MR feasibility study of global left ventricular myocardial oxygen consumption in normal volunteers: preliminary results

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Introduction: Ideally a comprehensive global left ventricular (LV) function evaluation should include an accurate LV systolic and diastolic function measurement [(1)]. However, in clinical practice the most frequently used function parameter such as left ventricular ejection fraction (LVEF) only reflects the systolic function of the LV. From a physiological perspective, myocardial oxygen consumption (MVO2) that reflects the overall myocardial oxidative metabolism may be a better functional parameter than LVEF in the evaluation of LV dysfunction. This is especially true in diastolic LV dysfunction that is commonly seen in patients with hypertension and hypertrophic cardiomyopathy. Among the nine determinants of MVO2 that had been defined by Braunwald, wall tension development, contractility and heart rate are the three primary factors [(2)]. About 80% of MVO2 is for contraction and the other 20% is for processes in cardiomyocytes such as basal metabolism and electrical conduction. The successful determination of MVO2 may also allow for an easier estimation of cardiac efficiency, defined as stroke work/MVO2, which might be the best parameter to describe the overall LV function. The purpose of this study is to investigate the feasibility of MR techniques that combine coronary sinus (CS) oximetry and cine phase contrast flow measurements to obtain global MVO2 non-invasively.

Materials and Methods: Our institutional research board had approved this study and every volunteer participated with informed consent. Seven male volunteers with ages of 37.6 ± 9.9 (Mean ± SD) years were enrolled to undergo this MRI examination in a GE 1.5T CVi system using ECG gating (3 cases) or peripheral gating (4 cases) and using a cardiac coil (6 cases) or a torso coil (1 case). The MRI protocol included the following four parts: 1). *In vitro* T2-%O2 calibration: 20 ml blood was collected from each volunteer in which 15 ml was manipulated to various oxygen saturations (%O2 ranging from 30% to 90%) in five 3-ml tubes for T2 measurements, as per the methods described in Wright et al [(3)]. Another 5 ml blood was used for hematocrit and hemoglobin (Hb) tests. 2). CS T2 measurement (**Fig.1 a-c**): We used a 3-plane localizer or Fiesta pulse sequence for CS localization followed by a robust and motion-insensitive T2 prep pulse sequence [(4)]. In 6 subjects, the Diminishing Variance Algorithm was applied for respiratory motion compensation (TR=2R-R interval, TE 12ms, 54ms and 97ms, spatial resolution= 1.36mm). The other subject was imaged with a breath-held version of T2 measurement (TR=1R-R interval, TE=12 and 97ms, spatial resolution=1.7mm). To reduce partial volume effect and sinus reflux, the imaging slice was placed perpendicular to the long-axis of CS at a location 15mm to 35 mm from the sinus ostium. 3). CS flow measurement (**Fig.1 d-e**): 2D cine phase contrast was used to obtain the flow parameters at the same positions as CS T2 measurement. The maximum velocity encoded was 80-100 cm/s [(5, 6)], TR ~30 ms, TE 4-6 ms, flip angle 30º, Matrix 256*256, cardiac phases=20. CS flow volume and velocity were calculated using the CV Flow software 3.1 on a GE Advantage workstation. 4). Global LV function evaluation: 2D Fiesta short-axis oblique (SAO) images were obtained for calculating LV mass using Mass plus software 5.1 on the workstation.

Results: Based on Fick's law, MVO2 was calculated from the following equation: MVO2={Q*(%aO2-%csO2)*[Hb]*Cm / LV mass} where the parameters are defined as follows: Q (ml/min): CS flow volume obtained from CS cine phase contrast measurement; %aO2: oxygen saturation in the artery that was assumed as 98%; %csO2: oxygen saturation in CS acquired from CS T2 and in vitro blood sample T2-%O2 calibration; [Hb] (g/ml) obtained from hematology test; Cm (maximal oxygen carrying capacity, ml of oxygen per gram Hb): a constant of 1.36 in normal situations. The final unit of MVO2 value was expressed as ml/min per gram LV mass. The results demonstrated that global LV MVO2 measurement by MRI was feasible in all seven volunteers. The measured MVO2 values were 0.15 ± 0.06 ml * min^{-1} * g^{-1} (mean ± SD). The correlation coefficient between MVO2 and age was 0.959 ($p<0.001$) using the linear regression statistical method.

