Microwave-induced thermoacoustic scanning CT for high-contrast and noninvasive breast cancer imaging

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A fast thermoacoustic computed tomography system with a multielement linear transducer array was developed to image biological tissues with circular scanning. The spatial resolution of the imaging system and the spectra of the thermoacoustic signals were analyzed. A modified integration backprojection algorithm using velocity potential was employed to recover the direct energy deposition distribution, signal processing methods, and reconstruction algorithms were validated by imaging a phantom. The differences of the microwave-frequency dielectric properties between malignant and normal adipose-dominated tissues in the breast are considerable, and the absorption contrast can reach as large as 6:1 at 1.2 GHz. An experiment of human breast tissue with a tumor was performed with this system; the thermoacoustic images reconstructed by a limited-field-filtered backprojection algorithm and a modified integration backprojection algorithm were also compared with a mammogram. Our results show that the system can provide a rapid and noninvasive approach for high-contrast breast cancer imaging. © 2008 American Association of Physicists in Medicine. [DOI: 10.1118/1.2966345]

Key words: thermoacoustic tomography, high contrast, breast cancer imaging, modified integration algorithm, velocity potential, absorption contrast

I. INTRODUCTION

Pure microwave imaging has the advantage of good imaging contrast but suffers from poor spatial resolution due to the long wavelength of microwave.12 Pure ultrasound imaging, an established medical imaging modality, can yield good spatial resolution but has poor contrast. Microwave-induced thermoacoustic computed tomography (CT), which is similar to photoacoustic imaging, combines the merits of both microwave imaging and ultrasound imaging, achieves excellent microwave absorption contrast and ultrasound spatial resolution, when compared to competing imaging techniques.3–8 Various tissues present particular characteristics in their absorption spectra; photoacoustic imaging can map optical absorption distribution whereas microwave-induced thermoacoustic imaging is related to the dielectric properties in the objects.

Thermoacoustic source wave is a result of microwave-induced thermal effect. A small temperature rise can be produced when a biological tissue is irradiated by a microwave pulse with adequate energy. Subsequently, the heated structure thermally expands and contracts, becoming a source of acoustic wave. By detecting the acoustic signals and via image reconstruction, thermoacoustic CT can be realized based on the heterogeneity in microwave absorption inside the object. High water or ion content tissues, such as muscle tissues, demonstrate high contrast to adipose tissues when employing microwave radiation. Besides, microwave radiation in thermoacoustic imaging provides a deeper penetration depth in biological tissues than optical radiation compared with photoacoustic imaging.

Thermoacoustic effect has been studied extensively, and more recently several groups have reported applications of microwave-induced thermoacoustic imaging for soft-tissue-mimicking phantoms and soft tissues in biomedicine. Wang et al. presented a thermocoustic imaging system and discovered potential applications in imaging a rhesus monkey brain through an intact skull, and the total data acquisition time was about 80 min due to mechanical rotation of the single detector used.9–11 Another group, under the leadership of Kruger, explored thermoacoustic CT at 434 MHz for breast cancer imaging and they have conducted clinical testing.12–14 Their experimental setup reduced the data acquisition time to 38 sec. However, their scanner was very complicated in structure with high construction cost and a spatial resolution of 1 mm. In comparison, our system has a spatial resolution of 0.5 mm.15 Our group developed an imaging system prototype utilizing 1.2 GHz microwave and demonstrated its feasibility of foreign body detection.16 Our current reported method for breast cancer imaging is simple and fast, and the data-acquisition time for a primary slice image is only 5 sec at one observing stop. It does not require complicated instrumentation and is modified from a commercial ultrasound system, and can be developed as a fast, low-cost, and noninvasive medical imaging alternative.

