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Original contribution

Effects of supplemental oxygen on cardiovascular magnetic resonance water proton relaxation time constant measurements (T_1, T_2 and T_2*)

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ABSTRACT

Objective: To study, the effects of supplemental oxygen on the measurement of native cardiovascular water proton relaxation time constants using commercially available protocols.

Methods: T_1, T_2 and T_2* relaxation time constant mapping were performed in twelve volunteers at 1.5 T breathing room air and supplemental oxygen supplied by nasal cannula and a non-rebreather mask. Regions-of-interest were drawn for quantitative measurements in the bloodpool of each ventricle and atria as well as septal myocardium. The effects of supplemental oxygen were investigated statistically using a mixed model analysis of variance. Intra- and inter-observer reproducibility were assessed using the Intraclass Correlation Coefficient and Coefficient of Variation.

Results: Blood T_1 relaxation time constants in the left ventricle (T_1 change = −241.0 ms) and left atrium (T_1 change = −247.0 ms) decreased significantly in every subject after oxygen inhalation with a non-rebreather mask ($p < 0.001$). No significant changes of T_1 in the right side of the heart were detected after oxygen inhalation with the non-rebreather mask ($p = 0.345$). Oxygen inhalation with nasal cannula did not significantly change blood T_1 in the study ($p = 0.497$). No significant changes in myocardial T_1 ($p = 0.390$), T_2 ($p = 0.960$) or T_2* ($p = 0.438$) were observed with supplemental oxygen supplied by nasal cannula or the non-rebreather mask. Results were similar in mid-short-axis and horizontal long-axis acquisitions.

Conclusion: Supplemental oxygen does not affect myocardial relaxation time constant measurements with current protocols. On the other hand, blood T_1 measurements with the inhalation of supplemental oxygen supplied by a non-rebreather mask change significantly and could affect myocardial tissue characterization if used for the calculation of extracellular volume. Additionally, current relaxation time constant mapping protocols do not reproducibly detect myocardial T_1 changes with supplemental oxygen inhalation.

1. Introduction

Cardiovascular magnetic resonance (MR) water proton relaxation time constant measurements are increasingly being used for tissue characterization in research and patient care applications. Most widely used are T_1, T_2 and T_2* measurements of the left ventricular (LV) bloodpool and myocardium. Although further technical developments and evaluation are being performed, software (pulse sequences and post-processing) and standardized protocols are currently commercially available for patient care [1]. Significant differences in native (without contrast agent administration) and gadolinium based contrast agent (GBCA) enhanced measurements have been associated with both ischemic [2,3] and non-ischemic cardiomyopathies [4], myocardial fat deposition [3], fibrosis and edema [5] as well as regional and global ventricular functional parameters. In cardiovascular imaging, a quantitative parameter's normal range is typically established for each technique and modality. Individual measurements outside of that normal range are deemed pathological [6]. For example, normal myocardial T_2* is widely considered to be higher than 20 ms and values < 20 ms are indicative of myocardial iron overload.

Confounding factors often complicate the usage of relaxation time constant measurements for patient care applications. For example, myocardial T_2* measurements are affected by susceptibility and vary significantly across the heart [7]. Another recent study [8] explored

Abbreviations: bSSFP, balanced steady-state free precession; ICC, intraclass correlation coefficient; CoV, coefficient of variation; ECV, extracellular volume; FLASH, Fast Low Angle SHot; GBCA, gadolinium based contrast agent; HASTE, Half-Fourier Acquisition Single-shot Turbo spin Echo imaging; HLA, horizontal long axis; LA, left atrium; LV, left ventricle; TE, echo time; TR, repetition time; MOLLI, Modified Look-locker imaging; MR, magnetic resonance; MYO, left ventricular myocardium; RA, right atrium; ROI, regions-of-interest; RV, right ventricle; SAX, short-axis

