Noninvasive Deep-Tissue Temperature Monitoring Based on Magnetic Mediated Thermoacoustics

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ISSN 2972-3418 **DOI:** 10.58567/bab01010005

Received 15 November, 2022; **Accepted** 12 December, 2022; **Available online** 26 December, 2022

Abstract Noninvasive acquisition of deep tissue temperature has important applications in home health monitoring, hyperthermia safety control, and other domains. In this work, we present here a novel magnetically mediated thermoacoustic temperature measurement method. Utilizing coil to stimulate amplitude modulated magnetic field and ultrasound transducer to receive the generated thermoacoustic wave from the inserted magnetic nanoparticles. Benefiting from the high sensitivity of thermoacoustic emission from nanoparticles and the deep penetration capability of both magnetic field and ultrasound propagation, the proposed thermoacoustic temperature measurement system enables a high measurement accuracy of 0.5 degrees Celsius in real time. This work potentially facilitates further development of closed loop magnetic hyperthermia for practical clinical applications.

Keywords: Thermoacoustic; Magnetically mediated thermoacoustic; Temperature sensing

1. Introduction

Real time noninvasive temperature measurement with relatively deeper penetration has been long pursued with limited success. The huge demand for such a device is revealed by routine temperature measurement and other medical applications in clinics and hospitals. With the aim of noninvasive measurement, penetrable solutions such as waves should be employed to establish the information connection between the biological tissue and the probe, either directly or indirectly.

Various waves have been utilized, including electromagnetic waves (e.g., light wave, microwave) and mechanical wave (e.g., acoustic wave), and even thermal waves as well. Being portable and low cost, diagnostic ultrasound-based methods can penetrate deep into the human body and provide real time temperature information. However, the accuracy of this method suffers due to its weak sensitivity to temperature (Pouch et al. 2010). Magnetic resonance thermometry is currently the golden standard in monitoring temperature *in-vivo* owing to its excellent accuracy and superior spatial resolution. Unfortunately, it is only suitable for scenarios where the temperature variation is relatively slow, and it is hindered by its high cost and large size (Zhang et al. 2017). Infrared thermography yields a high temperature measurement accuracy better than 0.1 degrees Celsius in real time, but it can only sense the temperature at the surface of an object (< 0.5mm). Conventional pure optical methods are sensitive to tissue physiological parameters including temperature, and thus are potential for its monitoring. However, the strong scattering of light within tissue precludes it from achieving high resolution monitoring of temperature at depths, for instance, in the carotid or pulmonary artery (Guo et al. 2019). In the recent several years, multiwave based thermal sensing techniques such as photoacoustics have been proposed and widely studied (Liu et al. 2019). Pramanik et. al (2020) proposed to use the photoacoustic method to measure the deep tissue temperature and verified it in an *ex vivo* tissue phantom. Benefiting from the high efficiency of photoacoustic generation and high sensitivity of temperature dependence (i.e., the Grueneisen parameter changes significantly with temperature), 0.15 degrees Celsius measurement accuracy and 2 s temporal resolution was obtained. Hereafter, Yao et al. (2013) proposed to measure absolute core temperature by taking ratiometric measurements at two adjacent temperatures. The temperature dependences of the Grüneisen parameter and the speed of sound are measured independently, and the intersection of the two dependence curves gives the value of absolute temperature.

In this work, the feasibility of deep tissue temperature measurement is explored in its twined technique—magnetically mediated thermoacoustics. A magnetic coil is employed to generate an amplitude modulated magnetic field and magnetic nanoparticles are utilized as the biomarkers to generate magnetically mediated thermoacoustic wave accordingly. Similar to in photoacoustics, temperature elevation would give rise to the increase of thermoacoustic pressure magnitude, facilitating the magnetically mediated thermoacoustic method to be employed for deep tissue temperature measurement.

