Methods for Quantification of Absolute Myocardial Oxygen Consumption with ^{17}O-CMR

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Purpose

Oxygen has an indispensable role in cardiac energetics, metabolism, and function. Decreased oxygen levels and consumption rate (MVO_2) are generally associated with myocardial ischemia, infarction, and heart failure. We have developed a cardiac MR acquisition method using $^{17}O_2$ labeled blood solution (^{17}O-CMR) to assess myocardial oxygenation [1]. The aims of this study were to develop a quantitative model to measure absolute MVO_2 and evaluate it in a canine model with and without myocardial ischemia.

Methods

Theory: ^{17}O water $H_2{}^{17}O$ is produced in myocardial tissue when $^{17}O_2$ is metabolized to water at the end of oxidative phosphorylation. Based on a theory developed in brain studies with inhaled $^{17}O_2$ gas [2], the concentration $[H_2{}^{17}O]$ of the myocardium after the injection of ^{17}O-labelled solution can be described in the following equation:

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

where $C_{myo}(t)$ is the $[H_2{}^{17}O]$ of myocardium; $C_{LV}(t)$ represents the concentration of $H_2{}^{17}O$ in the arterial blood pool, which is measured in the left ventricle (LV) 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 1.266 g myocardial tissue/g myocardial water. To solve Eq. (1), $C_{LV}(t)$ is first approximated with a gamma variate function as $C_0 \times t^{\alpha} e^{-\frac{t}{\beta}}$, and $A^{17O_2}(t) = A_0 \times e^{-\rho t}$, where C_0, A_0 and ρ are constants to be calculated. Eq. (1) can then be solved as:

$$C_{myo}(t) = \frac{2MVO_2 A_0 f_1}{m_2 - \rho}[e^{-\rho t} - e^{-m_2 t}] + m_1 \times C_0 \times e^{-m_2 t} \times \int_0^t x^{\alpha} e^{\left(m_2 - \frac{1}{\beta}\right)x} dx + 20 \quad (2)$$

The 20 (mM) represents the natural abundance of ^{17}O in the tissue water. Equation (2) can finally be fitted to the dynamic $C_{myo}(t)$ data set by a non-linear regression method in order to obtain MVO_2, as well as m_1 and m_2, as fitting parameters.

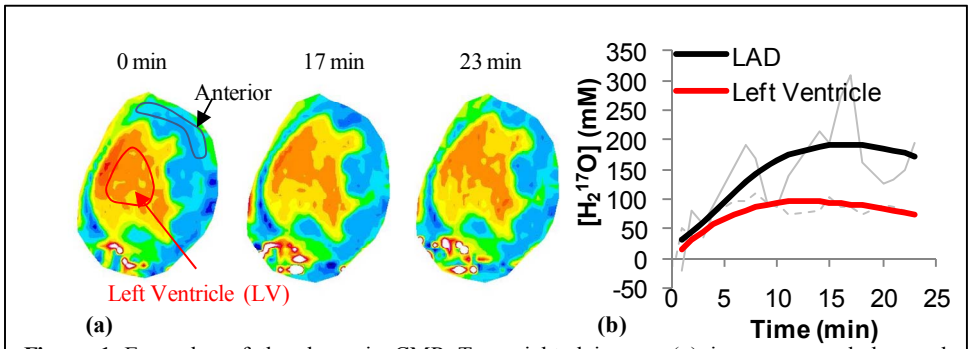

Figure 1 Examples of the dynamic CMR $T_{1\rho}$-weighted images (a) in one normal dog and calculated $[H_2{}^{17}O]$ after the injection of ^{17}O-PFD (b). The $T_{1\rho}$-weighted images demonstrate signal intensity reduction and recovery. The thick lines in (b) are the fitted data from our model.

Experiments: Six mongrel dogs were prepared for the evaluation of this method. Three dogs were in normal condition and three dogs were instrumented with 90-100% occlusion in two branches of the left anterior descending coronary arteries (LAD). Such acute high-degree stenosis was expected to reduce regional oxygen consumption. The study was 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). Each dog studied was injected with a dose of 2 mL/kg ^{17}O-PFD.

We have developed a CMR spin-locking ($T_{1\rho}$) technique [1] to measure $T_{1\rho}$-weighted signals from myocardial tissue that were correlated with $[H_2{}^{17}O]$ [3]. The dynamic $T_{1\rho}$-weighted images were acquired over a period of 30 min after the injection of ^{17}O-PFD. Absolute quantification of myocardial perfusion was also performed using first-pass perfusion imaging [4]. ROI measurements were carried out in the normal anterior myocardial regions and/or stenosis subtended lateral myocardial regions.

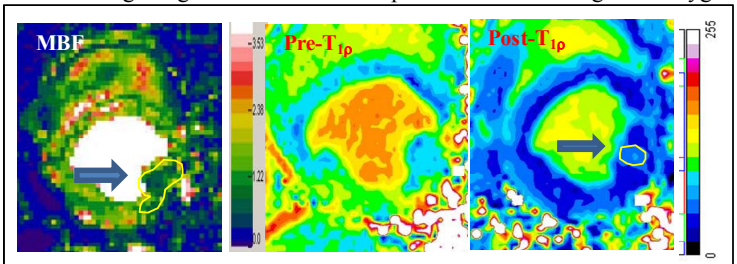

Figure 2 A 100% stenosis in the second diagonal branch of LAD resulted in perfusion deficit in lateral wall (arrow on MBF map). Resting $T_{1\rho}$-weighted ratio images show relatively uniform signal intensity in LV wall prior to injection of ^{17}O-PFD (pre-$T_{1\rho}$), but much less signal drop afterwards (arrow in post-$T_{1\rho}$). The deficit area in the post-$T_{1\rho}$ image (yellow circle) is much smaller than the hypo-perfusion area in MBF map (yellow ROI).

Results

Figure 1 shows myocardial images and $C_{myo}(t)$ or $[H_2{}^{17}O]$ (t) detected in a normal dog. The averaged MVO_2 in the anterior normal region was 3.96 ± 0.97 μmol/g/min in three normal dogs, which agrees well with MVO_2 measured by PET in mongrel dogs [5]. In stenotic dogs, Absolute myocardial blood flow (MBF) values at anterior and lateral regions were 2.38 ± 1.03 mL/g/min and 1.88 ± 0.91 mL/g/min, respectively. The corresponding MVO_2 values were calculated as 2.84 μmol/g/min and 1.57 μmol/g/min, respectively. **Figure 2** demonstrate MBF deficit area in the lateral region and a smaller area in less reduction in $T_{1\rho}$ signals, indicating reduced MVO_2 (lower $T_{1\rho}$ signal intensity correlate with higher MVO_2).

Conclusions

This is the first study to quantify absolute MVO_2 with ^{17}O-CMR methods using injected ^{17}O agent and a comprehensive model. Future validation study are warranted for establishment of this method to assess bioscale of regional myocardial oxygen metabolism.

References [1] McCommis KS, et al, MRM, 2010; 63:1442-1447. [2] Atkinson IC, et al, Neuroimage. 2010;51:723-733. [3] Reddy R, et al, JMR, 1995;108:276-279. [4] Goldstein TA, et al, MRM. 2008;59:1394-1400. [5] McCommis K, et al, MRI, 2004;26:11-9.