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variability in extracellular volume (ECV) measurements resulting from body posture variations during hematocrit sampling. Supplemental oxygen is often given to cardiac MR patients for improved breath-holding or therapeutically for hypoxia and emergency medicine [9,10]. Oxygen's effect on relaxation time constant measurements of blood have been studied in in-vitro [11,12], pre-clinical [13] and clinical settings [14–16]. More recently, high flow supplemental oxygen with a non-rebreather mask has been reported to reduce both myocardial and blood T_1 relaxation time constants [16] and was studied with Half-Fourier Acquisition Single-shot Turbo spin Echo imaging (HASTE) and Fast Low Angle SHot (FLASH) T_1 relaxation measurements [17–20]. The primary T_1 shortening mechanism is oxygen dissolved in blood acting as a paramagnetic contrast agent [21] and this phenomenon has mostly been utilized for oxygen-enhanced MR ventilation imaging [22]. Currently, it has not been studied whether supplemental oxygen is a confounding factor with quantitative myocardial relaxation time constant measurements using current technology. Additionally, if inhaled oxygen can be detected as a contrast agent with relaxation mapping techniques, it could lead to myocardial perfusion applications and a technique for the detection of myocardial ischemia.

In this study, the effects of supplemental oxygen delivered by nasal cannula and a non-rebreather mask on myocardial and blood relaxation time constant measurements using well-documented and widely available T_1, T_2 and T_2* protocols were studied. Relaxation time constant dependence on supplemental oxygen and its role as a potential confounder for myocardial tissue characterization were investigated by comparing myocardial and blood relaxation time constant measurements with supplemental oxygen to baseline room air acquisitions. Additionally, blood relaxation time constant variances and their association with heart chamber region-of-interest and venous hematocrit were explored.

2. Methods

2.1. Subjects

Twelve healthy subjects participated in this HIPAA compliant study (6 men and 6 women; mean age, 47.4 ± 5.3 years; age range, 37.8–55.9). The study was approved by the local Institutional Review Board. After the nature of the procedure had been fully explained, written informed consent was obtained. Subjects were screened to exclude respiratory and cardiac disease. Whole blood for venous hematocrit was drawn in all subjects by venipuncture and measured using routine clinical laboratory procedures before MR imaging. An MR compatible physiological monitor (Expression MR200, In Vivo, Orlando, FL) was used to measure and record oxygen saturation using a pulse oximeter and heart rate using a four lead electrocardiogram.

2.2. MR imaging

MR imaging was performed using a 1.5 T clinical scanner (Siemens Magnetom Avanto, Erlangen, Germany). Images were acquired during suspended respiration at end-expiration with ECG gating and a phased-array receive coil. In all subjects, the study protocol consisted of localizers, relaxation mapping with alternating supplemental oxygen and room air and lastly left and right ventricular CINE functional imaging. Relaxation mapping acquisitions were acquired in the four chamber and mid-short-axis imaging planes. Five measurement blocks spaced by 10 min were performed with supplemental oxygen supplied by nasal cannula and a non-rebreather mask alternating with subjects breathing room air. (Measurement 1: Room air, Measurement 2: Nasal cannula (oxygen 2 l/m), Measurement 3: Room air, Measurement 4: Non-rebreather mask (oxygen 15 l/m), Measurement 5: Room air). Ten minutes of continuous supplemental oxygen or room air was used to remove dynamic effects before relaxation mapping. Inhaled oxygen contents from room air, nasal cannula and a non-rebreather mask are approximately 20%, 35% and 70%, respectively [23].

Water proton relaxation time constant mapping was performed using vendor supplied software with T_1 and T_2 motion correction (Work-in-Progress Package # 448B, VB17A). T_1 mapping was performed using an inversion recovery balanced steady-state free precession sequence [24–26]: TR/TE(ms) = 2.8/1.2; Flip angle = 18°; Bandwidth = 1085 Hz/pixel; Matrix = 256 × 144, Resolution = 1.9 × 1.3 × 8 mm^3. 3-(3)-5 MOLLI (Modified Look-locker [27] imaging). TI start = 20 ms; TI increment = 80 ms. Pixel curve fitting was performed yielding T_1 and T_1* maps with two Eqs. (1) and (2).

$$I(x,y,TI_n) = A(x,y)\text{-}B(x,y) * \exp(-TI_n/T_1^*(x,y)) \quad (1)$$

$$T_1(x,y) = T_1^*(x,y) * (B(x,y)/A(x,y)\text{-}1) \quad (2)$$

where TI_n is the nth inversion time. I is the image signal intensity, [A, B, and T_1*] are estimated by a three parameter fit on the measured data and T_1 is calculated from the three parameters (Look-Locker correction). An additional correction for imperfect inversion was applied, multiplying the final value by 1.035.

