Published in final edited form as:

Magn Reson Med. 2018 March ; 79(3): 1545–1552. doi:10.1002/mrm.26808.

Cardiac Quantitative Susceptibility Mapping (QSM) for Heart Chamber Oxygenation

Yan Wen^{1,2}, Thanh D. Nguyen², Zhe Liu^{1,2}, Pascal Spincemaille², Dong Zhou², Alexey Dimov^{1,2}, Youngwook Kee², Kofi Deh², Jiwon Kim³, Jonathan W. Weinsaft³, and Yi Wang^{1,2}

¹Meinig School of Biomedical Engineering, Cornell University, Ithaca, NY, United States

²Radiology, Weill Cornell Medicine, New York, NY, United States

³Medicine, Weill Cornell Medicine, New York, NY, United States

Abstract

Purpose—To demonstrate the feasibility of *in vivo* quantitative susceptibility mapping (QSM) in cardiac MRI, and to show that mixed-venous oxygen saturation (SvO₂) can be measured non-invasively using QSM.

Methods—ECG-gated multi-echo 2D gradient echo data were collected at 1.5T from 14 healthy volunteers during successive breath-holds. Phase wraps and fat chemical shift were removed using a graph-cut based phase analysis and IDEAL in an iterative approach. The large susceptibility range from air in the lungs to blood in the heart was addressed by using the preconditioning approach in the dipole field inversion. SvO₂ was calculated based on the difference in blood susceptibility between the right ventricle (RV) and left ventricle (LV). Cardiac QSM quality was assessed by two independent readers.

Results—Nine out of fourteen volunteers (64%) yielded interpretable cardiac QSM. QSM maps showed strong differential contrast between RV and LV blood with RV blood having higher susceptibility values (291.5 ± 32.4 ppb), which correspond to $78.3 \pm 2.3\%$ SvO₂.

Conclusion—*In vivo* cardiac QSM is feasible and can be used to measure SvO₂, but improvements in data acquisition are needed.

INTRODUCTION

Mixed-venous oxygen saturation (SvO₂) is an important indicator of cardiopulmonary function that is widely used clinically to assess cardiac function in heart failure patients, and to measure shunt fractions in patients with congenital or acquired heart disease (1–3). Currently, conventional measurement of SvO₂ requires an invasive pulmonary artery catheterization procedure (2–4), and is thus both challenging and labor intensive for critically ill patients. Cardiac MRI has emerged as a promising non-invasive method for measuring SvO₂. It has been demonstrated that SvO₂ can be calculated based on blood T2 relaxation, which requires *in vitro* calibration of blood samples infused with oxygen at

different concentrations (5–12). This approach is highly dependent on pulse sequence parameters, field strengths, patient blood characteristics (7,12,13), and accurate blood calibration curves (14–16), thus complicating its clinical applicability (5,11). In contrast, magnetic susceptibility is a fundamental property of biomagnetic sources, with blood susceptibility being linearly dependent on the oxyheme concentration in blood. Therefore, a magnetic susceptibility based oxygenation measurement method would not require calibration (15,17) or blood withdrawal from patients.

Because of the difference in electron pairing in heme iron caused by oxygen binding, oxyheme is diamagnetic and deoxyheme is paramagnetic (18,19). Thus, blood oxygen saturation (SO_2) can be measured using Quantitative Susceptibility Mapping (QSM), which is an advanced phase-based MRI method for measuring the distribution of biomagnetic sources (19–26). Furthermore, QSM-based oxygenation quantification has been demonstrated to be feasible in the brain (17,18,27,28) and QSM has been used to study the mouse heart *ex vivo* (29), but it has not yet been applied to *in vivo* cardiac MRI due to several technical challenges: cardiac and respiratory motion, chemical shift effects from epicardial fat, and a large range in susceptibilities from air in the lungs and surrounding tissue. As known from coronary MRI, electrocardiogram triggering can be used to acquire data in mid-diastole to minimize cardiac motion, and breath-hold or navigator to minimize respiratory motion (30,31). Recent advancements in QSM precisely account for chemical shift effects using graph cuts (32), and deal with large range in susceptibility using preconditioning (33). By combining the knowledge from these advancements, this study aimed to investigate the feasibility of cardiac QSM for chamber blood SvO_2 quantification.

METHODS

Blood oxygenation quantification using QSM

The blood volume susceptibility, χ , depends linearly on the oxygen saturation, SO_2 , and can be estimated as follows (17,18) (ignoring the contribution from blood products other than oxy/deoxyheme):

$$\chi = H[(1 - SO_2)4\chi_{deoxyheme} + \chi_{oHb}] \quad [1]$$

where H is the heme concentration in blood (in $\mu\text{mol}/\text{ml}$), $\chi_{deoxyheme}$ is the molar susceptibility of deoxyheme, and χ_{oHb} is the susceptibility of oxyhemoglobin. H is a subject-specific physiological parameter which can be measured or estimated. The multiplicative factor of 4 indicates the number of deoxyhemes contained in a fully desaturated deoxyhemoglobin. Let χ be the blood susceptibility difference between the RV and LV measured on QSM, then the difference in blood oxygenation SO_2 can be calculated as:

$$\Delta SO_2 = \frac{-\Delta \chi}{4H\chi_{deoxyheme}} \quad [2]$$

The value of H is calculated as (18): $H = 4Hct \frac{\rho_{RBC,Hb}}{M_{Hb}}$, where $\rho_{RBC,Hb} = 0.34 \frac{g}{ml}$ is the mass concentration of hemoglobin in a RBC (34), $M_{Hb} = 64450 \times 10^{-6} \frac{g}{\mu mol}$ is the molar mass of deoxyhemoglobin (35), and the multiplicative factor of 4 refers to the 4 deoxyheme in a deoxyhemoglobin molecule. In this imaging study of healthy volunteers, we assumed Hct to be .45 for adult males and .4 for adult females (36), so $H_{male} = 9.49 \times \frac{\mu mol}{ml}$ and $H_{female} = 8.43 \frac{\mu mol}{ml}$. The value of 4χ deoxyheme is $151.054 ppb \frac{ml}{\mu mol}$ (18). Given the arterial blood oxygen saturation SaO_2 (measured by pulse oximeter), SvO_2 can be estimated as $SaO_2 - SO_2$.

Cardiac QSM experiments

This human study was approved by the Weill Cornell Medicine IRB committee and written informed consent was obtained from all subjects prior to imaging. Fourteen volunteers (13 male, 1 female, mean age $31.3 \text{ years} \pm 5.9$, age range = 24–45 years, no history of cardiopulmonary disease) underwent a cardiac MRI exam on a 1.5T clinical scanner (GE HD23.0, GE Healthcare, Waukesha, WI, USA; maximum gradient amplitude 33 mT/m, maximum slew rate 120 T/m/s). Subjects were imaged supine using a product 8-channel cardiac phased array coil (four anterior, four posterior elements) for signal reception and vector electrocardiographic (ECG) gating for cardiac synchronization. Prior to cardiac QSM, a breath-hold (BH) cine 2D balanced steady-state free precession (SSFP) scan was performed in the two-chamber view to determine the subject-specific optimal cardiac trigger delay time between the ECG trigger and the mid-diastolic diastasis. For cardiac QSM, a BH ECG-triggered 2D multi-echo fast gradient echo (FGRE) scan was performed in the short-axis view using the following typical imaging parameters: TR = 23 ms, TE = 3.6 ms, TE = 2.2 ms, number of echoes = 8, in-plane resolution $\approx 1.25 \times 1.25 \text{ mm}^2$, slice thickness = 5 mm, number of slices = 20, interleaved linear view ordering, first-order flow compensation in the readout and slice directions (for the readout direction, flow compensation gradients were applied to the first echo, and subsequent echoes were naturally flow compensated; for the slice direction, flow compensation gradients were applied to the slice-selection gradient), ASSET parallel imaging factor = 1.5, 10 views per heartbeat (HB) acquired during mid-diastolic diastasis, one slice per breath-hold of approximately 15 sec each. To maximize the consistency of respiratory position between imaging slices acquired in separate breath-holds, all subjects were instructed to completely exhale before holding their breath.

QSM reconstruction and blood oxygenation difference calculation

Figure 1 summarizes the main steps of cardiac QSM computation from the complex multi-echo GRE image data. First, an initial total field map was obtained by voxel based linear regression on the phase of the complex data obtained at multiple TEs. This field map estimate contains field wraps and includes contributions from fat chemical shift, both of which need to be removed for accurate QSM reconstruction (37). In this study, an advanced graph-cuts based unwrapping method called SPURS (32) was used in conjunction with the IDEAL water/fat separation algorithm (38,39) in an iterative manner (37) to accurately remove fat chemical shift. The susceptibility map was then computed from the total field using the recently developed Total Field Inversion (TFI) algorithm (40). Briefly, this

algorithm solves the total field-to-susceptibility source inversion problem by minimizing the following cost function:

$$\chi^* = \arg \min_{\chi} \frac{1}{2} \|w(f - d * P\chi)\|_2^2 + \lambda \|M_G \nabla P\chi\|_1 \quad [3]$$

where χ is the unknown susceptibility map in the whole field of view (FOV), f is the measured total field, d is a dipole kernel, $*$ is a convolution operator, ∇ is a gradient operator, λ is a regularization parameter, M_G is an edge mask computed from the magnitude image, and w is a weighting factor depending on SNR ($w \sim \text{SNR}$). P is a right preconditioner, designed to increase the convergence speed of the algorithm. As in (40), P was a binary mask that was equal to 1 inside the region of interest (ROI) and a larger value P_{outside} outside the ROI. In this study, both the optimal values of $P_{\text{outside}} = 20$ for the background air and lung region, and $\lambda = 1000$ were empirically determined in one subject by visual inspection of corresponding QSM maps and then fixed for the remaining subjects. For comparison with conventional QSM processing often used in brain imaging, a second set of QSM maps were computed using the PDF algorithm for background field removal (41) and the MEDI algorithm for dipole deconvolution (21). A manually segmented ROI centered on the heart was used as a data mask in MEDI (which typically produced QSM maps with less artifacts compared to those obtained with a full FOV ROI).