II. METHODS AND MATERIALS

II.A. Imaging principle and reconstruction

A small temperature rise can be produced when a microwave pulse irradiated a biological tissue, and the heated tissue thermally expands and contracts, becoming a source of...
acoustic wave. When microwave energy delivered in a pulse is short enough so that thermal diffusion can be ignored, the resulting thermoacoustic pressure \( p(r,t) \) that reaches a detector at position \( r \) and time \( t \) can be expressed as the following equation:\(^7\)

\[
p(r,t) = \beta I_0 c_0 \frac{d}{4\pi \rho C_p} \int_{\lvert r-r' \rvert=c} A(r') \frac{dt}{c_c}.
\]

where \( \beta \) is the isobaric volume expansion coefficient, \( I_0 \) is a factor proportional to the incident optical energy density, \( c_0 \) is the speed of ultrasound, \( C_p \) is the specific heat, \( \tau \) is the microwave pulse width, and \( A(r') \) is the absorbed optical energy density per unit volume of soft tissue at position \( r' \) at time \( t \). The induced thermoacoustic wave propagates from its originating region and can be detected by an ultrasonic detector; the strength and the profile of a thermoacoustic signal depend on the microwave absorption of the tissue.

Thermoacoustic pressure \( p(r,t) \) is also related to the velocity potential as follows:\(^8\)

\[
p(r,t) = -\rho \frac{\partial \phi(r,t)}{\partial t},
\]

where \( \rho \) is the density of the fluid medium, and \( \phi \) is the velocity potential. The received propagating thermoacoustic pressure comes from the absorption boundaries and reflects the absorbing differences of the test object since most transducers (except transducers made from PVDF) functions such as a bandpass filter and low-frequency signals are filtered out. The signals back-projected in limited-field-filtered back-projection (LFBP) reconstruction algorithm are the originally measured propagating acoustic pressures.\(^9\)–\(^22\)

The velocity potential is a useful physical quantity that can be written as a scalar solution of the wave equation. A modified integration backprojection (mIBP) algorithm using velocity potential is developed to derive inversely the direct microwave absorption distribution of the object. At a given time \( t \) from a certain initial distribution of absorbed energy \( W \) attenuated by a dependence of \( 1/(\lvert r-r' \rvert) \), the velocity potential is given by the integral of \( W \) over the surface of a sphere with radius \( c \cdot t \):

\[
\phi(r,t) = -\frac{\beta}{4\pi \rho C_p} \int_{\lvert r-r' \rvert=c} W(r') \left( t - \frac{\lvert r-r' \rvert}{c} \right) d^3r'
\]

where \( c \) is the speed of sound, \( \beta \) is the thermal expansion coefficient, and \( C_p \) is the specific heat capacity at constant pressure. Such integration can gather the contributions from various objects or from various parts of an extended irregular object. The \( \phi(r,t) \) is calculated as a function of time by repeated application of the above integral at different time points \( t \). The measured propagating acoustic pressures are used to compute the initial acoustic pressure, and through integration of the initial acoustic pressure, the velocity potential corresponds to the surface integral of the energy deposition. It is similar to x-ray imaging; the signal from the x-ray represents the integrated loss along the path. The measured propagating acoustic pressure, which is equivalent to the derivative quantity, is helpful for improving the sharpness of the boundaries between different tissues, whereas the mIBP algorithm is better suited for use in image reconstruction as velocity potential is nonnegative and represents the microwave energy deposition in tissue.\(^23\)–\(^24\)

II.B. Imaging system

The thermoacoustic CT prototype is illustrated in Fig. 1, a Cartesian coordinate system (X, Y, Z) is also depicted. A 1.2 GHz microwave generator (BW-1200HPT, China) transmitted 0.5 µs microwave pulses at a controlled repetition frequency. The to-be-imaged sample was placed on a rotary sample stage and immersed in a polyvinyl chloride tank, which was filled with transformer oil to couple thermoacoustic waves.

