

A Room-Temperature Susceptometer to Measure Liver Iron: Susceptometer Design and Performance

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Abstract

We describe a biomagnetic susceptometer using room-temperature magnetic sensors instead of Superconducting QUantum Interference Devices (SQUIDs). By oscillating the magnetic field, canceling the applied-field signal, and modulating the sensor-patient distance, the room-temperature system resolves magnetic-susceptibility signals roughly 10^8 times weaker than the applied magnetic field. The noise and drift of the susceptometer itself are well below other errors in the liver iron measurement, such as inconsistencies in the water bag, errors in patient positioning, and the susceptibility responses of the lung, bowel gas and tissues overlying the liver. Unlike earlier prototypes, the susceptometer is designed to sample approximately the same tissue volume as existing SQUID systems, so that errors due to the lung are anticipated to be no greater than in previous liver susceptometry. We have obtained encouraging results in our first measurements on human subjects, comparing the room-temperature susceptometer to an existing SQUID system.

1 Introduction

The work of Brittenham [1], Fischer [2], Farrell [1] and others has shown that biomagnetic susceptometry can measure liver iron with greater accuracy than any other noninvasive technique. However, existing biomagnetic susceptometers, using Superconducting QUantum Interference Devices (SQUIDs), require liquid helium, which is expensive and difficult to obtain in many parts of the world. In an effort to make liver iron measurements less expensive and more widely available, we are developing a biomagnetic susceptometer using room-temperature sensors.

In biomagnetic susceptometry, we apply a magnetic field to the patient's body, and measure the slight change in field produced by the magnetization of body tissues. Using a water bag to fill the space between the sensor system and the patient's body, we eliminate the background signal due to the difference in susceptibility between the body tissues and the surrounding air. The remaining signal is mainly due to the difference in susceptibility between the liver and the surrounding tissues [1,2]. This susceptibility difference is proportional to the iron concentration in the liver.

The change in magnetic field due to a liver iron concentration of $100 \mu\text{g}$ per gram of wet tissue is roughly 10^8 times weaker than the magnetic field that we apply to the patient's body. Measuring a response so much weaker than the applied field is one of the main technical challenges in liver susceptometry. This paper explains how we overcome these problems, describes the resulting noise performance of the susceptometer, and presents our first results on human subjects.

2 Susceptometer Design

SQUID susceptometers exploit several advantages unique to cryogenic systems, including the low noise of SQUID sensors, the tremendous stability of superconducting magnets, the ability of SQUIDs to ignore a large, constant background field and, most importantly, the freezing-out of thermal expansion at liquid-helium temperatures, which makes possible a very stable geometrical relationship between the superconducting magnet and the SQUID sensor. A room-temperature instrument must contend with Johnson noise in the magnetic sensors, fluctuations in the applied field, the limited dynamic range of the electronics, and temperature drifts that distort the geometry of the applied-field coils in relation to the magnetic sensors.

We use three main strategies to overcome these problems. First, we use an ac magnetic measurement, applying the magnetic field and detecting the sample response at a frequency of 570 Hz. At this frequency, our copper-wire sensing coil provides a noise level below $10^{-12} \text{ T/Hz}^{1/2}$. This, in turn, allows us to use a modest applied field, about $6 \times 10^{-4} \text{ T}$ (rms), minimizing ohmic heating and temperature drifts in the applied-field coils. Second, we design the sensor coil to cancel the signal due to the applied field, minimizing noise due to fluctuations of the current in the applied-field coils and avoiding the need to detect the susceptibility response on top of the full magnitude of the applied field. Third, we move the sensor unit, consisting of the applied-field coil and sensor coil, toward and away from the patient at a frequency of 1 Hz. This sensor motion modulates the magnetic susceptibility response, distinguishing

it from slow drifts in the ac magnetic signal that arise from thermal expansion and contraction in the applied-field coils.