For cardiac QSM analysis, the endocardial surfaces of the RV and LV were manually traced on GRE magnitude images. The mean susceptibility difference between RV and LV blood pools was measured, and SO_2 was calculated using Eq.2. SaO_2 was measured using pulse oximeter, and SvO_2 was estimated as $\text{SaO}_2 - \text{SO}_2$. The visual quality of each cardiac QSM map obtained with the TFI algorithm was scored by two cardiologists experienced in reading cardiac MRI using a three-point scale (1 = major artifacts and uninterpretable, 2 = moderate artifacts and reasonable quality, and 3 = minimum artifacts and excellent quality). To correlate the QSM scores with consistency of breath-holds, we quantified spatial slice consistency as follows: two perpendicular long-axis images clearly depicting the heart-lung interface were obtained by reformatting the acquired short axis slices. A simple signal intensity thresholding on these images was used to find the surface curve corresponding to this heart-lung interface. A second derivative along this curve was computed and the slice inconsistency was defined as the standard deviation of this second derivative curve. A high standard deviation corresponded to a greater slice inconsistency (less smooth heart-lung interface). The Wilcoxon rank-sum test with Bonferroni correction was used to assess the statistical differences in slice inconsistency among the three groups of QSM scores. Cardiac R2^* maps were also calculated using ARLO (42), and the average blood R2^* values were measured in the RV and LV using the same endocardial segmentations used in QSM analysis.

RESULTS

The average scan time of cardiac QSM was 11.7 ± 1.9 min. The average heart rate was 64.9 ± 4.7 bpm (beats per minute). All subjects were able to maintain good breath-holding during data acquisition for individual slices, leading to excellent GRE images free of motion

artifacts (Figs. 2–4). However, the consistency of end-expiratory breath-holding position between consecutive slices was variable among the subjects, this can be seen as slice misregistration on the long-axis reformatted images (Fig. 4). Of the 14 acquired cardiac QSM maps, 4 (29%) had excellent image quality (score=3), 5 (36%) were reasonable (score=2), and remaining 5 (36%) had significant artifacts and were uninterpretable (score=1). This resulted in a success rate of 64% (9/14, defined by scores ≥ 2). The average SaO_2 measured using pulse oximeter was 98.7%. The measured RV to LV susceptibility differences for QSM maps obtained with TFI with image quality scores of 1, 2, and 3 were 188.6 ± 64.9 ppb, 266.1 ± 22.2 ppb, and 323.3 ± 14.6 ppb, respectively. The corresponding values for QSM obtained with the conventional PDF+MEDI method were 98.1 ± 18.3 ppb, 122.6 ± 43.5 ppb, and 156.1 ± 54.2 ppb, respectively. The corresponding SvO_2 values were $85.6 \pm 4.6\%$, $80.1 \pm 1.2\%$, and $76.0 \pm 1.1\%$ for TFI versus $93.2\% \pm 1.28\%$, $91.4\% \pm 3.0\%$, and $89.1\% \pm 3.8\%$ for PDF+MEDI. The average RV to LV susceptibility difference for score 2 was 291.5 ± 32.4 ppb (vs. 136.0 ± 48.3 ppb for PDF+MEDI), which corresponds to a SvO_2 of $78.3\% \pm 2.3\%$ (vs. $90.5\% \pm 3.4\%$ for PDF+MEDI). The values obtained with TFI were in line with the normal range of SvO_2 in healthy adults at approximately 60–80%, while PDF+MEDI yielded values well above this range. There was weak contrast between LV myocardium and LV arterial blood on QSM (Figs. 2–3), with an average LV blood vs. myocardium susceptibility difference of 43.2 ± 32.5 ppb measured on the TFI derived QSM maps with score ≥ 2 , and 30.1 ± 17.8 ppb measured on the PDF+MEDI derived QSM maps ($p=0.44$, paired t-test). The average slice inconsistency (in pixels) was 2.15, 1.12, and 1.00 for datasets that produced QSM with image scores of 1, 2, and 3, respectively. There was a significant difference in slice inconsistency between QSMs with quality score of 1 and 2 ($p = 0.016$) and between those with score of 1 and 3 ($p = 0.016$). The average RV $R2^*$ value across subjects was 8.5 ± 0.8 Hz, which corresponded to a SvO_2 of $72.5 \pm 6.6\%$, $82.8 \pm 2.2\%$, and $82.2 \pm 7.5\%$ using the blood calibration curves reported in Silvennoinen et al. (14), Spees et al. (15), and Li et al. (16), respectively.