T_2 mapping was performed using a balanced steady-state free precession sequence with adiabatic T_2 preparation [28]: TR/TE (ms) = 2.6/1.2; Flip angle = 35°; Bandwidth = 1184 Hz/pixel; Matrix = 192 × 116, Resolution = 2.1 × 1.6 × 8 mm^3. Three T_2 prep acquisitions with equivalent TEs = 0, 25, 55 ms. Two parameter pixel curve fitting was performed yielding T_2 maps with Eq. (3).

$$I(x,y,TE_n) = M_0(x,y) * \exp(-TE_n/T_2(x,y)) \quad (3)$$

T_2* mapping was performed using a spoiled multiple gradient-echo sequence with dark blood preparation [29]: TR/TE(ms) = 22.6/(2.9–20.4 ΔTE = 2.5; flyback); Flip angle = 18°; Bandwidth = 814 Hz/pixel; Matrix = 256 × 115, Resolution = 2 × 1.2 × 8 mm^3. Two parameter pixel curve fitting was performed yielding T_2* maps with Eq. (4).

$$I(x,y,TE_n) = M_0(x,y) * \exp(-TE_n/T_2^*(x,y)) \quad (4)$$

Lastly, subjects underwent volumetric short and long axis CINE imaging using a balanced steady-state free precession CINE technique (TR/TE = 3.1/1.6 ms; Flip angle = 65°; Bandwidth = 1085 Hz/pixel; Matrix = 127 × 256; Resolution = 2.0 × 1.3 × 8 mm^2, Temporal resolution = 45–55 ms). 7–10 parallel short-axis slices with a 4 mm slice gap spanning the LV myocardium from the base to apex of the heart were acquired.

2.3. Image analysis

Regions-of-interest (ROIs) were manually drawn in the first measurement on four chamber and short-axis relaxation maps for each patient and the mean recorded: circular for T_1 and T_1* measurements in the bloodpool of each ventricle and atria and polygons for T_1, T_1*, T_2 and T_2* in septal myocardium. Bloodpool T_2 and T_2* measurements were not performed. Bloodpool ROIs were drawn to avoid any papillary muscles. ROIs were copied to measurements 2–5 and repositioned to adjust for changes in breath-hold location. ROI analysis was performed in a custom program (MATLAB Version R2014a, MathWorks, Natick, MA, USA). One observer (JWG) performed all measurements twice with a two week separation for intraobserver reproducibility analysis. A second observer (BH) independently performed all measurements for interobserver reproducibility analysis.

Right and left ventricular (RV and LV) functional values were measured from short-axis CINE-bSSFP images using Medis MASS (version 6.2.3, Leiden Netherlands). The RV and LV epicardial and endocardial borders were manually traced on all end-diastolic and end-systolic images. End-systolic/diastolic volumes, myocardial mass and ejection fractions were measured.

2.4. Statistical analysis

Continuous variables are summarized as mean ± standard deviation. Categorical variables are presented as frequency or percentage. Mixed-model analysis of variance was used to examine the influence of supplemental oxygen and location of bloodpool measurement on measured relaxation values. Mixed-model analysis of variance is used to test for differences between two or more independent groups while subjecting participants to repeated measures. The model included bloodpool location (right vs left, atria vs ventricle) and oxygen supplementation as fixed classification factors. The associations among hematocrit, T_1, T_1*, T_2, and T_2* were investigated using multivariate correlation analysis. Reproducibility was assessed using the Intraclass Correlation Coefficient (ICC) and Coefficient of Variation (CoV). A p-value of < 0.05 was considered to indicate a statistically significant difference. All statistical computations were performed using MATLAB (Version R2014a, MathWorks, Natick, MA, USA) and JMP (Version 12.0.1. SAS Institute Inc., Cary, NC).

