Ultrasound Microwave-Pumped Real-Time Thermoacoustic Breast Tumor Imaging System

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Abstract—We report the design of a real-time thermoacoustic (TA) scanner dedicated to imaging deep breast tumors and investigate its imaging performance. The TA imaging system is composed of an ultrashort microwave pulse generator and a ring transducer array with 384 elements. By vertically scanning the transducer array that encircles the breast phantom, we achieve real-time, 3D thermoacoustic imaging (TAI) with an imaging speed of 1.67 frames per second. The stability of the microwave energy and its distribution in the cling-skin acoustic coupling cup are measured. The results indicate that there is a nearly uniform electromagnetic field in each XY-imaging plane. Three plastic tubes filled with salt water are imaged dynamically to evaluate the real-time performance of our system, followed by 3D imaging of an excised breast tumor embedded in a breast phantom. Finally, to demonstrate the potential for clinical applications, the excised breast of a ewe embedded with an ex vivo human breast tumor is imaged clearly with a contrast of about 1:2.8. The high imaging speed, large field of view, and 3D imaging performance of our dedicated TAI system provide the potential for clinical routine breast screening.

Index Terms—Thermoacoustic imaging, ultrashort microwave, breast tumor, ultrasound.

I. INTRODUCTION

BRASST cancer is a disease with high morbidity and mortality rate. The survival rate of patients can be greatly improved by early diagnosis [1], [2]. X-ray mammography is the clinical gold standard technique to detect breast abnormalities. Nonetheless, the increased level of fibroglandular tissue in higher density breasts may obscure X-ray images of existing tumors. As a result, the overall sensitivity of mammography can be severely reduced. In addition, from the perspective of patients and health care providers, the high false-positive rate of X-ray mammography can potentially lead to unnecessary and expensive surgical interventions [3], [4]. Other imaging techniques (such as magnetic resonance imaging and ultrasound imaging) suffer from low specificity or low contrast in images, and are only sensitive for selected populations [5]. Therefore, it is urgent to develop a new technique that can surmount these difficulties.

Previous studies have shown that the dielectric property of tumor tissue is considerably different than that of the surrounding, normal tissue. There is a ratio of about 3.8:1 in tissue permittivity and 6:1 in tissue conductivity [6], [7] at a wide range of microwave frequencies. The fundamental difference is believed to be caused by increased vascularization and protein hydration in the malignant tumor [8]. Pulsed microwave pumped thermoacoustic (TA) signals carry the microwave absorption properties of the target, and local microwave absorption can be mapped by processing the collected TA signal [9]–[17], [25], [31], [32], [33] using limited-field filtered back-projection algorithms [18]–[20]. Therefore, thermoacoustic imaging (TAI), combining the benefits of deep penetration and high contrast from microwave stimulation and the high resolution of ultrasonic signal reception, has shown exciting potential applications in early breast cancer detection. However, long pulse microwave imaging technology has low efficiency and a lack of resolution which limits its clinical development. In recent years, an ultrashort microwave-pumped TAI technique has been studied by a few research groups as a novel approach to obtaining high-efficiency, high-resolution imaging [12], [23], [24]. Theoretical analysis and experimental results demonstrate that employing an ultrashort microwave pulse (USMP) generator leads to substantial enhancement in TA conversion efficiency and spatial resolution when compared with sub-microsecond microwave pulse excitation. In our previous work, we achieved a spatial resolution of 105 μm and an energy conversion efficiency that was about 2 orders of magnitude higher than that of the existing TAI [23]. Ultrashort microwave-pumped thermoacoustic imaging is a promising imaging method for breast cancer detection.

In this paper, we develop an ultrashort microwave-pumped thermoacoustic imaging (USMTAI) system to achieve breast tumor imaging. The overall performance of this system has been experimentally investigated, and the results show that it has the benefits of fast imaging, large visual field and low radiation dosage, which provide the possibility of clinical applications in the future.
II. Model and Method