Our sensor unit comprises a copper-wire sensing coil and applied-field coil, wound co-axially on a cylindrical fiberglass coil form. The applied-field coil has two opposed loops, forming a first-order gradiometer. The sensing coil is a second-order gradiometer with its center loop midway between the loops of the first-order field coil. This arrangement cancels the signal due to the applied field. The applied-field coil has a baseline of 9 cm, the sensing coil has a baseline of 11 cm, and the lower-most loop of the sensing coil lies 1 cm below the lower loop of the applied-field coil. All of the coils have mean diameters of 7 cm.

This sensor geometry, unlike those in our previous BioMag papers [3,4], approximates the larger of two coil sets in the SQUID system of Prof. Gary Brittenham at Columbia University [1]. The coil geometry is intended to sample approximately the same region of the body as the SQUID, so that we can compare the performance of the two systems without complications arising from possible differences in the interfering signals due to the lung and the tissue overlying the liver.

Our sensing coil has a resistance of approximately 150 ohms. With its Johnson noise of $1.4 \text{ nV/Hz}^{1/2}$ at 300K, plus comparable noise from the preamplifier, the theoretical noise in the 570-Hz magnetic measurement is about $0.25 \text{ pT/Hz}^{1/2}$ in the 550-turn lower coil of the gradiometer.



Fig. 1. Room-temperature biosusceptometer.

Fig. 1 shows the overall structure of the susceptometer. The instrument includes a motor and crank arm (top), connected by a 1.3-m fiberglass rod to a sensor unit that slides up and down in a plastic track (bottom). The entire assembly can be moved up and down to adjust the height of the sensor system above the patient.

3 Susceptometer Performance

We evaluate the noise in our sensor system measuring the fluctuations in the amplitude of the

570-Hz ac signal. With no ac field and no 1-Hz motion, the root-mean-square (rms) fluctuation is typically about 0.1 pT, or 0.8 nV at the output of the sensing coil, in a 1/8-Hz bandwidth centered at 1 Hz. This value is consistent with the Johnson noise and preamplifier noise described above. With the ac field, the noise typically increases by about 20%, indicating the effectiveness of field cancellation in minimizing noise due to applied-field fluctuations.

To measure the magnetic susceptibility response of a specimen, we record the modulations of the 570-Hz signal amplitude at multiples of the 1-Hz motion frequency. To relate this susceptometer response to its equivalent liver-iron concentration, we placed a water-filled cylindrical polyethylene bottle (length 30 cm, inner diameter 20 cm) under the susceptometer, with its inner circumference approximately 22.5 mm below the bottom enclosure of the susceptometer. This distance is in the upper range of the liver-surface distance for patients undergoing liver-iron measurements. We then emptied the water bottle, and measured the resulting change of the 1-Hz peak in the ac signal amplitude. Using the relative susceptibilities of water (8.8×10^{-5} SI units) and liver iron (1.6×10^{-5} SI units for 1000 micrograms per gram of wet tissue), we calculated the change in the 1-Hz peak amplitude corresponding to a given change in liver-iron concentration.

To assess the stability of the susceptometer, we measured the variation in the 1-Hz peak amplitude over time, with a specimen comprising a water bag and a water-filled phantom. Fig. 2 shows the results. Each data point represents an average over 10 successive data collection intervals lasting 8 seconds each. The susceptometer output is expressed in terms of liver iron concentration, based on the calibration described above. The short-term susceptometer noise, represented by the standard error of the mean for 10 successive 8-second measurements, is approximately $14 \mu\text{g/g}$ of wet tissue, while the background drift over 50 minutes is roughly $70 \mu\text{g/g}$.

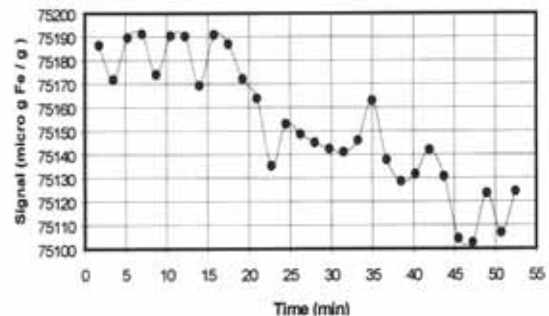


Fig. 2. Stability of susceptometer output over time.