The platform is composed of a B-mode system (Model CTS-200, SIUI, China) and a linear transducer array with 320 vertical transducer elements (EPU-PL21, SIUI, China).\(^9\)–\(^22\) The linear transducer array with a scanning width of 102 mm can be divided into 64 subgroups, and each subgroup consists of five transducer elements. A thin cylinder ultrasonic lens made from silicon rubber is mounted before the transducer elements; this technique can produce a geometric focus in front of the transducer array to select a 2D image plane and suppress the out-of-plane signals. Therefore, the cross-plane spatial resolution depends on the computed tomography ability of the linear transducer array. The slice-width profile was measured to be about 1.6 mm,\(^24\) which can be considered as the spatial resolution along the vertical direction. The transducer array has a resonance frequency of 3.5 MHz, a nominal bandwidth of 65%, and a response sensitivity of approximately 1 mV/Pa after internal amplification. Induced thermoacoustic waves received by the transducer array were digitized by a two-channel data acquisition system (DAS) card (Comuscope 12100, Gage Applied Co., Montreal, Quebec, Canada), and then transferred to a personal computer. The DAS card features a high-speed 12 bit analog-to-digital converter with a sampling rate of 100 MHz.

A custom-built control circuit provided a synchronized clock signal to a function generator. The function generator...
then divided the input frequency into a certain frequency but not on random bases, and the function generator triggered the sampling card and the microwave generator simultaneously at this frequency. Due to the angular response property of the transducer array, we applied a phase-controlled focus technique to detect thermoacoustic signals. At each time, 11 subgroups (each subgroup consisted of five elements; therefore, 320 elements were divided into 64 subgroups) out of 64 subgroups were selected through an internal control circuit to form one signal. Summing up signals from 11 different positions had the equivalent effect of averaging the signal 11 times and improved the SNR. The next adjacent signal in sequential order could then be gained by shifting another 11 subgroups in the way of permutation and combination (the second chosen 11 subgroups had intersections with the former 11 subgroups; one or two subgroups may be different between them). In general, the position of the synthesized signal had a synthetic effect of \( d/2 \) movement in the next period \( d \) is the space distance between two adjacent subgroups). Therefore, the received 128 lines were twice the number of the subgroups. Repeating acquisition of the data line by line in sequential order 128 times, a 2D image could be obtained.

Taking advantage of the phase-controlled technique, the captured signals received by the transducer elements from the test object, after preamplification and phase adjustment, were acquired without averaging, which can effectively reduce the time and microwave energy required for data acquisition. In our experiments, the data-acquisition time is only 5 s at each scanning stop for fast imaging. The system operation and data collection are controlled by the personal computer. The sample was rotated in the horizontal plane (X-Y plane) allowing the transducer array to capture signals around the sample in a circular configuration.

II.C. Imaging experiments

To evaluate the most important parameters in this thermoacoustic CT system, the spatial resolution of the imaging system, and average spectra intensity of the thermoacoustic signals, two absorption spots made of 15% gelatin, 85% water, and a drop of dark ink allowing the transducer array to capture signals are embedded in a piece of pork fat tissue as thermoacoustic sources. The diameter of the thermoacoustic points is 1.5 mm.

A round phantom was made from 15% gelatin, 12.5% milk, and 72.5% water to simulate the electromagnetic (EM) and acoustic properties of human tissue. The diameter of the round sample is 39 mm, and several notches with a slot width of 2.5 mm were carved carefully to simulate absorption heterogeneity, consequently, to verify the ability of the thermoacoustic CT data acquisition system and the reconstruction algorithms. The phantom model is used extensively for studying development, and reconstruction algorithm analysis and comparison, etc. \(^{25-27}\)

Breast cancer remains a leading cause of death among women in many parts of the world. According to the U.S. Institute of Medicine, the variety and sophistication of alternative imaging technologies under development have increased greatly. Film-screen x-ray mammography is still the first standard of breast imaging diagnosis, however it may miss up to 20% of existing lesions and identify many false positives. Thermoacoustic CT relies on microwave absorption that is sensitive to tissue abnormality. Breast tissue is also easily accessible to both EM energy delivery and ultrasound transmission; hence, thermoacoustic CT has promising potential for early cancer detection.