Two representative examples of cases with scores of 3 are shown in Figure 2. Strong contrast between the RV and LV blood pool can be seen on QSM, this reflects the differential oxygenation levels in the venous (paramagnetic) and arterial (diamagnetic) blood. In Figure 3, a case with a score of 2 shows a similar increase in susceptibility from LV to RV, though there are more apparent streaking and noise artifacts as compared to the cases shown in Figure 2. Figure 4 shows an example of a failed QSM map with a score of 1, in which major artifacts are present, resulting in poor or physiologically not meaningful RV-to-LV contrast. Figure 5 shows the comparison of the $R2^*$ map, the QSM map obtained with PDF+MEDI, and the QSM map obtained with TFI in one volunteer. In this example, compared to the $R2^*$ map, both of the QSM maps shows improved visual contrast between RV and LV blood. Both QSM maps are free of streaking artifacts, but TFI yielded a realistic SvO_2 of 77.0%, while the PDF+MEDI value was 90.1%, which was well outside the normal range in healthy subjects.

DISCUSSION

Our preliminary data in healthy volunteers showed that *in vivo* cardiac QSM is feasible, but requires improvements in data acquisition to increase success rate and improve QSM quality.

The difference in QSM between LV and RV blood can be used to indicate the changes in oxygenation between systemic and venous blood, however there is little QSM contrast between LV blood and myocardium in healthy subjects.

In this study, the average SvO_2 values derived from the susceptibility maps of healthy volunteers were found to be in reasonable agreement with those reported in the literature. For successful QSM scans (image score ≥ 2), the average SvO_2 was approximately 78%, which falls in the high end of the normal range (60–80%) (4), thus indicating an underestimation of susceptibility difference between RV and LV blood. This underestimation may be attributed to the fairly large voxel size (particularly in the slice direction) (43), which is needed to keep the scan time reasonably short. Another potential factor is the gradual decrease of arterial blood oxygenation in the LV during the length of the breath-hold (44). Lastly, the hematocrit value of 0.45 for adult male and 0.4 for adult female, which might need to be adjusted for individual subjects.

Normal myocardium is weakly diamagnetic, and thus appears isointense with oxygenated LV blood on QSM. This image feature may potentially enable cardiac QSM to detect pathological conditions that alter myocardial tissue properties. For example, intramyocardial hemorrhage is a known consequence of acute myocardial infarction that has been associated with adverse LV chamber remodeling and poor clinical outcomes (45,46). Given that hemorrhage would be expected to cause myocardium to become highly paramagnetic, (47) both diagnosis and quantification could potentially be well addressed by QSM. QSM has been used to measure intracerebral hemorrhage (ICH) and differentiate ICH from calcification (48). Whereas ICH risk has limited cerebral revascularization treatment to just to 1–8% of ischemic stroke patients (49), IMH damage to the heart as a long term causal factor for systolic heart failure after acute myocardial infarction is becoming more recognized (45,46).

While QSM is an established technique for mapping tissue and blood susceptibilities in the brain (19–23,25,27,48,50), this technology has not been applied to the chest due to several technical challenges. A major challenge common to heart imaging is respiratory and cardiac, which produce blurring and ghosting artifacts. In this first cardiac QSM study, a short breath-hold of 15 seconds was used to suspend respiration during acquisition, and data sampling was timed to the mid-diastolic cardiac rest period to minimize cardiac motion. In our cohort of healthy volunteers with good breath-holding ability and low heart rate (65 bpm on average), individual GRE image slices with excellent image quality could be obtained. However, significant variability in QSM maps was observed (Figs. 2–4), and cardiac QSM was deemed successful in only 64% of subjects. This low success rate could be explained by the spatial inconsistency between consecutive slices that were acquired in different breath-holds. This misregistration artifact is best visualized in the long-axis view (Fig. 4). Misregistration can lead to major errors such as artificial field discontinuities in the field map estimation, which propagate into the final QSM, ultimately leading to severe artifacts. Our results demonstrated that as the slice inconsistency increased, the resulting QSM quality decreased. Spatial misregistration between imaging slices can be a greater problem in older patients with cardiopulmonary diseases who have limited breath-holding capabilities (51). Slice inconsistency is not a challenge for $R2^*$ based oxygenation measurement methods, that

are voxel-based. One approach to overcoming the challenge from respiratory motion in cardiac QSM is to use a free-breathing navigator GRE acquisition (31), which will be a main focus of our future work.

In addition to the motion challenge during cardiac QSM acquisition, the quality of cardiac QSM depends on the ability of the post-processing algorithm to successfully remove the chemical shift effect of epicardial fat and accurately search through the large susceptibility range from near zero susceptibility sources of heart tissue and very high susceptibility sources of air in the lungs. In this study, a novel algorithm based on SPURS (32) and IDEAL (38) was used in an iterative chemical shift update scheme (37) to improve the quality of the field map in the fat regions (Fig. 1). To address the large susceptibility range, current state-of-the-art QSM methods generally perform background field removal first to estimate the local field, from which QSM is obtained through dipole field inversion. However, this two-step approach fundamentally contains errors in estimating background field from inaccurate boundary conditions (19,52), and these errors tend to carry over to the dipole inversion step, resulting in errors in the final QSM. In this work, the large susceptibility range is systematically managed using the preconditioning approach with TFI, which has been shown to be better than the background field removal methods at the interface between weak and strong susceptibility sources (40). As illustrated in Figure 5, we found that TFI yielded SvO₂ measurements within the expected range, while PDF+MEDl produced unusually high values well above the range expected from healthy volunteers. This strongly suggests that TFI is a more robust algorithm for cardiac QSM. While a simple binary mask was used for preconditioning in the TFI algorithm implemented in this study, a more complex preconditioner that relies on knowledge of strong susceptibility sources inside an ROI (i.e. RV blood, fat, bone, and possibly hemorrhage) may further improve QSM quality.

