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Conformal Hyperthermia of Superficial Tumor with Cylindrical Left-Handed Metamaterial Lens Applicator

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Abstract—In earlier time, we proposed a flat LHM-based hyperthermia scheme for conformal hyperthermia of a large superficial tumor. It is demonstrated that in this scheme by deploying multiple microwave sources in a specific array to shape the heating zone and properly setting the source-to-lens distance or phases of sources to adjust the inclination of heating zone, a heating zone better fit to large superficial tumor can be generated. In this paper, we propose a new hyperthermia scheme based on a cylindrical LHM lens which would be more maneuverable for tumors located in tissues with curved surface. It is shown that the same way adopted in the flat LHM-based scheme can be used in this new scheme to acquire desired heating zone for better fitting to tumor region. And large critical source intervals defined in this new applicator greatly relax the restriction to the size of practical antennas applied in this scheme.

1. INTRODUCTION

In microwave hyperthermia of malignant tumor, it is highly desired that most of the microwave in tissue is concentrated within tumor region to specify enough tumor damage and little normal tissue damage [1, 2]. Different antenna array applicators [3–6] have been designed to enhance localized microwave power deposition in tissue. Recently, conformal microwave array (CMA) applicators were reported to generate a heating zone of much better fit to superficial tumor of large size [7].

Left-handed metamaterials (LHM) provide new prospects for hyperthermia treatment of superficial tumors. Superficial tumors generally occur at depth no more than several centimeters beneath the skin [8], which is within the near-field focusing depth of LHM lens. Although losses of LHM will destroy Pendry's perfect lens [9], applicators with LHM lens are still very attractive to superficial tumor hyperthermia for two reasons. First, super-resolved focus of LHM lens characterized by half-power beam-width has been demonstrated in several experiments [10–13] with low-loss LHM slabs. It is the microwave power within half-power beam-width, not within the beam-width charactering the LHM lens resolution defined in [9], that makes dominant contribution to hyperthermia of tumor. Second, a focusing spot of moderate size in tissue is preferred for heating a large or diffusive superficial tumor. Tiny focal spots of LHM applicator, if acquired, will find application in tumor ablation or hyperthermia of early small size tumors.

Potentials of LHM lens applicator for tumor hyperthermia have been demonstrated both numerically and experimentally [14–16]. Furthermore, it is reported that with a flat LHM lens applicator, conformal hyperthermia can be performed by joint heating of multiple microwave sources (antennas) [17]. It is indicated that in the proposed hyperthermia scheme, by deploying multiple microwave sources in a specific array to shape the heating zone, and properly setting the source-to-lens

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distance or phases of sources to adjust the inclination of heating zone, a heating zone better fit to large superficial tumor can be generated.

Apparently, this flat LHM-based hyperthermia scheme should be useful for hyperthermia treatment of large superficial tumors. However, some kinds of tumors, especially superficial tumor, usually occur in tissues with curved surface, such as neck, leg, etc. Obviously, in these cases the flat LHM-based scheme can't well fit to the tissue, and so it would be hard to utilize this scheme to generate a heating zone completely fit to tumor. For these tumors, to achieve satisfactory hyperthermia effects, it is necessary to find a lens, such as cylindrical lens, resembling the tumor location in shape to substitute the flat lens. Fortunately, it has been reported that cylindrical LHM lens also have the capability to obtain a sub wavelength level focus, which can be easily adjusted by moving the microwave source [18]. In addition, the methods to fabricate cylindrical LHM lens have also been demonstrated [19, 20]. Taking all factors into consideration, it is favorable to apply cylindrical LHM lens in microwave hyperthermia of superficial tumor.

In this paper, we propose a new conformal hyperthermia scheme with a low-loss cylindrical LHM lens applicator. The hyperthermia is demonstrated by calculating the microwave power deposition in tissue with finite-difference time-domain (FDTD) simulations, and evaluating the temperature distribution in tissue by solving bio-heat equation (BHE). In Section 2, the requirement of deploying multiple sources to realize conformal hyperthermia is investigated. The critical source/antenna interval that defined in [17] is ascertained by further analyzing. In Section 3, methods to acquire a tilted heating zone in tissue are studied. As in the case of the system with a flat lens, we find that the inclination of heating zone can easily be controlled either by adjusting the source-to-lens distance or by adjusting the phase of microwaves. In Section 4, conformal hyperthermia of superficial tumor with the proposed scheme is demonstrated by an example.