A breast mastectomy specimen pathologically diagnosed as invasive ductal carcinoma and at the advanced stage with grade III features by the First Affiliated Hospital of Ji’nan University was used. The diameter of the actual mastectomy sample was approximately 10 cm and the size of the waveguide was \( 127 \times 63 \text{ mm}^2 \); therefore, the waveguide for this experiment was not large enough to cover the entire specimen, but could cover only the suspect region of interest. The tumor was deeply hidden in the breast tissue during the thermoacoustic imaging. However, in the process of mastectomy operation and artificially recovering the mastectomy specimen to its original morphology before thermoacoustic tomography, some connections such as coarse spiculum between the tumor and the normal breast tissue may have been destroyed to some extent. Two sets of the data processing procedure by LFBP and the mIBP algorithms are comparably analyzed in the experiments.

III. RESULTS

The spatial resolution of a thermoacoustic CT scanner is limited primarily by the duration of the microwave pulse and the frequency response (bandwidth) of the transducer. \(^{31}\) The longer the pulse width, the worse the spatial resolution. On the other side, the narrower the width of the microwave pulse used, the higher frequency of the thermoacoustic signals triggered, and the more ultrasound attenuation. A pulse width of 0.5 \( \mu \text{s} \) employed is a good compromise between spatial resolution and high-frequency ultrasound attenuation in thermoacoustic imaging.

The thermoacoustic image of the two absorbing points is realized through the LFBP reconstruction algorithm. Fig. 2(a) is the reconstructed thermoacoustic image with the inset showing the actual picture of the test sample. The relative location and fore-and-aft boundary of those small points are in excellent agreement with the original sample. A corresponding normalized line profile at position \( y=2.4 \text{ mm} \) of the image in Fig. 2(a) is shown in Fig. 2(b). The 40.5% amplitude line intercepts with the profile at points A, C and B, D. It also cuts across the centralines of the absorption peaks at E, F. \(^{19}\) Therefore, the minimum distinguishable distance \( R \) between two sources can be calculated as: \( |AC| + |BD| - 2r \approx 0.5 \text{ mm} \) according to Rayleigh Criterion, which is the generally accepted criterion for the minimum resolvable detail. The small thermoacoustic source in this experiment can be considered as a microwave point absorber; a Fourier transform to the thermoacoustic signal was performed corresponding to Figs. 2(b) and 2(c) shows the frequency spectrum of the impulse response of the transducer,
which was used in the image reconstruction process. All the signals are deconvoluted with the impulse response before reconstruction algorithms.

Induced thermoacoustic waves emanated from the boundaries and notches of the round block in virtue of microwave absorption heterogeneity, and the signals at 20 scanning stops around the sample were acquired to reconstruct the images. Fig. 3(a) shows the thermoacoustic CT image by the LFBP reconstruction algorithm with the real picture shown in the inset of Fig. 3(a), and for comparison Fig. 3(b) gives the image reconstructed by the mIBP algorithm. Owing to the MLTAS collecting thermoacoustic signals with a big step, some motion artifact is recognizable in the reconstructed images. However, the relative locations and sizes of the sample are clearly resolved with satisfactory contrast. A dashed profile [a] and a solid profile [b] both at position $x = 4.1$ cm of the images corresponding to Figs. 3(a) and 3(b), respectively, are shown in Fig. 3(c), the potential wells between the peaks in Fig. 3(a) are padded, and the hollow notches are accurately recovered in the latter image [Fig. 3(b)]. The image reconstructed using received acoustic pressure emphasizes sharp details, while the image reconstructed via mIBP reconstruction algorithm maps the realistic and direct microwave radiation absorption of the test sample.