The rest of this manuscript is organized as follows: In section 2, the theory of the magnetically mediated thermoacoustic temperature measurement and two major detection modes are briefly introduced. Afterward, systematic designs for the thermoacoustic temperature measurement and magnetic nanoparticle preparation are provided in Section 3. Section 4 illustrates the experimental demonstrations for thermoacoustic temperature monitoring and results analysis. Lastly, conclusions and prospects are drawn in Section 5.

2. Methods

In the magnetically mediated thermoacoustic method (Feng et al. 2013), as shown in Fig. 1, radio frequency field is generated by the current flowing in a magnetic resonance coil to excite the magnetic nanoparticle. The transient temperature of aggregated nanoparticles would increase following the modulation of magnetic field, which is caused by a combination of the hysteresis effect, the Brownian relaxation, and the Ne´el relaxation.

At a localized position, assuming magnetic field generated by the coil is expressed as $H(t)$ with an amplitude of H_0, we can obtain the averaged volumetric power deposition $\tilde{U}$, as

$$\tilde{U} = \frac{\mu_0}{2} H_0{}^2 \chi_0 \frac{\Omega^2 \tau}{1+\Omega^2 \tau^2}, \tag{1}$$

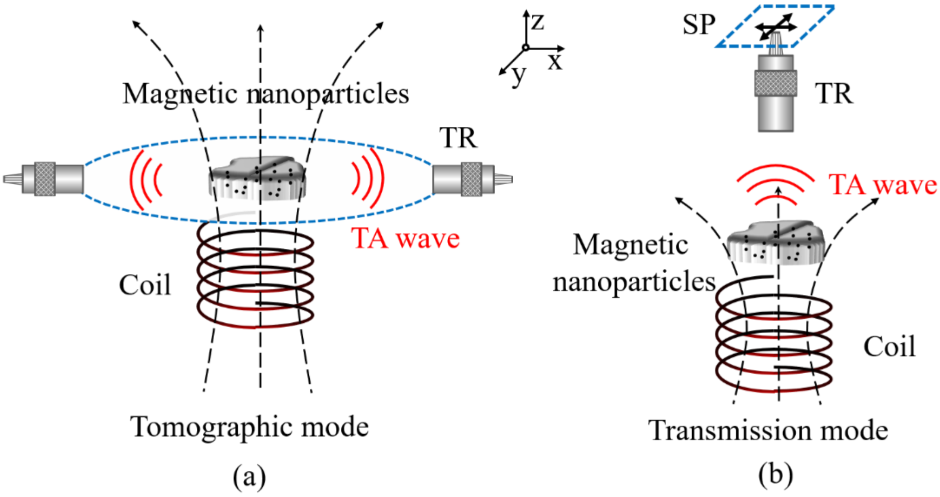

Figure 1. Two typical mode of magnetically mediated thermoacoustic detection: (a) tomographic mode; (b) transmission mode. Transducer: TR, thermoacoustic: TA, scanning plane: SP.

where Ω is the modulation frequency of short-time quasi single frequency magnetic pulse, τ is the effective relaxation time of the magnetic nanoparticles. With such energy absorption, temperature of the surrounding medium will be lifted up, which can be characterized by the Penns bioheat transfer equation .

$$\rho c_m \frac{\partial}{\partial t} T(t) = \nabla \cdot k \nabla T(t) + U(t) + c_b w(T_b - T(t)), \tag{2}$$

where ρ, c_m, and k are localized mass density, specific heat, and thermal conductivity of the surrounding medium; c_b and T_b are the specific heat and temperature of the external heat source (e.g. blood vessel). Under thermal confinement condition, the surrounding fluid medium will be heated according, and experience thermodynamic expansion. Subsequently, such vibrated energy will be emitted out in the form of ultrasonic wave. It is worth noting that the source of magnetically mediated thermoacoustic wave is the surrounding fluid medium, instead of the magnetic nanoparticles themselves (Liu et al. 2020). The initial thermoacoustic pressure can be derived as:

$$p = \phi \cdot U \cdot \Gamma(T), \tag{3}$$

where ϕ is the scaling coefficient that related to the amplitude and pulse width of the tone burst envelop,

