# MR-based R2* and quantitative susceptibility mapping (QSM) of liver iron overload: comparison with SQUID-based biomagnetic liver susceptometry

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**Target Audience:** Researchers and clinicians who are interested in the development and validation of QSM.

**Purpose:** Assessment of liver iron overload is essential for the longitudinal monitoring and treatment of patients with hereditary hemochromatosis and patients with transfusional hemosiderosis. Biopsy is often used to assess liver iron, however it is invasive, expensive, and suffers from high sampling variability[1]. Biomagnetic liver susceptometry (BLS) using a superconducting quantum interference device (SQUID) offers a noninvasive technique for the measurement of liver iron[2-4] that is based on a fundamental physical property of tissue (i.e. magnetic susceptibility). However, the lack of access to SQUID (only four systems available worldwide) has limited its widespread adoption in clinical practice. MRI is a widely available technology that is also sensitive to the presence of iron in the liver[5-7]. Recent works developing a confounder-corrected R2* technique[8] and a quantitative susceptibility mapping (QSM) technique[9] for measuring iron in the liver have been reported. However, these techniques have not yet been compared to SQUID. Thus, ***the purpose of this work*** was to investigate the relationship between confounder-corrected R2* and QSM-based BLS to SQUID-based BLS in patients with suspected liver iron overload.

**Methods:** Eleven patients were recruited for this study from a population undergoing cardiac MRI and SQUID-based BLS as part of routine monitoring for iron overload. Most of the patients receive regular chronic blood transfusions and chelation therapy. All patients gave informed written consent for this study. ***MRI R2* and QSM:*** MR imaging was performed on a 3T scanner (Philips Medical Systems, Best, The Netherlands) with a 28-channel torso array using a 3D six-echo, spoiled gradient-echo acquisition. Acquisition parameters included: $TE_1$ = 1.2 ms, $\Delta TE$ = 1.0 ms, TR = 7.7 ms, flip angle = 3°, acquired resolution = 1.6x2.2x8 $mm^3$, and matrix size = 256x144x32. The MR source images were processed using a complex-based chemical shift encoded reconstruction[10], yielding estimates of the R2* map and the $B_0$ field map. The $B_0$ field map was then processed using a QSM reconstruction developed for the abdomen[9] to estimate the susceptibility distribution. Both R2* and QSM measurements were made in the right lobe of the liver. The adjacent subcutaneous fat was used as the reference for the liver susceptibility estimate. ***SQUID Susceptometry:*** The SQUID-based BLS facility (Biomagnetic Technologies Inc., San Diego, USA) contains a sensor assembly with two symmetrical $2^{nd}$ order gradiometer sensors coupled to rf-SQUIDs aligned with superconducting magnetic field coils ($1^{st}$ order gradiometer, $B_{max}$=20mT), a water bellows coupling membrane as magnetic reference medium, and a workstation for process control, data acquisition, and analysis. The system was calibrated against an infinite water sphere making use of the magnetic air-water volume susceptibility difference of $\Delta\chi$ = 9.396 ppm. Pre-calculated magnetic flux integrals for liver and thorax tissue together with sonographically determined skin-liver distance and liver geometry allow real-time analysis of liver susceptibility[11].

**Results:** Figure 1 shows examples of estimated R2* and QSM-BLS maps for one patient without and one with liver iron overload. Figure 2 plots (left) liver R2* and (right) liver QSM estimates ($\Delta\chi_{QSM}$) versus susceptibility estimates from SQUID ($\Delta\chi_{SQUID}$). One of the eleven patients was excluded from data analysis due to extremely high iron overload (i.e. high R2*), which resulted in no measureable MR signal in the liver by the first echo time. The correlation between R2* and $\Delta\chi_{SQUID}$ was found as $R^2$ = 0.88. Linear regression analysis between $\Delta\chi_{QSM}$ and $\Delta\chi_{SQUID}$ yielded: slope = 0.63±0.09, y-intercept = -0.38±0.23 ppm, $R^2$ = 0.87.

**Discussion & Conclusion:** Both R2* and QSM-based BLS demonstrated strong correlation with SQUID-based BLS. The cause of the discrepancy in estimates between QSM and SQUID is unknown, but may be related to the MR imaging resolution[12]. Future work will be necessary to understand this difference. In conclusion, we have investigated the relationship between confounder-corrected R2* and QSM-based BLS to SQUID-based BLS. Strong correlation was found between both R2* and QSM-BLS with SQUID-BLS.

**References:** [1]Emond et al. Clin. Chem. 1999;45:340-6. [2]Brittenham et al. N Engl J Med 1982;307:1671–5. [3]Paulson et al. IEEE Trans Magnetics 1991;27:3249–52. [4]Marinelli et al. IEEE Trans Appl Superconductivity 2006;16:1513-57. [5]St. Pierre et al. NMR Biomed 2004;17:446-58. [6]Wood et al. Blood 2005;106:1460-65. [7]Hankins et al. Blood 2009;113:4853-55. [8]Hernando et al. MRM 2013;70:1319-31. [9]Sharma et al. MRM DOI:10.1002/mrm.25448. [10]Hernando et al. MRM 2010;63:79-90. [11]Fischer et al. Magn. Med. II 2007;529-549. [12]Zhou et al. Workshop on Phase Contrast and QSM 2014; p.94.

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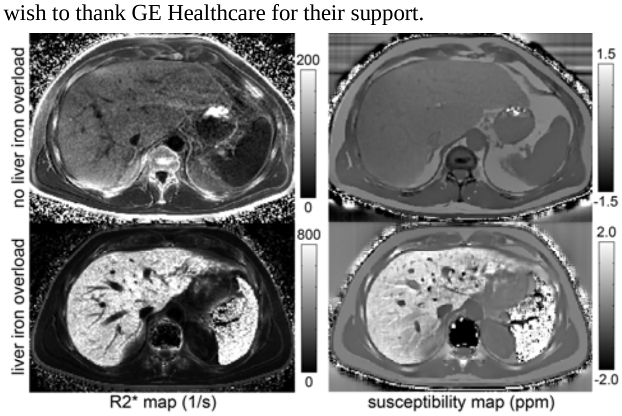


**Figure 1:** R2* maps (left) and QSM-BLS maps (right) for a patient without liver iron overload (top) and a patient with liver iron overload (bottom). Both R2* maps and QSM-BLS maps demonstrate sensitivity to the presence of liver iron.

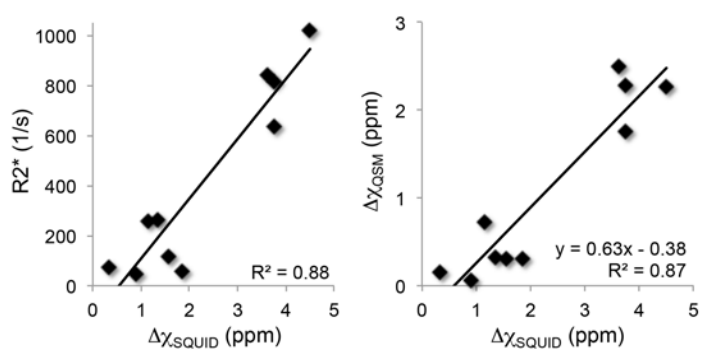


**Figure 2:** Scatterplots showing (left) R2* versus susceptibility from SQUID ($\Delta\chi_{SQUID}$), and (right) susceptibility from QSM ($\Delta\chi_{QSM}$) versus $\Delta\chi_{SQUID}$. Both R2* and $\Delta\chi_{QSM}$ demonstrate strong correlation with $\Delta\chi_{SQUID}$.