A. Experimental Setup

Fig. 1(a) presents a schematic of the proposed USMTAI system. A USMP generator is employed, which is capable of generating microwave pulse trains with a high-peak-power (10 MW), fast rise time (800 ps), and ultrashort pulse width (2–3 ns). The USMP generator makes use of a charging circuit and Tesla transformer to produce a high-voltage pulse which then discharges to the antenna, causing pulse-train microwave radiation. To obtain the fast rise time, a spark gap is used and sulfur hexafluoride (SF6) at high pressure (12 atm) is pressed into the spark chamber. A helical antenna with a central frequency of 434 MHz is designed to convert the high-voltage, short pulse to microwave radiation. The microwave generator operates at a maximum repetition rate of 100 Hz. The object to be imaged is placed in the cling-skin breast cup, and mineral oil with a negligible microwave absorption coefficient is used for the acoustic coupling. The TA signals are collected by a full ring transducer array with 384-elements, which then transmits to a homemade 64-channel data acquisition system (DAS) in sequence with a homemade 384-64 channel switching system. Meanwhile, the data processing is conducted by the onboard field programmable gate array (FPGA, 7965R, NI Inc. USA) of the DAS to obtain the real time imaging. The collected data can also be transferred to a computer for subsequent image processing. After the first layer of the object is imaged, the computer controls the movement of the micro-displacement mechanism for the imaging of the next layer. The TA images of each horizontal plane are reconstructed by a filtered back-projection algorithm. Slices of the sample are converted into a 3D volume using VolView (Kitware, Inc.) with a volume rendering mode. The detecting part of the USMTAI system is shown in Fig. 1(b).

B. Data Acquisition System

As shown in Fig. 2(a), the process of signal acquisition runs from the reception of the TA signal to the computer processing of the data. The full ring transducer (10C384-1.62 × 8-R100 AHA001, Doppler Ltd., China) is made up of three parts, and every part contains 128 detectors. The central frequency of the transducer is 10 MHz and the bandwidth ranges from 64.5% to 92.4%. In the imaging process, when the microwave pulses illuminate the object, the TA signals are detected by the 384 detectors simultaneously, and each group of 64 channel signals pass through the switching system in sequence and is acquired by two 32-channel data acquisition cards (NI5752, NI Inc. USA) at a sampling rate of 50 MHz. After switching six times, all 384 signals are acquired. Finally, the 384-channel signals are used to reconstruct a 2-D image via a filtered back-projection algorithm. Fig. 2(b), (c) and (d) show images of the full ring transducer, the 384-64ch switch system, and the 64ch data acquisition system, respectively.

C. Distribution and Stability of Microwave Energy

The performance of the USMP generator is experimentally investigated first. Fig. 3(a) shows the diagram setup for the measurement of the microwave energy distribution. In the cling-skin breast cup, we use 80 lard mixed with 20% water and the water is mixed with 3% guar gum by weight to simulate the real breast tissue. An integrated detector consisting of a transducer, a microwave absorber, and an acoustic coupling medium is used to detect the microwave energy distribution in the breast cup using the TA effect. The size of the absorber is 0.3 mm, small enough...
to be considered a point acoustic source. In thermoelastic mechanism, the amplitude of the TA signals is directly related to the microwave radiation energy, so we use a map of the TA amplitude to evaluate the microwave energy distribution. The energy density distribution is obtained by scanning the integrated detector across each XY-plane. The scanning region is divided into measurement points at uniform intervals, with a distance between two adjacent measurement points of 2 mm. The distance between each XY-plane is set at 2 mm. The 3D USMP energy density distribution reconstructed using VolView is displayed in Fig. 3(b). The cross section and vertical section is shown in Fig. 3(c) and (d), respectively. The line plots about the value of amplitude is also shown through the center pixel (in X, Y, Z direction) in Fig. 3(e). As shown in the figure, the microwave energy distribution is nearly uniform in each XY-plane and reduces with increasing Z-axis value. The energy density decreases from 200 to 90 a.u. when the detected plane moves 10 cm along the Z-axis. In the plane of Z = 0 cm, the microwave energy density, determined by the microwave output power and radiation area, is calculated using the pulse width and microwave power density. The energy density variation along the Z-axis can then be calculated using the obtained ratio of TA signal values [26]. The USMP system has an energy density as low as 135 μJ/cm². The maximum energy density of the USMPTAI system is about 300 μJ/cm², well below the safety standard set by the IEEE. The application of the USMPTAI system results in a large near-uniform radiation field, which would significantly reduce the possibility of thermal damage caused by the microwave energy deposition. Fig. 4 shows the stability of the microwave energy over a period of 10 minutes. The results show that the fluctuation of microwave energy for each different pulse repetition frequency is well within 10%, and that the pulsed microwave energy decreases by about 40% when the pulse repetition frequency changes from 10 Hz to 100 Hz, due to the limited charging time. The energy variation over time with no average is also shown in Fig. 4(b), the fluctuation is about 20%.

D. Real-Time Imaging

A dynamic imaging experiment is performed to test the imaging speed of the USMPTAI system. Three 3 mm-diameter plastic tubes filled with a saline solution is used and set in a row, then move the setup across the imaging area manually. Fig. 5 shows a movie sequence of this process. The images cover a region of 5.5 × 5 cm. As time progresses, the first plastic tube appears in the image, followed by the other two plastic tubes. There is no average of the imaging data and the repetition frequency of the microwaves is 100 Hz in this experiment. As is mentioned above, 6 pulses are needed to reconstruct an image, so the imaging speed about 16.7 frames per second is achieved and obtain real-time imaging.