$\Gamma(T)$ is the Grueneisen parameter which depends on the thermal coefficient of volume expansion β, acoustic speed c, specific heat capacity C_p in the ferrofluid and can be expressed as $\Gamma(T) = \frac{\beta c^2}{C_p}$. As the only term that is temperature dependent, the Grueneisen parameter $\Gamma(T)$ is linearly proportional to temperature in the range from 10 to 55 degrees Celsius (Liu et al. 2018) and therefore can be simply modelled as $\Gamma(T) = AT + B$. Substitute it into (4), one can get:

$$T = \frac{p}{p_0}(\frac{A}{B} + T_0) - \frac{A}{B}, \tag{4}$$

in which p_0 is the thermoacoustic signal amplitude at the baseline-temperature T_0, A and B are material dependent constants. Therefore, after pre-calibration (Liu et al. 2018), temperature measurement can be performed using (4) with the measured thermoacoustic amplitude. Fig. 1 depicts two different working modes of the proposed magnetically mediated thermoacoustic temperature measurement system. The tomographic mode employs the typical thermoacoustic tomography assembly in which the magnetic coil is placed in a vertical manner and the ultrasound transducer is scanned in a circular manner in the horizontal plane. The transmission mode works in a coaxial way and volumetric imaging is obtained by performing sectoral scanning in a rectangle area (Liu et al. 2017).

3. Results

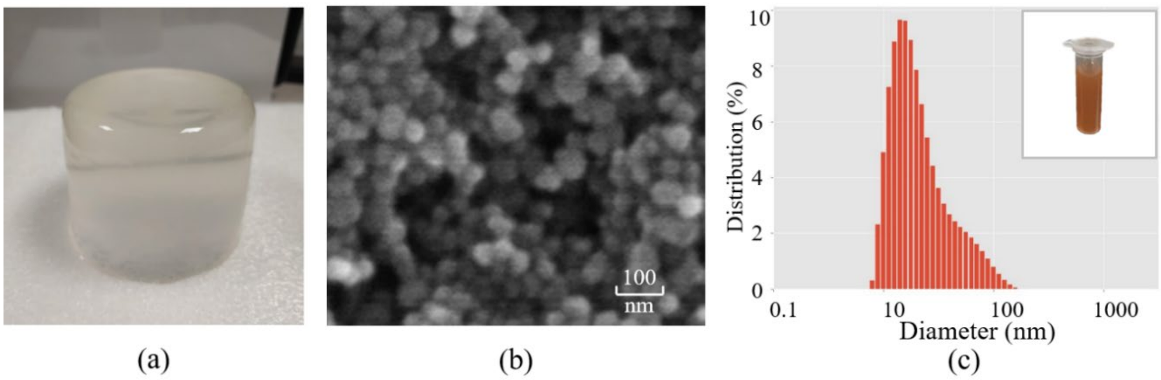

Figure 2. (a) Photograph of the prepared gelatin phantom, in which a magnetic nanoparticles tube is inserted. (b) Transmission electron microscopic image of the magnetic nanoparticles. (c) Size distribution of the magnetic nanoparticles.

Before demonstrating on temperature measurement capability of the proposed magnetically mediated thermoacoustic system, a home-made gelatin phantom was prepared for stable temperature control and thereby temperature monitoring. In this study, we used water soluble superparamagnetic nanoparticles EMG 304 (Ferrotec, NH, USA) as the magnetic ferrofluid. The EMG 304 has an average particle size of 10–15 nm in diameter [Fig. 2(b) and Fig. 2(c)] with a specific saturation magnetization being 153.8 emu/g. During temperature measurement and subsequent hyperthermia demonstration, such nanoparticles are diluted to a concentration of 50 mg/ml and injected into a nonmagnetic plastic tube with an inner diameter of 4mm.