This initial feasibility study of cardiac QSM has several limitations. First, the current 2D approach uses relatively thick slices (5 mm) and still requires a long scan time (over 10 min). The need for sustaining a consistent breath-holding over this extended period precluded the recruitment of cardiac patients who often have limited breath-holding capability. Potential approaches for accelerating cardiac QSM include the use of more efficient echo planar readout (53), parallel imaging (54) and echo sharing (55), as well as recent image reconstruction methods which combine k-space undersampling with compressed sensing (56). Second, the *in vivo* blood oxygenation difference between RV and LV obtained with QSM was not compared with the reference blood sampling method. Third, flow compensation was performed only in the readout and slice directions, which was needed to keep TR and the corresponding breath-hold length short. However, a previous study (27) has showed that 3D flow compensation can significantly improve the accuracy of QSM in regions with flow. Furthermore, the blood flow pattern in heart chambers during the mid-diastolic LV filling is complex, potentially resulting in phase errors that cannot be corrected with first-order flow compensation. As the result, the ventricular blood QSM values may have been affected by residual phase shift due to incomplete flow nulling, which may explain the slight increase in susceptibility of the LV blood in the apex compared to that at the basal slice (Figs. 2–3). Finally, it has been reported that 2D slice interleaved GRE acquisitions may produce inter-slice phase errors that can be corrected (53,57,58). We have carefully examined our GRE phase data and did not observe such errors, possibly because

this study used a single slice 2D acquisition (without slice interleaving). However, phase inconsistency remains a potential concern regarding data acquisition.

CONCLUSION

In this work, we demonstrated for the first time, the feasibility of *in vivo* cardiac QSM, and showed that a reasonable SvO₂ value can be measured non-invasively using this method.

Acknowledgments

We thank Kelly McCabe Gillen, PhD, for her assistance in manuscript editing.

This work was supported in part from NIH grant R01HL128278, R01NS072370, R01NS090464, and R01NS095562.

References

1. Robin E, Costecalde M, Lebuffe G, Vallet B. Clinical relevance of data from the pulmonary artery catheter. *Critical Care*. 2006; 10(3):1–10.
2. Brovman EY, Gabriel RA, Dutton RP, Urman RD. Pulmonary Artery Catheter Use During Cardiac Surgery in the United States, 2010 to 2014. *Journal of Cardiothoracic and Vascular Anesthesia*. 2016; 30(3):579–584. [PubMed: 26947712]
3. Judge O, Ji F, Fleming N, Liu H. Current Use of the Pulmonary Artery Catheter in Cardiac Surgery: A Survey Study. *Journal of Cardiothoracic and Vascular Anesthesia*. 2015; 29(1):69–75. [PubMed: 25440650]
4. Jesurum J. Svo2 Monitoring. *Critical Care Nurse*. 2004; 24(4):73–76.
5. Nield LE, Qi X-LL, Valsangiacomo ER, Macgowan CK, Wright GA, Hornberger LK, Yoo S-J. In vivo MRI measurement of blood oxygen saturation in children with congenital heart disease. *Pediatric Radiology*. 2005; 35(2):179–185. [PubMed: 15490150]
6. Wedegärtner U, Kooijman H, Yamamura J, Frisch M, Weber C, Buchert R, Huff A, Hecher K, Adam G. In vivo MRI measurement of fetal blood oxygen saturation in cardiac ventricles of fetal sheep: A feasibility study. *Magnetic Resonance in Medicine*. 2010; 64(1):32–41. [PubMed: 20572133]
7. Wright GA, Hu BS, Macovski A. Estimating oxygen saturation of blood in vivo with MR imaging at 1.5 T. *Journal of Magnetic Resonance Imaging*. 1991; 1(3):275–283. [PubMed: 1802140]
8. Langham MC, Magland JF, Epstein CL, Floyd TF, Wehrli FW. Accuracy and precision of MR blood oximetry based on the long paramagnetic cylinder approximation of large vessels. *Magnetic Resonance in Medicine*. 2009; 62(2):333–340. [PubMed: 19526517]
9. Thulborn KR, Waterton JC, Matthews PM, Radda GK. Oxygenation dependence of the transverse relaxation time of water protons in whole blood at high field. *Biochimica et Biophysica Acta (BBA) - General Subjects*. 1982; 714(2):265–270. [PubMed: 6275909]
10. Qin Q, Grgac K, van Zijl PCM. Determination of whole-brain oxygen extraction fractions by fast measurement of blood T2 in the jugular vein. *Magnetic resonance in medicine : official journal of the Society of Magnetic Resonance in Medicine / Society of Magnetic Resonance in Medicine*. 2011; 65(2):471–479.
11. Nield LE, Qi X, Yoo S-J, Valsangiacomo ER, Hornberger LK, Wright GA. MRI-based blood oxygen saturation measurements in infants and children with congenital heart disease. *Pediatric Radiology*. 2002; 32(7):518–522. [PubMed: 12107586]
12. Krishnamurthy LC, Liu P, Xu F, Uh J, Dimitrov I, Lu H. Dependence of blood T(2) on oxygenation at 7T: in vitro calibration and in vivo application. *Magnetic resonance in medicine : official journal of the Society of Magnetic Resonance in Medicine / Society of Magnetic Resonance in Medicine*. 2014; 71(6):2035–2042.
13. Zhao JM, Clingman CS, Närväinen MJ, Kauppinen RA, van Zijl PCM. Oxygenation and hematocrit dependence of transverse relaxation rates of blood at 3T. *Magnetic Resonance in Medicine*. 2007; 58(3):592–597. [PubMed: 17763354]

