renal qBOLD of PKD Patient

PKD patients has reduced cortical intra-renal oxygenation.
Renal qBOLD: Animal Model

(a) T1 W

(b) OEF, air

(c) OEF, 100% O2
Whole Organ Oxygen Consumption

Lu & Xu, JCBFM, 2011

Lu & Xu, MRM, 2012
Whole Kidney RVO$_2$

T2-Weighted

R2 (1/sec)

T2=127 ms

OEF~17%

T1-Weighted

Phase-Contrast

Renal Artery

Renal Vein

2.8

2.4

2

1.8

10 30 50 70 90

TE (ms)
Significance

- In patients with AKI, data on renal oxygen consumption, renal blood flow, glomerular filtration, and intra-renal oxygenation (renal oxygen supply/demand balance) are often lacking, and current views on intra-renal oxygenation and renal oxidative metabolism in the clinical situation of AKI are largely based on animal experimental studies;

- Combined with existing MRI techniques, renal qBOLD can provide a comprehensive and integrated approach to study renal cellular and organ function in sepsis patient with and without AKI;
  
  whole kidney/local perfusion; whole kidney RVO2, OEF; GFR and Filtration Fraction;
Innovation

- First attempt to non-invasively mapping of intra-renal oxygenation in AKI patients based on MRI qBOLD technique, utilizing deoxygenated blood as endogenous MRI contrast;
- First attempt to non-invasively quantify whole-kidney oxygen extraction fraction (OEF) and oxygen metabolism rate (RVO2);
- First attempt to investigate baseline intra-renal and RVO2 in sepsis patients with AKI, and investigate the effect of fluid management on kidney oxygen metabolism and kidney function
- Anticipate that these innovations will also apply to other chronic and acute diseases of the kidney, and to evaluate and manage kidney transplant patients.
Specific Aims

- **Aim 1:** To develop and optimize MRI-based techniques for non-invasive and absolute quantification of intra-renal oxygenation and renal oxygen consumption (RVO2) in human subjects.

  *Intra-renal oxygenation and global RVO2 can be robustly quantified by the proposed renal qBOLD techniques in the baseline state and under renal functional challenges.*

- **Aim 2:** To determine the pattern of distribution of intra-renal oxygenation and global RVO2 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.*
**Aim 1.1:** To Optimize and evaluate MR qBOLD-based non-invasive quantification of intra-renal oxygenation.

1. **Gradient Echo (GEPCI) vs. Spin Echo (GESSE)**
   - **GEPCI:** high SNR; fast; 
     low sensitivity; lipid/fast decay component
   - **GESSE:** high sensitivity, more lipid suppression
     lower SNR; slower; diffusion effect;

2. **Single breath-hold vs. Respiratory Triggering/Gating**
   - **BH:** minimum motion artifacts
     ~24 second (reduced with acceleration techniques)
   - **RT/RG:** free-breathing/shorter BH; whole-kidney 3D
     longer duration; motion correction

3. **Parallel imaging vs. Standard imaging**
   - balance of temporal/spatial resolution
**Aim 1.3:** To evaluate the changes on intra-renal oxygenation and global kidney oxygen consumption in healthy subject under renal functional challenges.

1. **Water-Loading**
   - robust change only in young healthy subjects
   - changes on RBF, GFR, RVO2, sodium re-absorption

2. **Loop diuretic furosemide**
   - sodium re-absorption ↓; oxygenation ↑; RVO2 ↔
**Expected Outcomes:** We expect that the renal qBOLD technique will accurately and reliably measure the intra-renal oxygenation and renal oxygen consumption in healthy subjects with high within-session and between-session repeatability. We also expect that our proposed method will be able to detect the improvement of intra-renal oxygenation during water diuresis, as demonstrated in our preliminary data.

**Anticipated Problems and Alternative Strategies:** For AKI patients may experience some difficulties with steady breath pattern, we will reduce the spatial resolution of the MRI image, or divide image acquisition into multiple short breath-holds (each less than 6 seconds). Siemens PACE technique may be used to ensure the same kidney position during different breath-holds.
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Kidney Perfusion & Metabolism

- $R_1\rho (\text{sec}^{-1})$
- $R_2^* (\text{sec}^{-1})$
- MR Perfusion Signal
- OEF (%)
Renal qBOLD: Acute Water Intake

Water Restriction

Water-Diuresis

OEF

R2* (1/sec)
qBOLD on Tumor Hypoxia

T1-W

OEF

DBV

Day 5  Day 8  Day 11

Garbow, Jost, He, et al
BOLD Signal and Blood Oxygenation

\[
S_{meso}(t) = Exp[-DBV \cdot f(t / t_c)]
\]

\[
R2' = \frac{4\pi}{3} \cdot DBV \cdot \gamma \cdot \Delta \chi_0 \cdot Hct \cdot (1-Y) \cdot B_0
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\[DBV = \ln \left( \frac{S_{extrapolated}(0)}{S_{measured}(0)} \right)\]

*DBV*: deoxyhemoglobin-containing blood volume  
*Y*: blood oxygenation level

Yablonskiy & Haccke, MRM, 1994
Renal qBOLD: Baseline

T1 Weighted

T2* Weighted

Y

R2* (1/sec)
Renal qBOLD: Summary

- MR-qBOLD based approach is capable of non-invasively measuring regional, in vivo, absolute renal blood oxygenation level in baseline and during kidney functional challenge;

- Renal qBOLD approach resolved oxygen gradient across kidney; provided experimental evidence for oxygen shunting in renal medulla;

- Renal qBOLD technique can provide a capability to clinicians for early detection of acute kidney failure, and monitoring treatment response in AKI patients;