3. Results

Imaging sessions were completed with good quality images in all subjects. Quantitative measurement from CINE images were within normal ranges: LV ejection fraction = 56 (%) ± 4.4, RV Ejection fraction = 55.6 (%) ± 4.5 and LV myocardial mass = 52.2 (g/m^2) ± 7.5. Hematocrit was 40.8 (%) ± 3.3 with a range of 33.1 to 44.3 (%). Fig. 1 shows representative T_1 maps from the three oxygen supplies (room air, nasal cannula and non-rebreather mask) along with exemplar region-of-interest placement for HLA and SAX imaging planes. Blood T_1 reduction during supplemental oxygen with the non-rebreather mask can be easily visualized in the left atrium and left ventricle (white stars). Neither heart rate (62.2 (bpm) ± 11.0; $p = 0.968$) nor peripheral oxygen saturation (97.9 (%) ± 1.4; $p = 0.065$) changed significantly during the study.

3.1. Effect of oxygen inhalation on water proton blood relaxation time constants

Values of T_1, T_1*, T_2 and T_2* in the chambers of the heart and myocardium are reported for HLA and SAX acquisitions in Tables 1–3. Both T_1 ($p < 0.001$) and T_1* ($p < 0.001$) relaxation time constants of the left ventricle (T_1 change = −241.0 ms; T_1* change = −241.5 ms) and left atrium (T_1 change = −247.0 ms; T_1* change = −233.6 ms) decreased significantly in every subject after oxygen inhalation with the non-rebreather mask. No significant changes ($p = 0.345$) of T_1 and T_1* in the right side of the heart (RV and RA) were detected after oxygen supplied with the non-rebreather mask. Oxygen inhalation with nasal cannula did not significantly change blood T_1 or T_1* in the study ($p = 0.497$).

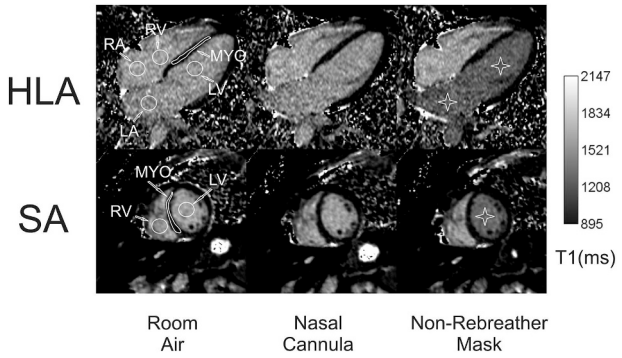

Fig. 1. Representative HLA and SAX T_1 relaxation time constant maps during inhalation of room air, oxygen via nasal cannula and a non-rebreather mask. Example region-of-interests in the four chambers of the heart and LV myocardium are shown. Statistically significant changes were only seen on the left side of the heart in this study (Star). In this example, there was a 260 ms decrease in the LV and a 250 ms decrease in the LA. LV = left ventricle, LA = left atrium, RV = right ventricle, RA = right atrium, MYO = ventricular septal myocardium.

3.2. T_1 and T_1* relaxation time constant differences in chambers of the heart

During room air inhalation (without supplemental oxygen), T_1 values in the four chambers of the heart did not differ significantly ($p = 0.994$), but T_1* values did differ significantly ($p < 0.001$) (see Table 2 and Fig. 2). There was a T_1* difference of 137 ms between the right and left atrium ($p < 0.001$) and a T_1* difference of 107 ms between the right and left ventricles ($p < 0.001$).

3.3. Effects of oxygen inhalation on myocardial relaxation time constants

No significant changes in myocardial T_1 ($p = 0.390$) or T_1* ($p = 0.363$) were observed with supplemental oxygen supplied by nasal cannula or the non-rebreather mask in both HLA and SAX imaging planes. Also, no changes were observed in myocardial T_2 ($p = 0.960$) or T_2* ($p = 0.438$) relaxation time constants with supplemental oxygen supplied by either nasal cannula or the non-rebreather mask.

3.4. Correlations of relaxation time constants with hematocrit

In the study, significant correlations of blood T_1 ($p < 0.002$) and T_1* ($p < 0.01$) with hematocrit were observed for all chambers of the heart (see Fig. 3). T_2* values were not correlated, but the T_2 values of myocardium were significantly correlated ($p < 0.001$). These correlations were maintained with supplemental oxygen.

3.5. Reproducibility of measurements

Blood T_1 showed excellent intra-observer and inter-observer reproducibility (Supplementary Table 1). RV bloodpool T_1 reproducibility was lower; presumably due to increased RV trabeculations. Myocardial relaxation measurements showed good to excellent reproducibility (Supplementary Table 2).

