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Magnetically mediated thermoacoustic imaging toward deeper penetration

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Magnetically mediated thermo-acoustic effect is predicted in theory and demonstrated in phantom studies in this letter. By applying transient current to a compact magnetically resonant coil at radio frequency below 20 MHz, large electric field is induced by magnetic field inside conductive objects which then undergoes joule heating and emanates acoustic signal thermo-elastically. The magnetic mediation approach with low radio frequency can provide deeper penetration into conductive objects which may extend thermoacoustic imaging to deep laid human organs. Both incoherent time domain and coherent frequency domain approaches are discussed with the latter demonstrated potential for portable imaging system. © 2013 AIP Publishing LLC.

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Microwave induced thermo-acoustic imaging (MI-TAI)¹⁻⁹ is an emerging multi-wave imaging modality that combines high dielectric contrast of tissues and good resolution of ultrasonography. In MI-TAI, tissue absorbs a small fraction of incident pulsed microwave energy and consequently produces ultrasonic emission thermal-elastically. The imaging depth depends on the microwave frequency used for irradiation. For commonly used frequencies such as 434 MHz and 3 GHz, the penetration depths for high water content tissues like skin and muscles are estimated to be 3.2 cm and 1.2 cm, respectively.² This impedes their applications for imaging deep organs. Exogenous contrast agents with enhanced microwave absorption show potential for imaging at deeper region,¹⁰⁻¹² however their toxicity for humans is not fully understood yet. Much deeper penetration can be achieved in principle by using lower frequencies, such as 20 MHz which offers at least 15 cm penetration. However, antennas for efficient electromagnetic radiation at such frequency is with size comparable to human body and therefore very difficult to confine the radiation to a specific region.¹³ Also, the radiation approach tends to decrease the effectiveness of depositing electric field inside materials with large permittivity, therefore, given the same conductivity, the large permittivity of tissues in microwave range will sacrifice the effectiveness of thermo-acoustic signal generation, which will be illustrated later.

To explore a more energy efficient solution and provide potentially deeper penetration, Piao *et al.*¹⁴ investigated theoretically the feasibility of applying alternating magnetic field (AMF) to heat magnetic nanoparticles (MNPs) for thermoacoustic imaging. Both time domain method and frequency domain method are discussed in great detail. This original approach is promising to achieve imaging guided therapy as hyperthermia can be readily fulfilled on that system. Here, we report a different method that adopt magnetic field operating at radio frequency below 20 MHz for mediating thermo-acoustic generation, which relies on joule heating for the heat generation and therefore is generally applicable to conductive objects. Meanwhile, a coherent frequency domain method for thermoacoustic imaging is proposed which exploits coded excitation methodology to

achieve larger signal to noise ratio (SNR). Under the same SNR requirement, it allows lower power to be used for effective imaging and is therefore potential for portable solutions. The rationale behind adopting magnetic field is based on the fact that human body is non-magnetic and responds to magnetic field nearly as free space.¹⁵ This enables magnetic field to penetrate tissues deeper and to circumvent large reflections (reflection coefficient > 70%) suffered by other radiation approaches. Furthermore, this approach is immune from the large permittivity of human tissues for depositing electric field inside tissues, providing a more efficient solution in terms of energy conversion. The feasibility of adopting low frequency magnetic field for thermoacoustic imaging, as proposed here and advocated in Ref. 14, is proved by the preliminary experimental results.

As shown in Fig. 1(a), a compact magnetically resonance solenoid coil formed with additional capacitors is used as the stimulator. The radio frequency current $I(t)$ is delivered to the coil, which produces alternating magnetic field for penetrating tissue. Since the radius of the coil R is much smaller than the wavelength λ of the current, i.e., $R \ll \lambda$, the coil shows negligible radiation and the current flowing in the coil is considered uniform in phase. Then the magnetic field at location $\vec{r}$ and time t can be computed analytically with the law of Biot and Savart

$$\vec{B}(\vec{r}, t) = \frac{\mu_0 N I(t)}{4\pi} \int \frac{\vec{e} \times (\vec{r} - \vec{r}')}{|\vec{r} - \vec{r}'|^3} dl', \quad (1)$$

