Quantitative Cardiac 17O MRI: Initial Validation Study

Jie Zheng[1], David Muccigrosso[1], Adil Bashir[1], Pradeep Gupte[2], and Robert J. Gropler[1]
[1]*Washington University, Saint Louis, Missouri, United States,* [2]*Rockland Technimed, Ltd, United States*

Purpose

Cardiac oxygenation was usually assessed by BOLD effects in MRI [1,2]. However, the BOLD signal reflects the mixture effects of myocardial blood flow (MBF), blood volume, and oxygen uptake. In the ISMRM meeting last year, we reported a new approach to quantify oxygen uptake based on dynamic changes in ^{17}O-labelled water after the administration of $^{17}O_2$-labelled contrast media. This technique directly links to the oxygen uptake. The purpose of this project aimed to validating this quantification method with improved data processing technique.

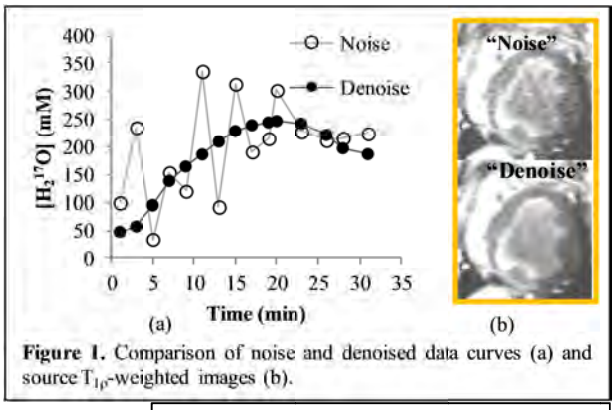

Figure 1. Comparison of noise and denoised data curves (a) and source $T_{1\rho}$-weighted images (b).

Methods

Theory: Briefly speaking, water $H_2{}^{17}O$ is produced in myocardial tissue when $^{17}O_2$ is metabolized to water at the end of oxidative phosphorylation in mitochondria. We have developed a single-compartment model to quantify oxygen uptake from myocardial [$H_2{}^{17}O$] after the injection of ^{17}O-labelled contrast media, as shown in the following equation:

$$\frac{dC_{myo}(t)}{dt} = 2MVO_2[A^{17O_2}(t)] \times f_1 + \{m_1 C_{LV}(t) - m_2 C_{myo}(t)\} \qquad (1)$$

where $C_{myo}(t)$ and $C_{LV}(t)$ are [$H_2{}^{17}O$] in the myocardium and blood pool, respectively. The later is measured in the left ventricle of the heart; m_1 and m_2 are two rate constants that describe the gain of [$H_2{}^{17}O$] from the blood and loss of [$H_2{}^{17}O$] into the draining veins, respectively. The constant f_1 is a unit conversion factor. *A(t)* is the concentration of $^{17}O_2$ in the blood pool.

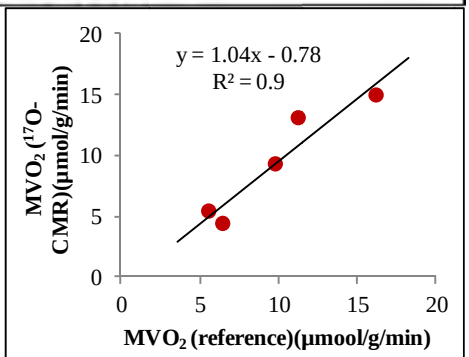

Figure 2 Correlation of MVO_2 measured by ^{17}O-CMR and reference method in normal dogs. A strong correlation was observed.