4. Discussion

Cardiovascular water proton relaxation time constants (both myocardial and blood) are reported to be associated with blood oxygen concentration [18,30–32]. We hypothesized that cardiovascular relaxation time constants measured with widely used relaxation mapping protocols might be dependent on the inhalation of supplemental oxygen and demonstrated that inhaled oxygen using a non-rebreather mask causes a significant decrease in left ventricular and atrial bloodpool T_1 using a popular MOLLI imaging protocol. No significant changes in the T_1 of right ventricular and right atrial bloodpool T_1s with the inhalation of oxygen through nasal cannula were observed. Also, no significant changes in myocardial T_1, T_2 or T_2* were observed with supplemental oxygen.

These results indicate that using a commercially available protocol: 1) blood T_1 measurements with inhalation of supplemental oxygen with a non-rebreather mask would be problematic if blood T_1 values are used for estimation of hematocrit for synthetic extracellular volume quantification; 2) blood and myocardial relaxation measurements with oxygen supplied by nasal cannula do not change markedly and 3) the MOLLI protocol does not reproducibly detect myocardial T_1 changes with oxygen inhalation.

An inverse association of hematocrit with blood T_1 is widely reported [31,33,34] and observed in this study (−1.2% T_1 change per % HCT change). Myocardial T_2 was significantly associated with

Table 1
T_1 and T_1* bloodpool and myocardial values measured during breathing of room air and supplemental oxygen with the four chamber imaging plane.

		RA	LA	RV	LV	MYO	O_2SAT (%)
T_1 (ms)	Room air 1	1612.8 ± 62.8	1598.1 ± 63.7	1608.8 ± 82.3	1603.3 ± 65.6	1023.1 ± 38.3	97.7 ± 1.4
	Nasal cannula	1623.3 ± 69.2	1588.5 ± 62.9	1614.3 ± 77.0	1602.0 ± 69.7	1045.1 ± 39.7	98.1 ± 1.2
	Room air 2	1612.1 ± 63.4	1604.5 ± 53.9	1613.6 ± 79.0	1604.8 ± 70.8	1049.5 ± 39.4	97.6 ± 1.2
	Non rebreather mask	1613.5 ± 74.9	**1363.0 ± 32.0****	1611.5 ± 86.6	**1363.8 ± 42.7****	1059.1 ± 60.7	98.8 ± 0.6
	Room air 3	1595.8 ± 54.7	1616.6 ± 73.4	1614.4 ± 67.6	1598.0 ± 100.3	1046.0 ± 41.2	97.25 ± 1.8
	p-Value	0.893	< 0.001	0.994	< 0.001	0.390	0.065
T_1* (ms)	Room air 1	1649.3 ± 96.9	1491.6 ± 56.1	1609.1 ± 108.1	1514.2 ± 47.5	866.3 ± 48.2	97.7 ± 1.4
	Nasal cannula	1648.9 ± 87.5	1471.2 ± 100.0	1615.1 ± 82.4	1507.9 ± 78.7	877.4 ± 52.2	98.1 ± 1.2
	Room air 2	1612.0 ± 94.1	1469.3 ± 58.4	1604.4 ± 107.6	1497.3 ± 77.4	897.0 ± 46.3	97.6 ± 1.2
	Non rebreather mask	1620.4 ± 103.5	**1235.7 ± 41.2****	1580.3 ± 79.7	**1250.3 ± 44.2****	904.7 ± 54.9	98.8 ± 0.6
	Room air 3	1591.6 ± 100.6	1480.4 ± 48.7	1598.6 ± 87.5	1477.9 ± 115.2	891.5 ± 52.2	97.25 ± 1.8
	p-Value	0.535	< 0.001	0.907	< 0.001	0.363	0.065

RA = right atrium, LA = left atrium, RV = right ventricle, LV - left ventricle, MYO = left ventricular myocardium.
** Significant changes with supplemental oxygen ($p < 0.05$) are indicated with bold.

Table 2
T_1 and T_1* bloodpool and myocardial values measured during breathing of room air and supplemental oxygen with the short-axis imaging plane.

