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An Ultrasensitive Magnetoelectric Sensor System For the Quantitative Detection of Liver Iron

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Abstract

Ultrasensitive magnetoelectric (ME) sensors have been developed using magnetostrictive/piezoelectric laminate heterostructures. This paper discusses a highly interdisciplinary design of a room temperature biomagnetic liver susceptometry system (BLS) based on the ME sensors. The ME-sensor based BLS maintains the ultrahigh sensitivity to detect the weak AC biomagnetic signals and introduces a low equivalent magnetic noise. The results reveal a “turning point” and successfully indicate the output signals to be linearly responsive to iron concentrations from normal iron level ($0.05 \text{ mgFe/g liver phantom}$) to $5 \text{ mgFe/g liver phantom}$ iron overload level (100X overdose). Further, the introduction of the water-bag technique shows the promise on the automatic deduction of the background (tissue) signal, enabling an even higher sensitivity and better signal-to-noise (SNR). With these improvements, it becomes feasible to get improved characterization flexibility and the field distribution mapping potential via signal processing from the correlations of multiple sensors in the system. Considering the wide presence of biomagnetic signals in human organs, the potential impact of such biomagnetic devices on medicine and health care could be enormous and far-reaching.

Keywords

Magnetoelectric sensors; Composite sensors; Piezoelectricity; Magnetostriction; Liver iron quantification; Biomedical application

I. Introduction

Over the past two decades, remarkable progress has been made on the details of the iron absorption mechanism [1–3]. It is concluded that absorbing and accumulating excessive iron in body organs (iron overload) can damage or even destroy an organ, such as the liver [4–7]. The concentration and total amount of iron in different tissues are critical parameters that determine the clinical outcome in all forms of iron overload that can be caused by hereditary hemochromatosis, thalassemia intermedia, iron loading anemia, thalassemia major, sickle cell disease, aplastic anemia, and other pathological disorders or genetic mutations [8–17]. According to the Centers for Disease Control and Prevention (CDC), even hereditary hemochromatosis alone affects as many as 1 in every 200 people in the U.S. Therefore, it is critical to develop effective methods for early and quantitative iron overload detection [18].

It has been established that liver iron concentration (LIC) is a direct indication of body iron level [19–21]. While the liver biopsy method remains the “golden standard” for the quantification of the LIC, due to its invasiveness, studies conducted in the past have proven that biomagnetic liver susceptometry (BLS) is effective in quantifying LIC at levels from normal level ($<0.05 \text{ mg}_{\text{Fe}}/\text{g}_{\text{liver}}$) to overloads [19–24]. However, as the conventional BLS requires the dynamic range of the superconducting quantum interference devices (SQUID) to measure the susceptibility of the liver tissue, which brings high cost ($> \$1$ million) and complexity to operate (with liquid cryogen), the general clinical adoption of the SQUID BLS have been greatly restricted.

Recently, a low-cost, compact-size, room temperature operated and ME sensor based BLS has been demonstrated, making use of the unique opportunity afforded by the advancements in multiferroic composites with giant magnetoelectric (ME) effect [25]. The discussion here focuses on the investigations of the liver-tissue-mimicking samples of assorted iron concentrations (known as liver phantoms). The results not only indicated the output signals to be linearly responsive to iron concentrations from normal iron level ($0.05 \text{ mg}_{\text{Fe}}/\text{g}_{\text{liver phantom}}$) to $5 \text{ mg}_{\text{Fe}}/\text{g}_{\text{liver phantom}}$ iron overload level (100X overdose) but revealed a “turning point”, which marks one specific iron concentration that effectively neutralizes the magnetic responses from the water-like tissue. Further, inspired by the turning-point phenomenon, a water-bag technique is introduced to automatically deduct the signals due to the water in the phantom, or, in other words, the background signals, so that the signals from iron in the phantom will stand out and get highlighted. This water-bag technique enables an even better sensitivity and signal-to-noise ratio (SNR) for the system and, therefore, shows promise to allow the correlation analysis of multiple sensors in the system, and ultimately towards improved characterization flexibility and the field distribution mapping potential.

Considering the wide presence of biomagnetic signals in human organs, the potential impact of such biomagnetic devices on medicine and health care could be enormous and far-reaching.

II. System Design

A. The Magnetoelectric Sensor

Recent advances in the multiferroic materials, especially, in the magnetoelectric (ME) composites, create a unique opportunity for developing piezoelectric sensors for magnetic field sensing. In particular, the laminate composites consisting of ferromagnetic phases (e.g. Terfenol-D) and ferroelectric phases (e.g. $\text{Pb}(\text{ZrTi})\text{O}_3$) have shown strong electromagnetic coupling effect between the two phases, as in Fig. 1 (top) [26], which derive large ME coupling coefficients at room temperature and have potential to be used as high-sensitivity magnetic sensors [27–38]. The direct elastic coupling between the piezoelectric layer and magnetostrictive layer transmits the strain to the piezo-layer, which in turn produces an electric output through the piezoelectric effect, as schematically shown in Fig. 1 (bottom).