where N is the number of turns of the coil, μ_0 is the permeability of tissue, $\vec{r}'$ denotes the position of current element dl' of the coil whose direction is indicated by unit vector $\vec{e}$. According to the Maxwell's equation: $\nabla \times \vec{E} = -\frac{\partial \vec{B}}{\partial t}$, an alternating electric field $\vec{E}$ is thereby generated by the alternating magnetic field, which is derived as

$$\vec{E}(\vec{r}, t) = \frac{\mu_0 \omega N I(t) \vec{e}}{4\pi} \int \frac{dl'}{|\vec{r} - \vec{r}'|}, \quad (2)$$

where ω is the radian frequency of the applied current. Assume tissue conductivity is $\sigma(\vec{r})$, then according to Ohm's

FIG. 1. (a) Schematic of magnetically mediated thermoacoustic generation. (b) Illustration on incoherent time domain and coherent frequency domain TA signal.

law, the electric field will induce conductive current $\vec{J}(\vec{r}, t) = \sigma(\vec{r})\vec{E}(\vec{r}, t)$ flowing in the tissue, which causes absorption of incident radio frequency energy through joule heating.

The heating function, defined as the absorbed energy per unit time and per unit volume, is calculated as $H(\vec{r}, t) = \langle \vec{J}(\vec{r}, t) \cdot \vec{E}(\vec{r}, t) \rangle = \langle \sigma |\vec{E}|^2 \rangle$ where operator $\langle \rangle$ denotes short time average and $||$ represents absolute value. The absorbed energy disturbs tissues' original thermodynamic equilibrium and rises its temperature slightly, causing thermal expansion that launches acoustic waves propagation¹⁶

$$\nabla^2 p(\vec{r}, t) - \frac{1}{c^2} \frac{\partial^2}{\partial t^2} p(\vec{r}, t) = -\frac{\beta}{C_p} H(\vec{r}, t), \quad (3)$$

where $p(\vec{r}, t)$, c , β , C_p represent the thermoacoustic (TA) pressure, speed of sound, isobaric volume expansion coefficient, and specific heat capacity of tissues, respectively. The acoustic signal is then received systematically by an ultrasound transducer to form images. The wave equation can be solved with Green's function method¹⁶ under linear acoustic theory

$$p(\vec{r}, t) = \frac{\beta}{4\pi C_p} \iiint \frac{d^3}{|\vec{r} - \vec{r}'|} \sigma(\vec{r}') \frac{d\langle |\vec{E}(\vec{r}', t')|^2 \rangle}{dt'} \bigg|_{t' = t - \frac{|\vec{r} - \vec{r}'|}{c}}, \quad (4)$$

where $\vec{r}'$ indicates points inside tissue while $\vec{r}$ represents the location of receiving transducer. Note that the thermoacoustic generation is proportional to the square of electric field, which means the efficiency in generating electric field is of crucial importance. To make it complete, thermoacoustics in coherent frequency domain is also discussed here. Taking the Fourier transform of the wave equation and its solution in time domain, we obtain

$$\nabla^2 P(\vec{r}, \omega) + k^2 P(\vec{r}, \omega) = -\frac{j\omega\beta}{C_p} H(\vec{r}, \omega), \quad (5)$$

$$P(\vec{r}, \omega) = -\frac{j\omega\beta}{4\pi C_p} \int \frac{e^{jk|\vec{r} - \vec{r}'|}}{|\vec{r} - \vec{r}'|} H(\vec{r}', \omega) d^3 \vec{r}', \quad (6)$$

where k is the acoustic wave number. It is observed that the produced acoustic signals will share the same spectrum with the heating function, which is proved to be the envelop of the carrier signal.⁹ Modulating the carrier signal's envelop with chirp signals¹⁷ or other special codes¹⁸ will therefore

result in the generation of "coded" TA signal (chirped TA signal for instance), as shown in Fig. 1(b), together with incoherent time domain TA signal. Subsequent correlation of the noisy but "coded" TA signal with the known modulation reference renders significant improvement in the SNR. Specifically, consider here a chirp signal sweeping from ω_0 to ω_1 within a time duration T is used to modulate the envelop of the radio frequency current. The analytical result of the cross-correlation between the modulation reference and the received acoustic signal is