		RV	LV	MYO	O_2SAT (%)
T_1 (ms)	Room air 1	1576.2 ± 87.3	1602.1 ± 69.5	1018.5 ± 29.6	97.7 ± 1.4
	Nasal cannula	1585.6 ± 87.8	1596.2 ± 70.8	1032.1 ± 33.2	98.1 ± 1.2
	Room air 2	1568.1 ± 79.5	1607.8 ± 74.1	1028.4 ± 31.8	97.6 ± 1.2
	Non rebreather mask	1585.7 ± 82.0	**1376.6 ± 52.9****	1022.5 ± 30.2	98.8 ± 0.6
	Room air 3	1574.3 ± 73.4	1599.2 ± 56.4	1026.6 ± 31.5	97.25 ± 1.8
	p-Value	0.981	< 0.001	0.390	0.065
T_1* (ms)	Room air 1	1590.4 ± 108.9	1611.7 ± 77.9	855.5 ± 48.2	97.7 ± 1.4
	Nasal cannula	1580.5 ± 95.6	1595.5 ± 71.1	868.7 ± 53.9	98.1 ± 1.2
	Room air 2	1567.7 ± 108.4	1621.0 ± 70.9	863.8 ± 54.8	97.6 ± 1.2
	Non rebreather mask	1570.1 ± 89.3	**1359.5 ± 43.5****	868.3 ± 49.7	98.8 ± 0.6
	Room air 3	1578.4 ± 100.0	1600.2 ± 68.0	864.6 ± 43.9	97.25 ± 1.8
	p-Value	0.983	< 0.001	0.363	0.065

RV = right ventricle, LV = left ventricle, MYO = left ventricular myocardium.
** Significant changes with supplemental oxygen ($p < 0.05$) are indicated with bold.

Table 3
Myocardial T_2 and T_2* values measured during breathing of room air and supplemental oxygen.

	HLA		SAX		O_2SAT (%)
	T_2 (ms)	T_2* (ms)	T_2 (ms)	T_2* (ms)	
Room air 1	49.6 ± 3.0	35.2 ± 4.7	48.6 ± 1.83	31.3 ± 3.2	97.7 ± 1.4
Nasal cannula	49.6 ± 3.0	36.5 ± 5.0	48.9 ± 2.5	32.0 ± 2.9	98.1 ± 1.2
Room air 2	49.0 ± 4.0	37.4 ± 3.3	49.0 ± 2.0	31.3 ± 4.3	97.6 ± 1.2
Non rebreather mask	48.8 ± 3.5	38.2 ± 3.4	48.7 ± 2.34	31.92 ± 4.2	98.8 ± 0.6
Room air 3	48.6 ± 3.2	36.8 ± 2.4	47.9 ± 2.0	31.5 ± 3.8	97.25 ± 1.8
p-Value	0.956	0.438	0.702	0.985	0.065

Data are presented as mean ± standard deviation. No significant changes were observed.

hematocrit (−1.5% T_2 change per %HCT change) and myocardial T_1 trended towards an association. Also, a significant T_1* difference of the right and left bloodpools of the heart was observed, but not with T_1. The derivation for the so-called "Look-Locker" correction factor (B/A - 1) is based on a continuous readout with a Fast Low Angle SHot (FLASH) pulse sequence [35,36]. Even though the MOLLI technique uses a gated balanced Steady-State Free Precession (bSSFP) sequence, the signal model behaves as a 3-parameter model where the Look-Locker correction is reasonably effective at low readout excitation flip angles. The reason for this right/left heart T_1* difference is not known but could be due to the different T_2 values of venous and arterial blood seen across the heart as the MOLLI bSSFP readout is sensitive to T_2 [37]. In a MOLLI acquisition, shorter T_2 species show greater modulation of magnetization [38]. MOLLI has the unexpected effect of essentially averaging out errors introduced by the three parameter (Look-Locker) correction [36].