Discussion: Although many methods like rate-pressure product, triple product, tension-time index and pressure-work index could indirectly estimate the global MVO2, these methods are inaccurate and the measured values do not fully reflect the LV function status in patients with heart diseases. Currently PET is considered as the most accurate *in vivo* tool to measure MVO2 using tracers of ^{11}C-acetate and ^{15}O2 non-invasively [(7, 8)]. General disadvantages with PET such as high expense, low availability, and potential radiation of tracers preclude its wide application in clinical practice. Moreover, the spillover radioactivity from the lung and chamber could be a potential limit for the PET MVO2 measurement. Direct measurement of MVO2 could be realized by the invasive catheterization of coronary sinus to acquire the arterial-venous oxygen saturation difference and multiplied by flow obtained via catheterization based on Fick's law. However, this direct method could not be applied widely due to its invasiveness.

To the best of our knowledge, this study represented the first successful quantification of global LV MVO2 by MR techniques. CS flow represents 85% to 90% of the venous return from the left ventricle. Using CS flow measurement by phase contrast to get coronary flow reserve has become a useful tool in evaluating patients with heart diseases [(5, 6)]. By combining CS relaxometry and phase contrast MR techniques, we successfully obtained the value of global LV MVO2. The results showed that this non-invasive MR technique for global LV MVO2 measurement was feasible. Comparing with MVO2 values in the normal or control groups from PET studies which indicated an expected MVO2 of 0.10 ± 0.03 ml * min^{-1} * g^{-1} and 0.15 ± 0.03 ml * 100g^{-1} * $beat^{-1}$ [(9, 10)], our measured MVO2 values are reasonable. Moreover, our limited data also demonstrated that MVO2 values were closely related to age in healthy volunteers. This result was consistent with reports by others based on PET scans in which the possible mechanism might be an age-related shift in myocardial substrate metabolism [(11)]. *In vitro* blood T2-%O2 calibration might be a limiting factor. However, the blood collection for the hematology test is a standard protocol for patients with heart diseases, and we could reduce the amount of blood collection to 6ml by manipulating %O2 and repeating the *in vitro* MR scan. The major advantages of this MR technique are the direct application of Fick's law to accurately calculate MVO2, more equipment availability than PET, no requirement for radioactive tracers and an entirely non-invasive study. Due to the non-invasive nature of MRI and the central role of MVO2 in cardiac physiology, wide application of MR MVO2 measurement in clinical practice could be expected. Another potential of this technique is to get organ-specific oxygen consumption like oxygen uptake in brain, kidney, or liver if we could obtain flow parameters of the venous system in a specific organ combined with in vitro blood sample calibration. In the future, real-time MR CS localization and flow quantification might be beneficial. In order to reduce the measurement errors from the anatomical variations of CS, MR angiography of the CS might also be needed to accurately localize MVO2 MR measurement.

Conclusions: In this study we established the feasibility of an MR technique that combines coronary sinus T2 and phase-contrast flow measurements using Fick's law in the quantification of MVO2 non-invasively in healthy volunteers. The limited data also demonstrated that MVO2 values seem to be age-related although more data needed to confirm this.

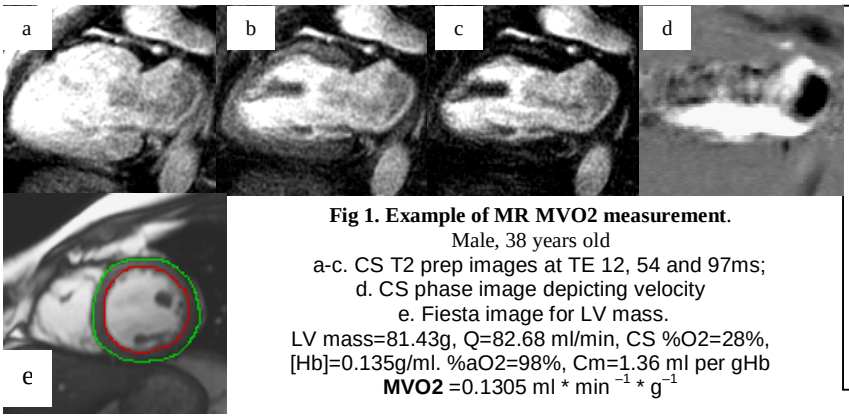

Fig 1. Example of MR MVO2 measurement.
Male, 38 years old
a-c. CS T2 prep images at TE 12, 54 and 97ms;
d. CS phase image depicting velocity
e. Fiesta image for LV mass.
LV mass=81.43g, Q=82.68 ml/min, CS %O2=28%, [Hb]=0.135g/ml. %aO2=98%, Cm=1.36 ml per gHb
MVO2 =0.1305 ml * min^{-1} * g^{-1}

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