$$S(t) = \frac{A_0 A_1 T^2}{2\pi m(t - \tau)} \sin \left[\frac{m\pi(t - \tau)}{T} \left(1 - \frac{t - \tau}{T} \right) \right] \cos(\omega_c(t - \tau)), \quad (7)$$

where A_0 and A_1 are the amplitude of the reference and received signal, respectively, $\omega_c = \frac{(\omega_0 + \omega_1)}{2}$ represents the center frequency, $m = (\omega_1 - \omega_0)T$ denotes the time-bandwidth product, and $\tau = \frac{|\vec{r} - \vec{r}'|}{c}$ is the propagation delay. With this approach, the SNR improvement is $\sqrt{m}$, which could be over 30 times while still achieving a fast enough repetition rate. For instance, a burst chirp signal sweeping from 0.5 MHz to 1.5 MHz that lasts 1 ms can yield an improvement in SNR by 31 times (30 dB). With a duty cycle of 10% for the burst chirp signal, the repetition rate can be 100 Hz, high enough for real time imaging (50–60 Hz).

To compare with the EM radiation approach, consider a power density of Pd is deposited into a medium. The accompanying electric field generated in the medium can be proved to be: $E = 2\sqrt{\frac{\mu_0}{\epsilon}} \times \sqrt{Pd} \propto \frac{1}{\sqrt{\epsilon}}$, where ϵ is the permittivity of the medium. It is seen that the electric field is inversely proportional to the square root of permittivity and thus will be decreased inside tissue compared to that in air since the former has a much larger permittivity. This problem is considerably circumvented in magnetically mediated approach. As seen from Eq. (1), only permeability, not the permittivity, affects the generation of magnetic field. As long as magnetic field can penetrate into region of interest, electric field can be generated effectively. The fact that human body shows the same permeability as vacuum and pertains low conductivity ensures the deep penetration at the proposed frequencies. Another advantage of the proposed method is its superior energy efficiency in delivering energy on demand. This can be understood by modelling the energy transfer process by a transformer whose primary is the magnetically resonance coil and the secondary being connected to a resistor that emulates lossy tissue. The turn ratio of the transformer is determined by the coupling between coil and tissue. Unlike radiation approach that keeps dissipating large peak power on the order of tens of kW,^{19,20} the transformer "circuit" only draws energy by tissue absorption, which is small even though large current is flowing in the primary side. Due to the absence of huge radiation power dissipation in the magnetic resonance coil, customized circuits delivering low power but large current can be designed to be compact for the proposed approach.

Experiments are conducted at both incoherent time domain and coherent frequency domain to demonstrate the signal generation in phantoms with some imaging results. The

FIG. 2. (a) Experiment setup for magnetically mediated thermoacoustic signal generation and imaging. (b) Photography of the experimental system.

experimental system setup along with its photography is illustrated in Fig. 2. A customized Helmholtz coil separated by 4.5 cm is placed below and above the phantom for magnetic mediation. Each coil has 5 turns and the diameter of the coil is 4.5 cm. The resonance frequency of the magnetic resonant tank (the coil with capacitor network) is fixed at 12.4 MHz and the measured quality factor is about 20. No cooling of the coil is applied thanks to the low duty cycle for both the incoherent time domain method (0.01%) and coherent frequency domain method (0.5%). However, for the coherent frequency domain method with a longer chirp duration and higher repetition rate, adequate cooling may be necessary.

The phantom is immersed in the water tank and is placed 2 cm away from the bottom coil. DI water is used as ultrasound coupling agent. A function generator (Tektronix, AFG3252) is used to produce desired radio frequency signal at repetition frequency of 100 Hz which is fed into the an RF pulse amplifier (BT00200-AlphaSA-CW, Tomcorf) to drive the resonance coil. A 2 ohm resistor in series with the coil monitors the current flowing in the coil. The focused ultrasound transducer with center frequency of 1 MHz and focal length of 0.8 inch (Olympus, V303) is immersed in the water tank and fixed on a linear translation stage to receive thermoacoustic signal. The detected signal is first amplified by 76 dB with a customized two-stage low noise amplifier and then digitized by the oscilloscope (Waverunner 6Zi, Lecroy).

FIG. 3. Time domain TA signals at two different separations between transducer and the phantom (a) 2.7 cm, blue: with phantom, red: no phantom. (b) 3.8 cm, blue: with phantom, red: no phantom.