This susceptometer noise is small compared with the overall error, roughly $200 \mu\text{g/g}$ of wet tissue, that is typically attained in liver iron measurements with SQUIDS [1,2]. This error, much larger than

the noise of the SQUID itself, is believed to arise from factors such as inconsistencies in the water bag, errors in positioning the patient, and the susceptibility responses of the lung, bowel gas and tissues overlying the liver. In principle, these errors should be approximately the same for the room-temperature susceptometer as for existing SQUIDS, since our sensing and applied-field coils are designed to sample approximately the same tissue volume as those of the existing SQUIDS. Thus, for the room-temperature susceptometer as for the SQUID systems, we believe that the noise and drift in the susceptometer itself are low enough that they will not significantly affect the overall precision of the liver iron measurement.

4 Human Subjects: First Results

We recently made our first liver-iron measurements on human subjects, in the laboratory of Dr. Gary Brittenham at the Columbia Presbyterian Hospital, New York, NY, USA. The 10 subjects, 1 normal control and 9 patients with thalassemia major and thalassemia intermedia, ranged from 13 to 51 years in age, 157 to 184 cm in height and 11 to 20 mm in liver-surface distance. On each subject, 5-7 measurements were made with Dr. Brittenham's SQUID and 2-4 with our room-temperature susceptometer, repositioning the patient and/or refilling the water bag for each measurement. Each measurement with the room-temperature system was an average of 5-10 8-second data records.

As a preliminary analysis, we compared the room-temperature and SQUID results in the following way: We assumed that the liver iron concentration was given by

$$C[Fe] = S_{RT} a \exp(-b(z_{LS} + z_{SS})) + c, \quad (1)$$

where S_{RT} is the difference in signal between the patient and a water phantom, as measured by the room-temperature susceptometer, z_{LS} is the depth of the liver below the skin, as measured using ultrasound, and z_{SS} is the distance from the body surface to the sensor coils, as measured using a locator loop. We used $b = 0.076 \text{ mm}^{-1}$, as obtained by Dr. Brittenham using the SQUID. We estimated a and c from a least-squares linear regression of the SQUID data as a function of the room-temperature susceptometer signal. In estimating these constants, we omitted one anomalous data point that differed from the SQUID result by more than 7 times the rms deviation of the other measurements from their corresponding SQUID values.

Fig. 3 compares the liver iron value from the room-temperature susceptometer (closed symbols) with that from the SQUID instrument (open symbols). The small diamonds and larger squares represent, respectively, the individual measurements and average values for each patient. Using the averages

for each patient, the rms difference between the room-temperature and SQUID results is approximately $630 \mu\text{g/g}$ if we include the anomalous result, and $260 \mu\text{g/g}$ if we exclude it.