III. RESULTS

A. Phantom Experiment

A simulated breast phantom was made to verify the 3D imaging capability of the system. All of the experiments involved animal and human tissues in this paper have passed a protocol approved by the Institutional Review Board of the South China Normal University. The phantom is mainly composed of excised human breast tumor and mimicked normal breast tissue. The excised human breast tumor was obtained from the Sun Yat-Sen University Cancer Hospital, and its size is about 9.5 × 6.2 × 5.5 mm. The mimicked normal breast tissue is made of pork fat tissues [10]. As shown in Fig. 6(a), the excised breast tumor is embedded in the mimicked normal breast tissue with which the cling-skin breast cup is filled. The labeled box in (a) is the imaging region, with a size of 25 × 12 × 5.5 mm. The corresponding three-dimensional TA image is shown in Fig. 6(b). For demonstration purposes, the TA images of the three slices labeled in (b) are extracted from the three-dimensional image, as shown in (c), (d), and (e), respectively. The corresponding X-ray images obtained by a commercial X-ray system (piXarray100, Bioptics, InC., U.S.A.), which were taken after slicing in the corresponding positions, are taken at one minute time intervals. The results show that the fluctuation of microwave energy for each different pulse repetition frequency is well within 10%, and that the pulsed microwave energy decreases by about 40% when the pulse repetition frequency changes from 10 Hz to 100 Hz, due to the limited charging time. The energy variation over time with no average is also shown in Fig. 4(b), the fluctuation is about 20%.
shown in (f), (g), and (h), respectively. We do calculation about the correlation coefficients of the TA images and X-ray images. The method used is the maximum correlation algorithm (MAC), which is a traditional algorithm in image matching. The correlation coefficients between TA image (c), (d), and (e) to X-ray images (f), (g), and (h) is 0.76, 0.81, and 0.78, respectively. This system, therefore, possesses three-dimensional imaging capability. The same tumor embedded in the bottom, the side, and the top of the breast phantom is also imaged in Fig. 6(i) 1, 2, and 3, respectively. The mean contrast of the imaging is 3.6:1, 2.4:1, 1.9:1, and 2.2:1 at the position 1, 2, 3, and 4, respectively.

B. Breast of Ewe Experiment

In order to further demonstrate the imaging ability, another breast phantom is built, composed mainly of excised human breast tumor and the excised breast of an adult ewe. A medial layer with a diameter of 5 cm was chosen to be imaged. The TA images of the normal breast and the tumor embedded breast are shown in Fig. 7(a) and (b), respectively. The location of tumor is illustrated by the dashed box. The corresponding X-ray image, which is taken after slicing in the corresponding positions, is shown in (c); We also do calculation about the correlation coefficient of Fig. 7(b) and (c), the correlation coefficient is 0.72.

To explore the imaging contrast, the normalized pixel values of the normal tissue, tumor, and the background in the TA and X-ray images are shown statistically in (d), all error bars represent three times experimental statistical results. It can be seen that the mean contrast between the normal tissue and the background in the TA image is much lower than in the X-ray image. On the other hand, the difference between the normal tissue and the tumor can be clearly seen in the TA image in three experiments, with a mean contrast of about 1:2.8, while it has a mean contrast of about 1:1.7 in the X-ray image. The TA image, therefore, has a higher contrast.

C. Energy/Temperature Estimation

When the pulse width of the excited microwave is less than the thermal relaxation time, the instantaneous temperature rise in tissue can be expressed by $\Delta T = \frac{E_0/(C_{\text{water}})}{}$, where $E_0$ is the energy density per volume. If muscle is taken as an example,
the parameters are $C_p \approx 3.7 \text{ J/(gK)}$ and $\rho \approx 1.06 \text{ g/cm}^3$. A traditional 6 GHz microwave generator (BW-6000HPT, China) with a 500 ns pulse width and 350 KW peak power [11] is used for comparison. Traditional microsecond microwave pulses are coupled into a rectangular waveguide with a cross section of $\pi \times 50 \text{ cm}^2$, and irradiate the sample uniformly, with an energy density per area of 2.23 mJ/cm$^2$. If we suppose that the penetration depth of microwaves is 1.2 cm, the energy density per volume due to pulse microwave excitation is $2.23/0.72 = 3.09 \text{ mJ/cm}^3$. The instantaneous temperature rise is therefore $3.09/(3.7 \times 1.06) = 0.79 \text{ mK}$. In contrast, our nanosecond pulsed microwave with a 10 ns pulse width, 4-40 MW peak power and an energy density per area of 0.318 mJ/cm$^2$ and a penetration depth of about 3.7 cm will result in an instantaneous temperature rise of $0.318/3.7/(3.7 \times 1.06) = 0.022 \text{ mK}$, which is about 1/36 that from traditional long microwave pulses. To acquire a two-dimensional image, six pulses are required. Thus, with a traditional long pulsed microwave, the total temperature rise is $6 \times 0.79 = 4.74 \text{ mK}$. On the other hand, the total temperature rise using a nanosecond pulsed microwave will be 0.132 mK, which can be almost ignored. Meanwhile, the human body has certain temperature regulating functions that make the temperature increment even less. Therefore, it can be theoretically predicted that thermal damage is less likely using the proposed pulsed microwave.