14. Silvennoinen MJ, Clingman CS, Golay X, Kauppinen RA, van Zijl PCM. Comparison of the dependence of blood R2 and R2* on oxygen saturation at 1.5 and 4.7 Tesla. *Magnetic Resonance in Medicine*. 2003; 49(1):47–60. [PubMed: 12509819]
15. Spees WM, Yablonskiy DA, Oswood MC, Ackerman JJH. Water proton MR properties of human blood at 1.5 Tesla: Magnetic susceptibility, T1, T2, T2*, and non-Lorentzian signal behavior. *Magnetic Resonance in Medicine*. 2001; 45(4):533–542. [PubMed: 11283978]
16. Li D, Wang Y, Waight DJ. Blood oxygen saturation assessment in vivo using T2* estimation. *Magnetic Resonance in Medicine*. 1998; 39(5):685–690. [PubMed: 9581597]
17. Jain V, Abdulmalik O, Probert KJ, Wehrli FW. Investigating the magnetic susceptibility properties of fresh human blood for noninvasive oxygen saturation quantification. *Magnetic Resonance in Medicine*. 2012; 68(3):863–867. [PubMed: 22162033]
18. Zhang J, Zhou D, Nguyen TD, Spincemille P, Gupta A, Wang Y. Cerebral metabolic rate of oxygen (CMRO2) mapping with hyperventilation challenge using quantitative susceptibility mapping (QSM). *Magnetic Resonance in Medicine*. 2016; doi: 10.1002/mrm.26253
19. Wang Y, Liu T. Quantitative susceptibility mapping (QSM): Decoding MRI data for a tissue magnetic biomarker. *Magnetic Resonance in Medicine*. 2015; 73(1):82–101. [PubMed: 25044035]
20. Schweser F, Deistung A, Reichenbach JR. Foundations of MRI phase imaging and processing for Quantitative Susceptibility Mapping (QSM). *Zeitschrift für Medizinische Physik*. 2016; 26(1):6–34. [PubMed: 26702760]
21. Liu J, Liu T, de Rochefort L, Ledoux J, Khalidov I, Chen W, Tsiouris AJ, Wisnieff C, Spincemille P, Prince MR, Wang Y. Morphology enabled dipole inversion for quantitative susceptibility mapping using structural consistency between the magnitude image and the susceptibility map. *NeuroImage*. 2012; 59(3):2560–2568. [PubMed: 21925276]
22. de Rochefort L, Liu T, Kressler B, Liu J, Spincemille P, Lebon V, Wu J, Wang Y. Quantitative susceptibility map reconstruction from MR phase data using bayesian regularization: Validation and application to brain imaging. *Magnetic Resonance in Medicine*. 2010; 63(1):194–206. [PubMed: 19953507]
23. Haacke EM, Liu S, Buch S, Zheng W, Wu D, Ye Y. Quantitative susceptibility mapping: current status and future directions. *Magnetic Resonance Imaging*. 2015; 33(1):1–25. [PubMed: 25267705]
24. Liu C, Li W, Tong KA, Yeom KW, Kuzminski S. Susceptibility-weighted imaging and quantitative susceptibility mapping in the brain. *Journal of Magnetic Resonance Imaging*. 2015; 42(1):23–41. [PubMed: 25270052]
25. Eskreis-Winkler S, Zhang Y, Zhang J, Liu Z, Dimov A, Gupta A, Wang Y. The clinical utility of QSM: disease diagnosis, medical management, and surgical planning. *NMR in Biomedicine*. 2016; doi: 10.1002/nbm.3668
26. Deistung A, Schweser F, Reichenbach JR. Overview of quantitative susceptibility mapping. *NMR in Biomedicine*. 2016; doi: 10.1002/nbm.3569
27. Xu B, Liu T, Spincemille P, Prince M, Wang Y. Flow compensated quantitative susceptibility mapping for venous oxygenation imaging. *Magnetic Resonance in Medicine*. 2014; 72(2):438–445. [PubMed: 24006187]
28. Fan AP, Bilgic B, Gagnon L, Witzel T, Bhat H, Rosen BR, Adalsteinsson E. Quantitative oxygenation venography from MRI phase. *Magnetic Resonance in Medicine*. 2014; 72(1):149–159. [PubMed: 24006229]
29. Dibb R, Qi Y, Liu C. Magnetic susceptibility anisotropy of myocardium imaged by cardiovascular magnetic resonance reflects the anisotropy of myocardial filament α -helix polypeptide bonds. *Journal of Cardiovascular Magnetic Resonance*. 2015; 17(1):60. [PubMed: 26177899]
30. Wang Y, Riederer SJ, Ehman RL. Respiratory motion of the heart: kinematics and the implications for the spatial resolution in coronary imaging. *Magn Reson Med*. 1995; 33(5):713–719. [PubMed: 7596276]
31. Wang Y, Rossman PJ, Grimm RC, Riederer SJ, Ehman RL. Navigator-echo-based real-time respiratory gating and triggering for reduction of respiration effects in three-dimensional coronary MR angiography. *Radiology*. 1996; 198(1):55–60. [PubMed: 8539406]