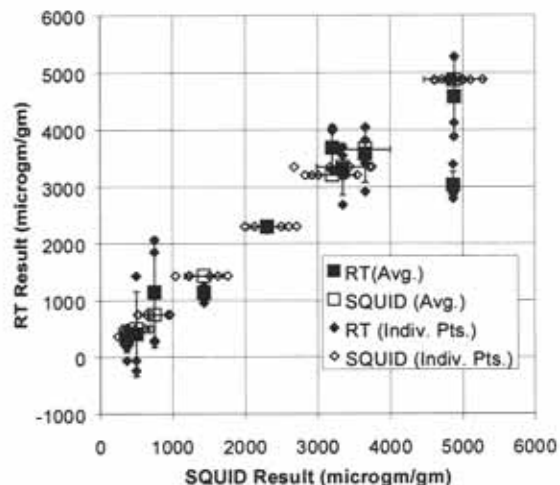


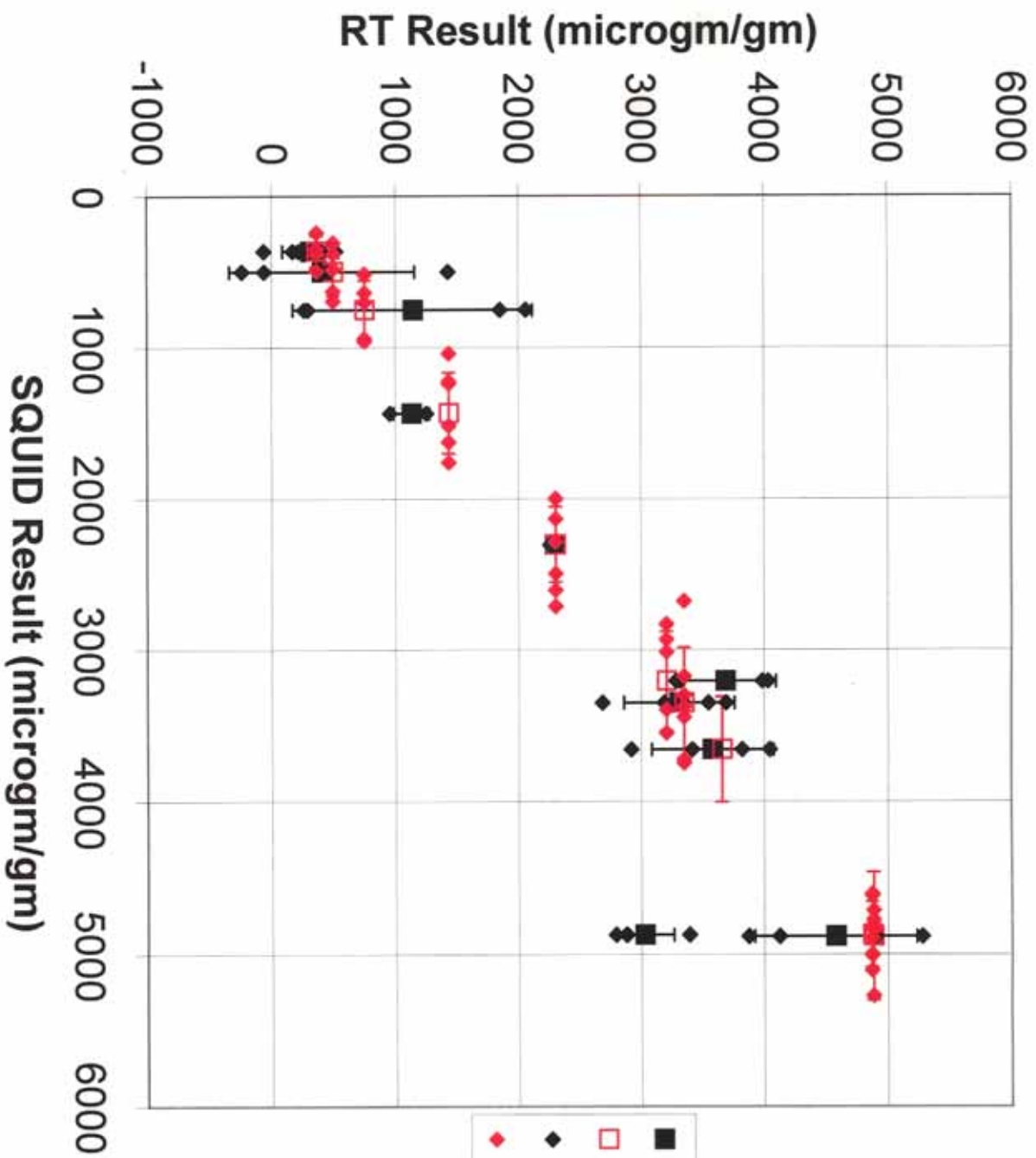
Fig. 4. Liver iron measurements with SQUID and room-temperature susceptometers.

More data are clearly needed to determine the true performance of the room-temperature system. These first experiments did indicate three areas for improvement. First, our locator loop provided much poorer resolution than that of the existing SQUID system, in the lateral positioning of the patient. Second, our water bag was less pliable than that of the SQUID, and our results varied considerably with the amount of water in the bag, suggesting that the water bag was not reliably conforming to the patient's body. Third, a smaller sense-coil diameter may be needed to reduce errors on small patients. With improvements in these areas, we hope to achieve higher accuracy in future liver iron measurements.

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5 References

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- RT (Avg.)
- SQUID (Avg.)
- ◆ RT (Indiv. Pts.)
- ◆ SQUID (Indiv. Pts.)