IV. DISCUSSION

A typical plot of generated microwave pulse is shown in Fig. 8(a), where two typical TA signals of tumor and saline solution is presented in (b) and (c), respectively. In Fig. 8(a), the waveform is represent for the electric field of microwave, rather than energy, and according to the theory of thermoacoustic effect, the tails of the microwave pulse has less influence than the rising edge's. In addition, the tails of the microwave pulse has lower main frequency, for which the absorption coefficient of material is much smaller. As for the TA signals, the main reason for the relative large tails is that the bandwidth of the transducer is not wide enough.

From the [27], the contrast between malignant tissues and normal breast glandular tissues is no more than 10%. In terms of the current TA imaging technology, when such small differences appear in actual tissues, it seems that is difficult to distinguish the fibroglanular tissue and tumor. From the study in microwave imaging [28], [29], although the dielectric contrast between malignant tissue and dense fibroglanular tissue clutter is low, it can also be distinguished by improving the detection sensitivity, so to improve the TAI detection sensitivity may become a new development direction. In addition, using the tumor-specific contrast agent in TAI is also a method to solve this problem [30].

It is difficult to obtain the exact value of the microwave absorption coefficient in the reconstructed TA image. The reason is that some factors influence the amplitude of TA signal, such as the ultrasonic transmission path and physical structure of tissue. In the actual detection, it is very difficult to control these parameters consistently. In addition, the iterative algorithm is inevitable in the process of reconstructing the image due to circular-scanning, which brings more obstacles to obtain the accurate value of the microwave absorption coefficient. The unavailability of the exact value cause the missing of object properties except morphology. In other words, for the strong pixel value region (such as tumor, foreign body, calculi, or hematocele) displays in the reconstructed image, only the morphological characteristics can be identified. Point by point scanning instead of circular-scanning may be an alternative method to solve this problem. Furthermore, obtain additional information by combining with other imaging modalities, like X-ray mammography or ultrasonography, is a possible direction for the development of TA imaging.

The imaging speed is limited by the mechanical speed, sampling speed, microwave repetition frequency, and imaging reconstruction speed. In our system, the transducer does not need to rotate, reducing the mechanical speed to the microsecond-level electronic switch speed. In other words, mechanical scanning is replaced by electrical scanning. Sampling speed and imaging reconstruction speed are not the main limiting factors on the imaging speed, as hardware response is measured in microseconds. The main factor limiting the imaging speed of our system is the microwave repetition frequency, which must wait dozens of ms for the next pulse. Therefore, a 384-channel signal, which is sufficient to reconstruct a TA image and is captured in 0.06 s at a repetition frequency of 100 Hz, results in a faster microwave generator which can speed up the imaging process.

In the current system, the radiated microwave energy is relative weak due to large radiation area, and the microwave frequency is 434 MHz, where the microwave absorption coefficients are relative low. This caused a low signal to noise ratio (SNR), and then makes the contrast low. Increasing the operating frequency of the microwave source can increase the microwave absorption coefficients, and therefore can improve the imaging contrast. However, higher absorption means lower penetration depth. In the future, a more suitable operating frequency will be chosen that can balance the contrast and penetration depth. In addition, we can also improve the radiated microwave
energy appropriately under the condition that the microwave energy is absolutely safe to the human body.

V. CONCLUSION

This paper has presented the design and imaging performance of our TA breast imaging system. We used a ring transducer array with 384 elements vertically scanning the breast to realize real-time, 3D imaging.

Results indicate that this system can achieve an imaging speed of about 16.7 frames per second. 3D imaging is performed successfully, and an ex vivo human breast tumor is imaged clearly with a contrast about 1:2.8. In summary, the proposed ultrashort microwave-pumped thermoacoustic imaging system possesses obvious advantages, such as fast imaging, a large visual field and high safety, that make it a promising option for breast cancer detection.

REFERENCES