The microwave absorption coefficient of biological tissues can be expressed:

$$\alpha = \omega \sqrt{\frac{\mu e}{2} \left[ \sqrt{1 + \left( \frac{\sigma}{\omega \epsilon} \right)^2} - 1 \right]},$$

where $\omega$ is the angular frequency of microwave irradiated, $\mu$ is the permeability, $e$ is the relative dielectric constant, and $\sigma$ is the conductivity. In our thermoacoustic CT system, the electric field is much stronger than the magnetic field; therefore, the dielectric properties of tissues determine the absorption of microwave at various microwave frequencies. In the frequency range of 0.2–2 GHz, the relative dielectric constant and conductivity of malignant tissues are much greater than those of normal breast tissue as shown in Fig. 4. Most of the soft tissues have an absorption coefficient between those for water and adipose tissue. This wide range of values among various tissues can provide a high imaging contrast for biological tissues. Imaging strategies that measure absorption of microwave energy may be effective in differen-
tiating malignant tissue from normal tissue since a relation-
ship between malignant tissue and cell-membrane
glycoproteins, which is mostly bound with increased water
and ions, has been proposed.34 According to the data in Fig.
4, cancerous breast tissues are six times more strongly ab-
sorbing than surrounding normal adipose-dominated tissues
in breast tissue at 1.2 GHz; therefore, microwave-induced
thermoacoustic imaging may potentially be used to detect
early-stage breast cancers with high contrast.

The thermoacoustic images of the malignant breast tissue
were compared with the corresponding radiograph in Fig. 5.
The transducer scanned around the sample at different stops
and the microwave beam vertically illuminated on the
sample in the way as shown in Fig. 5(a), the mammogram of
the specimen in Fig. 5(b) indicates a cancerous area marked
in the dashed area. In the coronal plane, the bright elliptical
areas in the reconstructed thermoacoustic images [Figs. 5(c)
and 5(d)] represent stronger microwave absorption, the ob-
ject was measured to be approximately 25×31 mm², and
on the mammogram the size of the tumor was about
26×30 mm². A strong contrast was observed in the thermo-
aoustic images [Figs. 5(c) and 5(d)] with satisfactory consist-
tency in tumor position and shape, and the tumor-to-
background contrast was estimated to be about 5.5:1, which
demonstrates the imaging contrast advantage of thermo-
aoustic CT over the few-percent contrast obtained with an
x-ray mammogram. The boundaries are somewhat empha-
sized with sharp details in the image of Fig. 5(c) recon-
structed by the LFPB algorithm; the latter image recon-
structed by the mIBP algorithm in Fig. 5(d) is a little blurred
but recovers the realistic absorption distribution accurately.

The outer bright rings in the thermoacoustic images rep-
resent the boundary between the tumor and the normal
adipose-dominated tissue in breast. The remarkable, well-
defined ring pattern depicts vascular distribution in the tumor
whose periphery is the cancer invasion front with rapid cell
proliferation and robust angiogenesis.35–37 The accompany-
ing proliferation and angiogenesis is avidly bound with ions
and water, which would cause enhanced dielectric properties
contrast at the cancer invasion front. Ring patterns have also
been reported in dynamic magnetic resonance imaging
(MRI) and photoacoustic imaging with rim enhancement
correlating well with ratios of tumor periphery-core mi-
crovessel densities.38,39 A small increase in ionic conductiv-
ity or water content can produce a significant increase in
microwave absorption at the margin of the tumor. It should
be noted that the thermoacoustic images of the breast cancer
reveal similar margin morphological features based on intrin-
sic contrast.