B. The Prototype System

The compact device footprint ($< 300 \text{ cm}^2$) makes it easily be integrated into various device configurations such as gradiometers in different forms, which will be exploited for and developed into the BLS.

Fig. 2 shows the schematic illustration of the sensing unit (top) and the related instrumentations (bottom). From these schematics, it is obvious that our design has a compacted size and simpler configuration, which significantly enhance its portability and adaptability for routine clinic application.

III. Analysis, results and discussion

Piezo-sensors are well known for their high sensitivity. By employing ME composite principle, as illustrated in Fig. 1. (Bottom), a high-magnetic-field sensitivity can also be realized. The sensitivity of the ME sensor system in Fig. 1. (Top) can be expressed as [39, 40],

$$\frac{V_{out}}{\Delta H_a} \approx \frac{\Delta q_p}{C_f \Delta H_a} = \frac{d_p A_p}{C_f s_p^E (1 + \frac{s_m^H t_p}{s_p^E t_m})} \frac{\Delta S}{\Delta H_a} \quad (1)$$

where S/H_a is the piezomagnetic coefficient in the magnetostrictive layer, d_p is the piezocoefficient, A_p is the total electrode area of the piezolayer, t_p , t_m , s_p^E and s_m^H are the thicknesses, the compliances of the piezolayer and magnetic layer, respectively, and q_p is the charge generated in the piezolayer [39, 40].

Fig. 3 shows that, from investigations on liver-tissue-mimicking samples of assorted iron concentrations (known as liver phantoms), the output signals of the ME sensor based BLS to be linearly responsive to iron concentrations from normal ($0.05 \text{ mg Fe/g liver phantom}$) to $5 \text{ mg Fe/g liver phantom}$ iron overload level (100X overdose).

Furthermore, a turning point is found at $4 \text{ mg Fe/g liver phantom}$. This is because at this particular iron concentration, the paramagnetic contribution, or the paramagnetic response, due to iron is equal to that of diamagnetic water, resulting an effective magnetic susceptibility of zero.

The existence of such turning point indicates that it is the difference, between the diamagnetic signals from water and the paramagnetic ones from iron, the net signal, $|V_{\text{phantom water}} - V_{\text{phantom iron}}|$, that is being measured. Since our main interest lies on the signals from iron, the signals due to water in the phantom are considered “background signals”. Therefore, in order to eliminate the background signals and highlight the iron signals, a water bag is introduced right above the phantom for the horizontal scan, as in Fig. 4.

As shown in Fig. 4, the introduction of a water bag not only keeps a constant the interface between the sensing unit and the liver phantom, but, more importantly, it also has water signal automatically deducted. This is because, in this case, the net signal becomes $|V_{\text{water bag}} - (V_{\text{phantom water}} - V_{\text{phantom iron}})|$, that is, the signals from iron only, $|V_{\text{phantom iron}}|$, since $V_{\text{water bag}} = V_{\text{phantom water}}$. Therefore, as a result, only the signals from iron get measured and heightened, which is to our interest.

Investigations on the water phantoms, which contain no iron but only water, confirmed the analysis above. As shown in Fig. 5, almost no signal was found when the measurements were performed with the water bag, while a strong water signal appeared when without it. This water-bag technique enables an even better sensitivity and signal-to-noise ratio (SNR) for the system and, therefore, shows promise to allow the correlation analysis of multiple sensors in the system, and ultimately towards improved characterization flexibility and the field distribution mapping potential.

IV. Conclusion

In summary, the LIC level is of extreme importance in determining one’s overall body iron status. We successfully developed an ME-sensor-based BLS and demonstrated that its sensitivity and dynamic range for assessing LIC were comparable to those of the SQUID-based ones. A water-bag technique is introduced and enables an even better sensitivity and signal-to-noise ratio (SNR) due to the automatic deduction of the background signals.

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Fig. 1. (Top) Configuration of ME laminates. (Bottom) The schematic illustration of the operation principle for the ME sensors.

Fig. 2.
 (Top) The schematic illustration of the sensing unit. (Bottom) The Related instrumentations of ME-Sensor-Based Susceptometry.

Fig. 3.
The output signals of the ME sensor based BLS.

Fig. 4.
The schematic illustration for the application of a water bag.

Fig. 5.
The output signals for the investigations on water phantoms with and without the water bag.