Quantitative Cardiac 17O MRI: Initial Validation Study
Jie Zheng1, David Muccigrosso1, Adil Bashir1, Pradeep Gupta2, and Robert J. Gropler1
1Washington University, Saint Louis, Missouri, United States, 2Rockland 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 17O-labelled water after the administration of 17O-labelled contrast media. This technique directly links to the oxygen uptake. The purpose of this project aimed to validate this quantification method with improved data processing technique.

Methods
Theory: Briefly speaking, water H217O is produced in myocardial tissue when 17O 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 [H17O] after the injection of 17O-labelled contrast media, as shown in the following equation:

\[ \frac{dC_{mVO}(t)}{dt} = 2MV_{O_2} \left[ A(t) \right] \times f_1 + \left[ m_1C_{LV}(t) - m_2C_{myo}(t) \right] \]  \( \text{(1)} \)

where \( C_{myo}(t) \) and \( C_{LV}(t) \) are [H17O] 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 [H17O] from the blood and loss of [H17O] into the draining veins, respectively. The constant \( f_1 \) is a unit conversion factor. \( A(t) \) is the concentration of 17O in the blood pool.

Experiments: Four normal mongrel dogs (mean weight = 18 kg) were used for the initial validation study to the model. Dobutamine was infused to increase MVO2. 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 17O gas (OxyToT, Rockland Technimed Ltd, Airmont, NY). The dose of 17O-PFD was 2 mL/kg for each injection.

A special CMR spin-locking (T1p) technique [1] was applied to measure T1p-weighted signals from myocardial tissue. It was found that T1p signals were negatively correlated with the concentration of 17O-labelled water [H17O] [3]. These T1p-weighted images were dynamically acquired over a period of 30 min after the injection of 17O-PFD. Absolute quantification of myocardial oxygen 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-denosing method was applied to all dynamic data sets [4]. Reference MVO2 was calculated using Fick’s law: MVO2 = ([O2]o - [O2]o) x MBF.

Results
Figure 1 shows original and denoised myocardial [H17O] 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 H217O from this region. The calculated MVO2 after denoising processing in normal dogs was 5.02 ± 0.56 at rest and 12.45 ± 2.89 \( \mu \text{mol/g/min} \) during the dobutamine stress. Figure 2 shows the correlation of measured MVO2 using 17O-CMR and reference values, demonstrating a strong agreement.

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 MVO2 values were calculated as 6.5 ± 1.7 and 3.1 ± 0.8 \( \mu \text{mol/g/min} \), 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 T1p signals, relative to the orange lateral region. This indicates increased MVO2 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 bioclue of regional myocardial oxygen metabolism.