Inhaled supplemental oxygen has been used in studies of the lung [39], brain [14,15,40] and tumors [41] as an MRI contrast agent. Increasing blood oxygenation initially causes an increase in T_1, T_2 and T_2* [32,42] due to the magnetic susceptibility difference between the inside of the erythrocyte and plasma, which is proportional to the concentration of deoxyhemoglobin. Once hemoglobin is fully saturated, the primary relaxation mechanism is oxygen dissolved in blood acting as a paramagnetic contrast agent [21]. This results in a T_1 decrease similar to conventional gadolinium based contrast agents. Observed blood T_1 and T_1* shortening (−15% and −17%, respectively) in the left heart chambers with supplemental oxygen supplied by a non-rebreather mask are consistent with this theory. The detected T_2* invariance in healthy subjects confirm previous results [43,44] and is in contrast to another report [45]. The results of this paper do differ from another manuscript [18] which reported a significant small decrease in myocardial T_1 relaxation and are consistent with a number of published reports showing

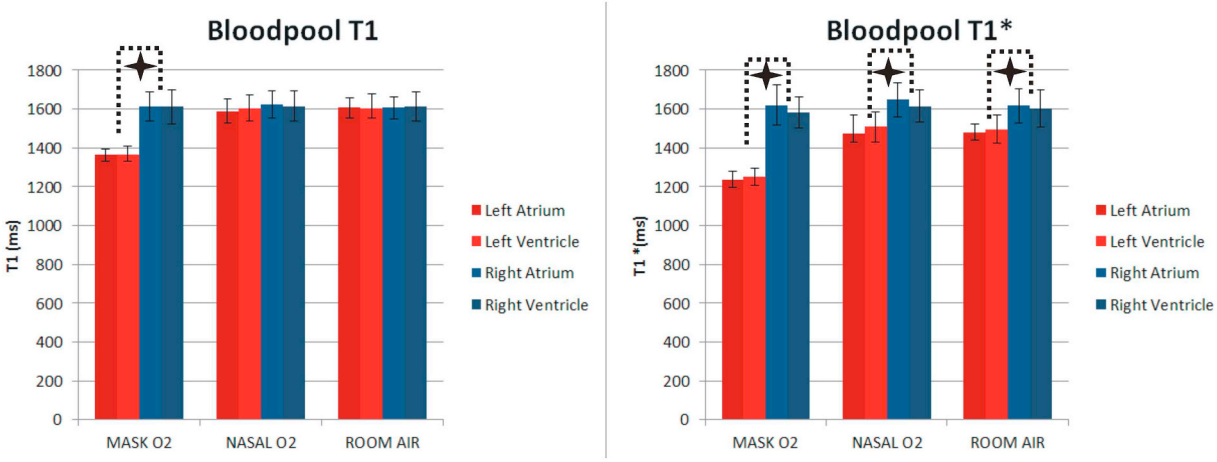

Fig. 2. Graphs show T_1 and T_1* differences in the chambers of the heart and with supplemental oxygen supplied by nasal cannula and a non-rebreather mask. Compared to room air, there was a significant decrease in both T_1 and T_1* for the left atrium and ventricle when oxygen was supplied by a non-rebreather mask ($p < 0.001$) but not with nasal cannula ($p = 0.389$). There was a significant difference in T_1* between the left and right side of the heart with room air ($p < 0.001$) and nasal cannula ($p < 0.001$), but no significant difference in T_1 was seen ($p = 0.685$).

a relatively large reduction in arterial blood T_1 relaxation with inhaled oxygen.

4.1. Limitations

This study is limited by use of fixed imaging protocols, use of a single vendor and MR machine. Sample sizes were small, and a significant difference may be detected with much larger sample sizes, but this study clearly demonstrates that blood T_1 changes with a non-rebreather mask are consistent, while myocardial relaxation changes are not reproducibly detected. A further limitation is that only healthy subjects were studied and not subjects with disease: pulmonary, ischemic or non-ischemic cardiomyopathy. Additionally, we did not study the effects of oxygen on contrast enhanced blood and myocardium or on the subsequent calculation of extracellular volume. We expect that the results would be similar in the above situations, but additional studies may be warranted. Blood T_2 and T_2* were not measured due to the use of established protocols. Newly developed protocols and pulse sequences would allow the assessment of supplemental oxygen's effect on blood T_2 [46]. An optimized MOLLI protocol was used for T_1 measurements with due to its high accuracy. Newer pulse sequences such as ShMOLLI [47], SASHA [48], SAPHIRRE [49] and STONE [50] have been developed with trade-offs of accuracy and precision [1].

