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 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:

$$\frac{d[H_2^{17}O]}{dt} = 2MVO_2[A^{17}O_2(t)] \times f_1 + \{m_1C_{LV}(t) - m_2C_{myo}(t)\}$$

(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 $C_0 \times x^\alpha e^{-x^\beta}$, and $A^{17}O_2(t) = A_0 \times e^{-\rho \tau}$, where $C_0$, $A_0$ and $\rho$ are constants to be calculated. Eq. (1) can then be solved as:

$$C_{myo}(t) = \frac{2MVO_2 A_0 f_1}{m_2^2 - \rho^2} \left[ e^{-\rho t} - e^{-m_2 t} \right] +$$

$$m_1 \times C_0 \times e^{-m_2 t} + \frac{1}{\rho} \int_0^t x^\alpha e^{-m_2 x} dx + 20$$

(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.

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$_{1p}$) technique [1] to measure T$_{1p}$-weighted signals from myocardial tissue that were correlated with [H$_2^{17}$O] [3]. The dynamic T$_{1p}$-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.

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$_{1p}$ signals, indicating reduced MVO$_2$ (lower T$_{1p}$ 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.