The data is averaged 2048 times before being transferred to MATLAB 2010 b on a PC for offline processing. A tapering metal strip with 5 mm width (at the center) and 20 mm length is used to demonstrate thermoacoustic signal generation by the radio frequency pulses. In this case, the RF pulses are with a width of 1 μ s and a carrier frequency at 12.4 MHz. Driving with a power of 250 W, the peak current flowing in the coil is about 10 A and the magnetic field intensity is estimated to be 2 kA/m. The distance between the transducer and phantom is around 2.7 cm. The received thermoacoustic signal is shown in Fig. 3(a), which appears at 18 μ s, as expected from the propagation delay. The TA signal shifts to 25 μ s (Fig. 3(b)) when the phantom is moved away from the transducer and disappears when the phantom is removed. The time domain TA image of the metal strip along with its optical photography is shown in Fig. 4(a). It is formed by linearly scanning with the focused transducer manually and then performing back projection along each A-line signal. The anatomic structure can be clearly identified and agrees well with the optical photography. To further enhance the SNR of thermoacoustic signal induced by magnetic mediation, the coherent frequency domain experiment with a flat transducer (1 MHz, Olympus, V323) is carried out. A chirp signal sweeping from 0.5 MHz to 1.5 MHz within 50 μ s is used to modulate the current envelop and the carrier frequency is maintained at 12.4 MHz. The chirp modulation frequency is chosen so that the generated acoustic signal will fall within the bandwidth of the ultrasound transducer. The repetition rate for the chirp modulated current is kept at 100 Hz and the time-bandwidth product is 50 so that a SNR improvement of 17 dB is achieved. Fig. 5 presents, from (a) to (d), the time domain signal for the current, its extracted envelop, received TA signal and the correlation results. TA signal is time-gated to avoid direct electromagnetic coupling, which is applicable here as the chirp modulated current is

FIG. 4. TA image of tapering metal strip reconstructed by (a) incoherent time domain method and (b) coherent frequency domain method.

FIG. 5. (a) Time domain linear frequency chirp modulated current signal, (b) extract current envelope (reference chirp signal for correlation), (c) thermoacoustic signal generated by frequency domain method, and (d) normalized correlation results.

still in burst mode with low duty cycle (0.5%) and the chirp duration ($50\ \mu\text{s}$) is shorter than the propagation delay ($70\ \mu\text{s}$). Good electromagnetic shielding is necessary to eliminate the direct electromagnetic coupling for longer chirp durations. Correlation is then performed between the extracted envelope signal and received TA signal, which yields a peak at $70\ \mu\text{s}$, agreeing with the distance ($10.5\ \text{cm}$) between the transducer and the phantom. The time domain signal shows amplitude variation as the frequency changes due to the limited bandwidth of the transducer. The TA image is formed by the back projection method and is shown in Fig. 4(b). It is noted the image is distorted somewhat in lateral (x) direction as the flat transducer used here lacks lateral focusing capability. Still, the image shows much less noise than that in time domain, verifying the SNR improvement of the frequency domain method. Even finer image can be got by advanced imaging reconstruction methods.^{21–24}

It is worth mentioning that the coherent frequency domain approach is actually preferred since the magnetic mediation approach relies on the resonance of coils to benefit from its current amplifying capability. The resonance necessitates relatively long pulse width to build up, which translates directly to reduced resolution in the incoherent time domain method. However, the elongated duration of chirp signal can accommodate this easily without sacrificing the resolution since the correlation will compress the pulses to achieve a resolution determined by the center frequency ω_c , which is $1\ \text{MHz}$ in this case. The resolution can be scaled up by using higher ω_c and corresponding high frequency ultrasound transducers.

To conclude, thermoacoustic signal generation and imaging by the magnetically mediated approach is demonstrated experimentally. It can provide deeper penetration than high frequency microwave irradiation. The associated reduced power budget offered by coherent frequency domain operation can lead to miniaturized systems and achieves comparable SNR and resolution to high peak power incoherent time domain solution. Future works will aim to customize the power amplifier and extend the time-bandwidth product of chirp signals in order to demonstrate the significant thermoacoustic signal generation in human tissues and its imaging performance therein.

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