In conclusion, the use of supplemental oxygen has the potential to change measured cardiovascular T_1 relaxation values. As measured using a documented MOLLI T_1 protocol, there are significant changes in left atrial and ventricular T_1 relaxation time constants with

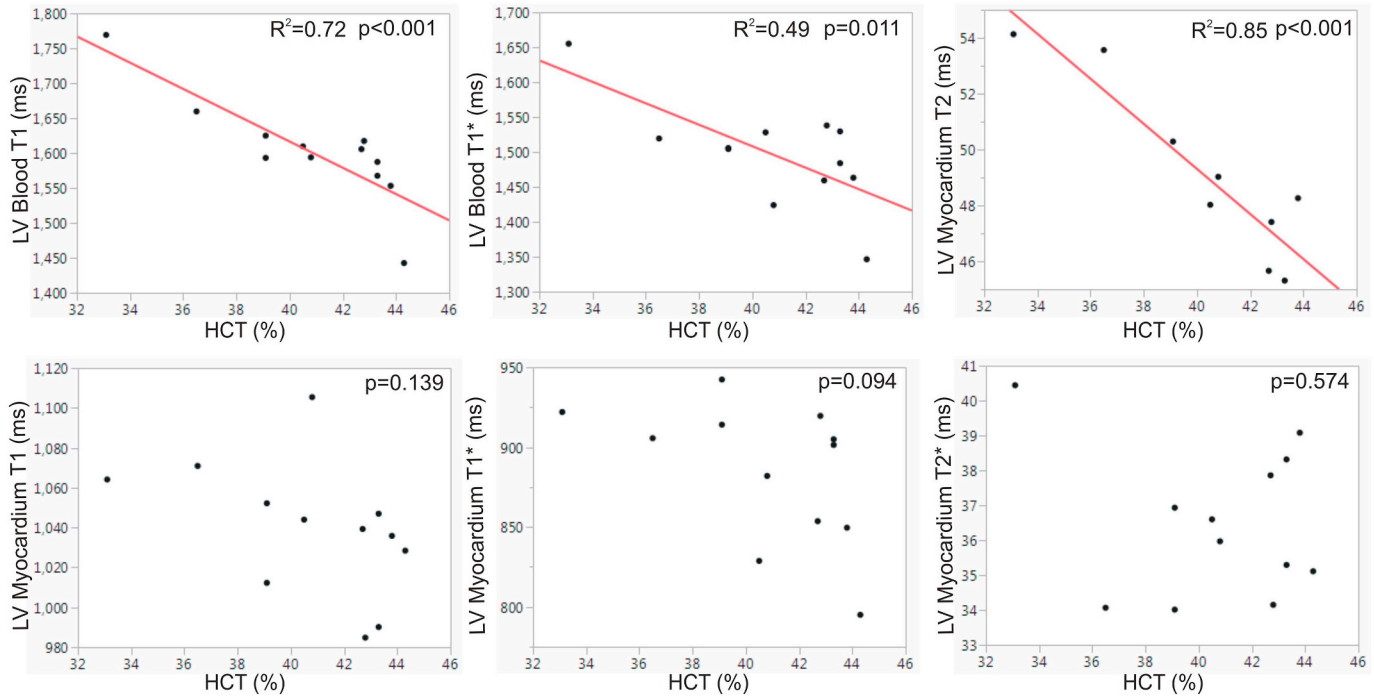

Fig. 3. Association of relaxation time constants with venous hematocrit. Left ventricular blood T_1 and T_1* relaxation time constants and myocardial T_2 were correlated with hematocrit (top row), but myocardial T_1, T_1* and T_2* relaxation time constants were not (bottom row).

supplemental oxygen supplied by a non-rebreather mask. Clearly, use of high flow oxygen with a non-rebreather mask will alter arterial blood T_1 times and consequently synthetic hematocrit and ECV calculations. If supplemental oxygen was used during MR imaging, one could alternatively measure blood T_1 relaxation time constants from the right rather than the left side of the heart. Lastly, myocardial T_1, T_2 and T_2* values did not change with oxygen supplied by a non-rebreather mask or nasal cannula. Therefore, large observed changes in myocardial T_1 relaxation time constants (for example in cardiac amyloidosis) should not be affected by supplemental oxygen.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.mri.2019.05.004.

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