In addition, the reconstructed thermoacoustic images in
Figs. 5(c) and 5(d) were subjected to thresholding in order to
display only the higher bits of brightness and to suppress the
background, so that the boundary can be enhanced at the cost
of dynamic range of the contrast, which can be found from
the image processing artifacts around the ellipses. The inner
bright ring next to the outer ring in Fig. 5(d) is equivalent to
the beginning of the positive integral in a mIBP reconstruc-
tion algorithm, which brings the promotion effect. The ther-
moacoustic CT image recovered by mIBP algorithm is more
uniform than the image using originally received thermo-
aoustic signals on account of the smoothing effect of this
integration.
IV. CONCLUSION AND DISCUSSION

The experimental results show that objects with sufficiently dielectric contrast in biological tissue can be imaged using our microwave-induced thermoacoustic CT system. The scanning thermoacoustic CT system with the mIBP algorithm is a promising imaging configuration and can be characterized by acquisition rapidness and recovery accuracy. Compared with cumbersome and expensive x-ray computed tomography (CT) and magnetic resonance imaging (MRI), thermoacoustic CT is low cost, convenient, noninvasive, and different from the current medical imaging modalities in contrast mechanisms; it can be used to image dielectric properties of the tissue, which usually relates with physiological and pathological symptoms. Because malignant breast tissue absorbs microwaves more strongly than benign breast tissue, and microwave even can reach deep objects hidden in the tissue, such capability is suitable and can be potentially developed as a reliable, fast, and low-cost imaging clinical diagnosis apparatus for early-stage breast cancer detection and imaging.

The pressure and temperature rise excited by a pulse microwave in tissue can be deduced from Eq. (1) and computed by $\Delta p = (\beta c_0^2)/(C_p E_a)$ and $\Delta T = (E_a)/(C_p \cdot p)$, where $E_a$ is the energy density per volume. Muscle can be taken as a uniform sample with an energy density per area of 0.4 mJ/cm², 10−4 K−1, the specific heat is $C_p = 1500 \text{ mJ/g K}$, the mass density is $\rho = 1.06 \times 10^3 \text{ g/cm}^3$, and the speed of ultrasound is $c_0 = 1500 \text{ m/s}$; therefore, the Grüneisen parameter $(\beta c_0^2)/(C_p\rho)$ is approximately 2.3. The microwave pulses were coupled into a rectangular waveguide with a cross section of $127 \times 63 \text{ mm}^2$, and the microwave pulses irradiated a sample uniformly with an energy density per area of 0.4 mJ/cm². Suppose the penetration depth of microwave is 2.4 cm, the energy density per volume due to a pulse microwave excitation is $E_a = (0.4 \text{ mJ})/(1 \text{ cm}^2 \times 2.4 \text{ cm}) = 0.17 \text{ mJ/cm}^3$, the pressure and temperature rise are $\Delta p = (\beta c_0^2)/(C_p\rho) \cdot E_a = 40 \text{ Pa}$, and $\Delta T = (E_a)/(C_p \cdot p) = 0.04 \text{ mK}$, respectively. Hence, the values are within the working response range of the transducer, and even if there is no heat conduction to dissipate the heat, this small heating rise effect should be noninvasive for clinical applications.

Thermoacoustic CT is based on tissue radiation interaction properties that are different from other medical imaging modalities currently used. Since thermoacoustic CT can potentially be implemented at virtually any EM frequency, many regions of the EM spectrum may now be usable for medical imaging. The microwave system employed has a maximum trigger repetition rate of 500 Hz, and a 128-channel parallel data acquisition system is our ongoing work. Although the data-acquisition time for initial structural and function monitoring of the test object was 5 s, multiple view angles were required for a complex network with higher resolution and comprehensive tissue information. Our current system by combined scanning of electronic scan and mechanical scan indicates that adopting several multielement transducer arrays spaced around the rotation center with the same angle and same distance, mechanical rotation of the transducer is no longer needed, and real-time imaging for breast cancer could become reality.

Thermoacoustic CT can be further improved by choosing optimal detection bandwidth, detection electronics, and proper data processing. Moreover, in order to make our detecting system portable and convenient, we can use movable antenna to illuminate the tissue. A 3D thermoacoustic CT and a more homogeneous microwave illumination with higher energy are expected to further improve the imaging quality.

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