As illustrated in Fig. 3, the magnetic nanoparticle tube is embedded into the turbid gelatin phantom with a depth of 2.0 cm to form the biological phantom to demonstrate the deep penetrability of the proposed thermoacoustic system. Environmental temperature variation in the process of calibration and measurement is realized by external water heating and natural cooling (heat diffusion from external hot water to the gelatin phantom). A fiber-optical thermometer (FOT-M, Fiso) with a small sensor head in the scale of sub-millimeter is inserted into the phantom tube to monitor the actual temperature of magnetic nanoparticle tube for calibration. This thermometer features complete immunity to electromagnetic interference (EMI) and a high accuracy of ± 0.3 degrees in a wide temperature range (10 ~ 85 degrees Celsius). In the process of hot-water cooling, the temperature is recorded by the thermometer and the thermoacoustic method, simultaneously.

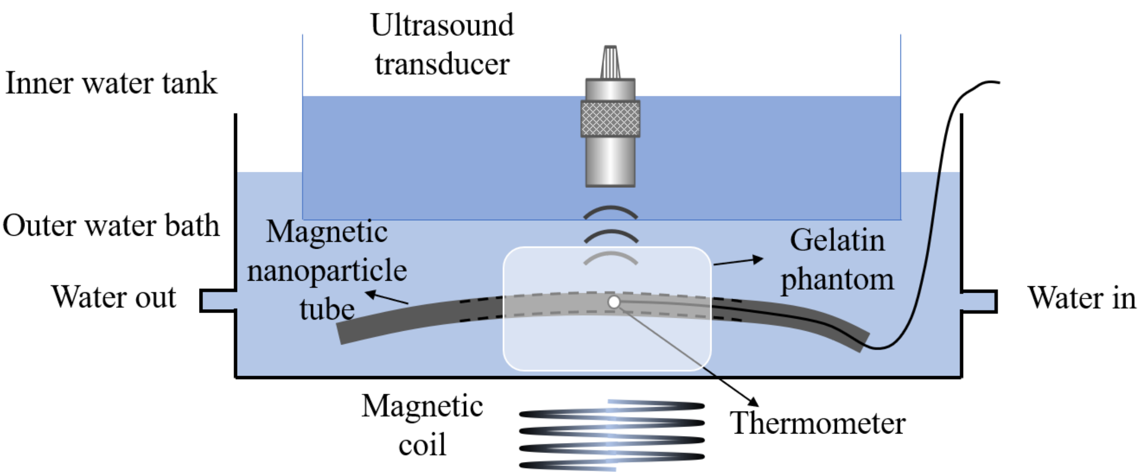

Figure 3. Experimental setup of the magnetically mediated thermoacoustic temperature measurement.

The results of temperature measurement are shown in Fig. 4. Fig. 4(a) illustrates the tendency of temperature variation as hot water is gradually pumped into the water bath. As expected, the temperature increases rapidly at the early stage and gradually saturated. This is consistence with the fact that the heat diffusion decreases as the temperature difference between the external hot source and the gelatin phantom. It is noted that at about the 60^{th} measurement point, a step change of temperature (of about 0.4 degrees) is observed, which may be caused by the instant movement of the whole gelatin phantom. Utilizing a more stable heating solution (such as environmental heating or heating pad) instead of the hot water pumping may avoid this temperature jumping.

Fig. 4(b) illustrates the relationship between the thermoacoustically measured temperature and the thermometer measured temperature. The readout of the thermometer constitutes the horizontal axis, while the amplitude in the axial axis represents the thermoacoustically measured temperature. Two thermoacoustic waveforms captured by ultrasound transducer respectively at the start and the end of temperature measurement are depicted in the insets, where a 40% increase of thermoacoustic signal amplitude occurs for a 6 degrees elevation in temperature, which is consistent with the thermal property of Grueneisen parameter in previous literature (Pramanik et al. 2009). As can be observed, the thermoacoustically measured temperature follows tightly with the thermocouple readings with an average error of about 0.4 degrees and a maximal error of about

0.9 degrees. Considering the extra comparison error that is additionally introduced by the fiber-optical temperature sensor, an actual accuracy of better than ± 0.5 degrees should be obtained in the current system.