32. Dong J, Liu T, Chen F, Zhou D, Dimov A, Raj A, Cheng Q, Spincemaille P, Wang Y. Simultaneous Phase Unwrapping and Removal of Chemical Shift (SPURS) Using Graph Cuts: Application in Quantitative Susceptibility Mapping. *IEEE Transactions on Medical Imaging*. 2015; 34(2):531–540. [PubMed: 25312917]
33. Liu Z, Kee Y, Zhou D, Wang Y, Spincemaille P. Preconditioned total field inversion (TFI) method for quantitative susceptibility mapping. *Magn Reson Med*. 2016
34. Hoffman, R., Silberstein, LE., Heslop, H., Weitz, J. *Hematology: Basic Principles and Practice*. Saunders/Elsevier; 2013. p. 2520-2521.
35. Dickerson, RE., Geis, I. *Hemoglobin: Structure, Function, Evolution, and Pathology*. Benjamin/Cummings Publishing Company; 1983.
36. Sadava, DE., Hillis, DM., Heller, HC. *Life: The Science of Biology*. W. H. Freeman; 2011. p. 954
37. Dimov AV, Liu T, Spincemaille P, Ecanow JS, Tan H, Edelman RR, Wang Y. Joint estimation of chemical shift and quantitative susceptibility mapping (chemical QSM). *Magnetic Resonance in Medicine*. 2015; 73(6):2100–2110. [PubMed: 24947227]
38. Reeder SB, Pineda AR, Wen Z, Shimakawa A, Yu H, Brittain JH, Gold GE, Beaulieu CH, Pelc NJ. Iterative decomposition of water and fat with echo asymmetry and least-squares estimation (IDEAL): Application with fast spin-echo imaging. *Magnetic Resonance in Medicine*. 2005; 54(3):636–644. [PubMed: 16092103]
39. Reeder SB, Wen Z, Yu H, Pineda AR, Gold GE, Markl M, Pelc NJ. Multicoil Dixon chemical species separation with an iterative least-squares estimation method. *Magnetic Resonance in Medicine*. 2004; 51(1):35–45. [PubMed: 14705043]
40. Liu Z, Kee Y, Zhou D, Spincemaille P, Wang Y. Preconditioned QSM to Determine a Large Range of Susceptibility Over the Entire Field of View from Total Field. *Proc Int SocMagn Reson Med*. 2016; 24:0032.
41. Liu T, Khalidov I, de Rochefort L, Spincemaille P, Liu J, Tsiouris AJ, Wang Y. A novel background field removal method for MRI using projection onto dipole fields (PDF). *NMR in biomedicine*. 2011; 24(9):1129–1136. [PubMed: 21387445]
42. Pei M, Nguyen TD, Thimmappa ND, Salustri C, Dong F, Cooper MA, Li J, Prince MR, Wang Y. An Algorithm for Fast Mono-exponential Fitting Based on Auto-Regression on Linear Operations (ARLO) of Data. *Magnetic resonance in medicine : official journal of the Society of Magnetic Resonance in Medicine / Society of Magnetic Resonance in Medicine*. 2015; 73(2):843–850.
43. Zhou D, Zhang J, Spincemaille P, Wang Y. Susceptibility Underestimation in a High Susceptibility Phantom: Dependence on Imaging Resolution, Magnitude Contrast and Sample Orientation. *Proc Int SocMagn Reson Med*. 2016; 24:1550.
44. Sasse SA, Berry RB, Nguyen TK, Light RW, Kees Mahutte C. Arterial Blood Gas Changes During Breath-holding From Functional Residual Capacity. *Chest*. 1996; 110(4):958–964. [PubMed: 8874252]
45. Betgem RP, de Waard GA, Nijveldt R, Beek AM, Escaned J, van Royen N. Intramyocardial haemorrhage after acute myocardial infarction. *Nat Rev Cardiol*. 2015; 12(3):156–167. [PubMed: 25403783]
46. Hamirani YS, Wong A, Kramer CM, Salerno M. Effect of Microvascular Obstruction and Intramyocardial Hemorrhage by CMR on LV Remodeling and Outcomes After Myocardial Infarction: A Systematic Review and Meta-Analysis. *JACC: Cardiovascular Imaging*. 2014; 7(9): 940–952. [PubMed: 25212800]
47. Goldfarb JW, Hasan U, Zhao W, Han J. Magnetic resonance susceptibility weighted phase imaging for the assessment of reperfusion intramyocardial hemorrhage. *Magn Reson Med*. 2014; 71(3): 1210–1220. [PubMed: 23776036]
48. Chen W, Zhu W, Kovanlikaya I, Kovanlikaya A, Liu T, Wang S, Salustri C, Wang Y. Intracranial Calcifications and Hemorrhages: Characterization with Quantitative Susceptibility Mapping. *Radiology*. 2014; 270(2):496–505. [PubMed: 24126366]
49. Fassbender K, Balucani C, Walter S, Levine SR, Haass A, Grotta J. Streamlining of prehospital stroke management: the golden hour. *Lancet Neurol*. 2013; 12(6):585–596. [PubMed: 23684084]