Experiments: Four normal mongrel dogs (mean weight = 18 kg) were used for the initial validation study to the model. Dobutamine was infused to increase MVO_2. Blood sampling in artery and coronary sinus, as well as microsphere measurement for myocardial blood flow (MBF), were performed at rest and during the dobutamine stress. In addition, three dogs were instrumented with 90-100% occlusion in 2-3 branches of the left anterior descending coronary arteries (LAD) for resting study. Acute high-degree stenosis was expected to induce changes in regional oxygen consumption at rest. All imaging experiments were performed in a clinical 3T Siemens Trio scanner with 6-element phased-array coils. An artificial blood perfluorodecalin emulsion (PFD), was used as the carrier for the $^{17}O_2$ gas (OxyToT, Rockland Technimed Ltd, Airmont, NY). The dose of ^{17}O-PFD was 2 mL/kg for each injection.

A special CMR spin-locking ($T_{1\rho}$) technique [1] was applied to measure $T_{1\rho}$-weighted signals from myocardial tissue. It was found that $T_{1\rho}$ signals were negatively correlated with the concentration of ^{17}O-labelled water [$H_2{}^{17}O$] [3]. These $T_{1\rho}$-weighted images were dynamically acquired over a period of 30 min after the injection of ^{17}O-PFD. Absolute quantification of myocardial perfusion were also performed in stenotic dogs using the first-pass perfusion imaging technique [4] to confirm the stenosis.

Data Analysis: ROI measurements were carried out in the anterior and lateral myocardial regions. A spatial-temporal wavelet-denoising method was applied to all dynamic data sets [4]. Reference MVO_2 was calculated using Fick's law: $MVO_2 = ([O_2]_a - [O_2]_{cs})$ x MBF.

Results

Figure 1 shows original and denoised myocardial [$H_2{}^{17}O$] time course data sets from a myocardial region in one normal dog. The fluctuation of the data points are dramatically suppressed after the denoising, clearly showing the wash-in and wash-out phases of water $H_2{}^{17}O$ from this region. The calculated MVO_2 after denoising processing in normal dogs was 5.02 ± 0.56 at rest and 12.45 ± 2.89 μmol/g/min during the dobutamine stress. **Figure 2** shows the correlation of measured MVO_2 using ^{17}O-CMR and reference values, demonstrating a strong agreement.

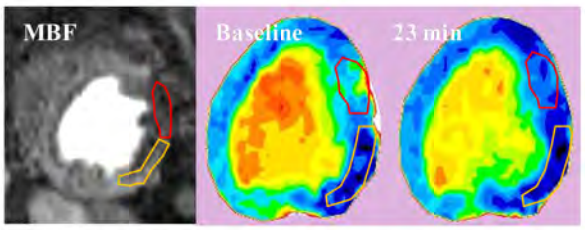

Figure 3. From left to right: perfusion weighted image, $T_{1\rho}$-weighted image at baseline and 23 min after injecting ^{17}O-PFD. Red and orange ROIs indicate stenosis subtended region and adjacent normal region, respectively. Corresponding MBF at these regions were 0.85 and 2.3 mL/g/min.

In stenotic dogs, absolute MBF at anterior and lateral regions was measured as 1.1 ± 0.3 and 2.2 ± 0.1 mL/g/min, respectively. Using our model in Eq (1), the corresponding MVO_2 values were calculated as 6.5 ± 1.7 and 3.1 ± 0.8 μmol/g/min, respectively, indicating increased oxygen extraction in stenosis subtended anterior regions. **Figure 3** demonstrates MBF deficit area (red ROI) in the anterior region from one stenotic dog and a smaller area in the same region with larger reduction in $T_{1\rho}$ signals, relative to the orange lateral region. This indicates increased MVO_2 or oxygen uptake to compensate the loss of oxygen supply due to the stenosis, even at rest.

Conclusions

This study represents our continuing effort to develop non-invasive approach to quantify cardiac oxygenation for both basic science research and clinical diagnosis. Future study in more diseased models and clinical trial are warranted for establishment of this method to assess bioscale of regional myocardial oxygen metabolism.

References [1] Friedrich MG, et al, Circulation, 2003; 108: 2219 - 2223. [2] McCommis KS, et al, Circ Cardiovasc Imaging, 2010; 3: 41-46. [3] Reddy R, et al, JMR, 1995;108:276-279. [4] Goldstein TA, et al, MRM. 2008;59:1394-1400.