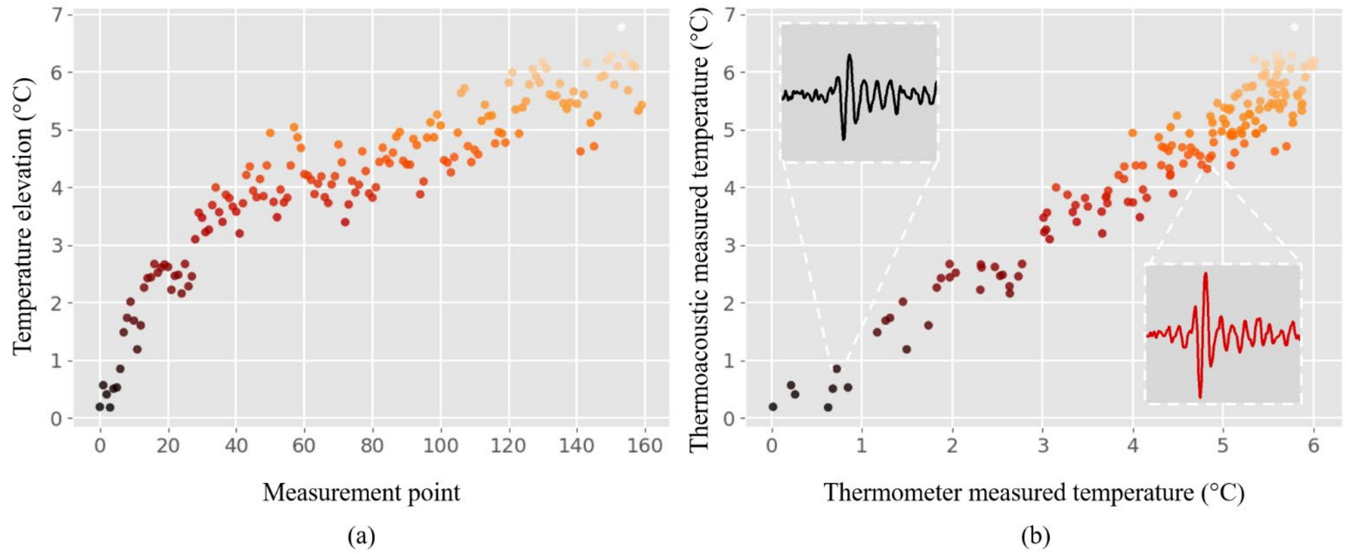

Figure 4. Magnetically mediated thermoacoustic temperature measurement results. (a) Temperature variation as hot water is gradually pumped into the water bath. (b) The relationship between the thermoacoustically measured temperature and the thermometer measured temperature. The insets show the thermoacoustic waveforms at two different measurement points.

4. Conclusions

In this work, we present here a novel magnetically mediated thermoacoustic temperature measurement method. Utilizing coil to stimulate amplitude modulated magnetic field and ultrasound transducer to receive the generated thermoacoustic wave from the inserted magnetic nanoparticles. Benefiting from the high sensitivity of thermoacoustic emission from nanoparticles and the deep penetration capability of both magnetic field and ultrasound propagation, the proposed thermoacoustic temperature measurement system enables a high measurement accuracy of 0.5 degrees Celsius in real time. This work potentially facilitates further development of closed loop magnetic hyperthermia for practical clinical applications.

Funding Statement

This work was supported by National Natural Science Foundation of China (Grant No. 12204242) and Natural Science Foundation of Jiangsu Province (Grant No. BK20210323).

Conflict of interest

The author claims that the manuscript is completely original. The author also declares no conflict of interest

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