50. Chen W, Gauthier SA, Gupta A, Comunale J, Liu T, Wang S, Pei M, Pitt D, Wang Y. Quantitative Susceptibility Mapping of Multiple Sclerosis Lesions at Various Ages. *Radiology*. 2014; 271(1): 183–192. [PubMed: 24475808]
51. Funk E, Thunberg P, Anderzen-Carlsson A. Patients' experiences in magnetic resonance imaging (MRI) and their experiences of breath holding techniques. *Journal of Advanced Nursing*. 2014; 70(8):1880–1890. [PubMed: 24456491]
52. Zhou D, Liu T, Spincemaille P, Wang Y. Background field removal by solving the Laplacian boundary value problem. *NMR in Biomedicine*. 2014; 27(3):312–319. [PubMed: 24395595]
53. Sun H, Wilman AH. Quantitative susceptibility mapping using single-shot echo-planar imaging. *Magnetic Resonance in Medicine*. 2015; 73(5):1932–1938. [PubMed: 24938830]
54. Deshmane A, Gulani V, Griswold MA, Seiberlich N. Parallel MR imaging. *Journal of Magnetic Resonance Imaging*. 2012; 36(1):55–72. [PubMed: 22696125]
55. Quick HH, Ladd ME, Hoevel M, Bosk S, Debatin JF, Laub G, Schroeder T. Real-time MRI of joint movement with trueFISP. *Journal of Magnetic Resonance Imaging*. 2002; 15(6):710–715. [PubMed: 12112522]
56. Uecker M, Lai P, Murphy MJ, Virtue P, Elad M, Pauly JM, Vasanawala SS, Lustig M. ESPIRiT— an eigenvalue approach to autocalibrating parallel MRI: Where SENSE meets GRAPPA. *Magnetic Resonance in Medicine*. 2014; 71(3):990–1001. [PubMed: 23649942]
57. Kaaouana T, de Rochefort L, Samaille T, Thiery N, Dufouil C, Delmaire C, Dormont D, Chupin M. 2D harmonic filtering of MR phase images in multicenter clinical setting: Toward a magnetic signature of cerebral microbleeds. *NeuroImage*. 2015; 104:287–300. [PubMed: 25149849]
58. Wei H, Zhang Y, Gibbs E, Chen N-K, Wang N, Liu C. Joint 2D and 3D phase processing for quantitative susceptibility mapping: application to 2D echo-planar imaging. *NMR in Biomedicine*. 2016; doi: 10.1002/nbm.3501

Figure 1.
Flow chart of cardiac QSM post-processing.

Figure 2.

Two representative high quality cardiac QSM examples, demonstrating differential susceptibility between the left and right sides of the heart. Magnitude images reformatted into long axis in the top row, short axis magnitude images in the middle row, and corresponding QSM in the bottom row. QSM demonstrated oxygenation differences throughout the basal (left), mid, and apical (right) chambers, in both examples.

Figure 3.

A representative cardiac QSM example with reasonable quality. Differential susceptibility between the left and right sides of the heart can be seen. Magnitude images reformatted into long axis in the top row, short axis magnitude images in the middle row, and corresponding QSM in the bottom row. Columns represent basal (left), mid, and apical (right) chambers.

Figure 4. Representative cardiac QSM example with poor quality. The susceptibility contrast is mostly degraded by the shadowing artifacts. The long axis magnitude image (top) showed that there were a few misregistered slices (red arrows), suggesting inconsistent breath holding positions.

Figure 5.

Comparison of $R2^*$ map, and QSM maps computed using PDF+MEDI and TFI algorithms. In this example, both QSM maps demonstrated much improved blood contrast between the right and left ventricles than the $R2^*$ map does. Between the two QSM maps, the result from TFI has better RV to LV contrast. The susceptibility difference between RV and LV blood was 327.4 ppb (corresponding to 77.0% SvO₂) with TFI, and 138.6 ppb (90.1% SvO₂, well above the normal range) with PDF+MEDI.