2. HYPERTHERMIA WITH JOINT HEATING

2.1. The New LHM-Based Conformal Microwave Hyperthermia

The new hyperthermia scheme with cylindrical LHM lens is shown in Fig. 1. The hyperthermia is demonstrated by calculating the microwave power deposition in tissue. To be comparable, the cylindrical LHM lens applied in this scheme is supposed to have the same thickness $d = 4\,\text{cm}$ as the flat LHM lens used in the scheme proposed in [17]. Similarly, several microwave sources ($S_1, S_2, \ldots S_n$, *representing antenna phase centers in practice*) may be set behind the cylindrical LHM lens. The LHM lens will also focus microwave emitted from source $S_i\,(i = 1, 2, \ldots, n)$ at a corresponding focal point $F_i\,(i = 1, 2, \ldots, n)$ in tissue. Therefore, different heating zones enclosing focal point $F_i\,(i = 1, 2, \ldots, n)$ can be generated. Further, conformal hyperthermia can be realized if we properly combine these heating zones.

It is demonstrated that to make sure conformal hyperthermia performance, two neighboring heating zones should be seamlessly joined in tumor region. Therefore, the distance between two neighboring sources should be restricted by simulating hyperthermia with two sources. In other words, a critical source interval for joint heating, viz., heating adjacent zones utilizing multiple sources, should be defined.

For demonstration, we investigate joint heating of two neighboring sources in the proposed scheme by simulating hyperthermia with two sources of microwave of 2.45 GHz. In the simulation, the circular biological tissue of radius $r = 5\,\text{cm}$ to be heated is assumed to be homogeneous, muscle-like tissue covered by a skin layer of 0.2 cm thickness. Outside the skin layer, water bolus of thickness of 0.5 cm is used to protect the skin from being overheated. And the inner and outer diameter radius of the lens is set to be $r_{in} = 5.5\,\text{cm}$ and $r_{out} = 9.5\,\text{cm}$.

Emitting and focusing of microwave can be simulated by using FDTD method. In our FDTD codes, the LHM is supposed to be isotropic and characterized by relative permittivity ε_{rLHM} and μ_{rLHM} of the form

$$\varepsilon_{rLHM}(\omega) = 1 - \frac{\omega_{pe}^2}{\omega^2 + 2j\delta\omega}, \tag{1}$$

$$\mu_{rLHM}(\omega) = 1 - \frac{\omega_{pm}^2}{\omega^2 + 2j\delta\omega}. \tag{2}$$

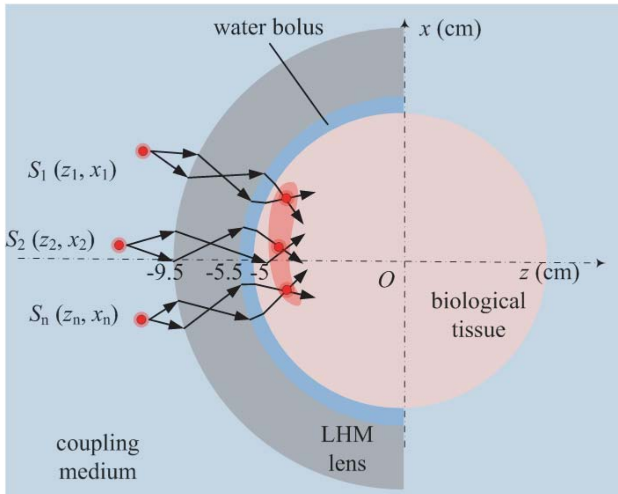

Figure 1. Conformal hyperthermia by using multiple sources behind a cylindrical.

Proper permittivity ε_{rLHM} and permeability μ_{rLHM} of LHM can be defined by setting ω_{pe}, ω_{pm} and loss factor δ in (1) and (2). As used in [14], ten-cell extended uniaxial anisotropic perfectly matched layer is considered, and transition layer between the LHM and its surrounding medium is introduced to avoid sharp interface.

To make sure the comparability, in simulation the parameters of this scheme are set to the same value as that of the scheme proposed in [17], except the shape of the applied lens and the treated tissue, which means that the parameters of skin, fat, muscle and water bolus are defined following [17]. And we set $\omega_{pe} = 9\omega$, $\omega_{pm} = 1.414\omega$, $\omega = 2\pi f$ and $\delta = 3.3 \times 10^5$ in Equations (1) and (2) so that $\varepsilon_{rLHM} \approx -80 + j1.4 \times 10^{-3}$, $\mu_{rLHM} \approx -1 + j8.57 \times 10^{-5}$ for the LHM lens, which indicates a low loss of $0.006i$. The coupling medium is supposed to have dielectric constant $\varepsilon_{rm} = 80$ so that reflection occurring at the LHM lens surface can be suppressed. Considering our former researches indicating that the loss of water has little influence on the reflection and the distribution of specific absorption rate (SAR) in tissue, we use water as coupling medium. And considering the size of lens and tissue, the computational space is set to have 2200×2200 cells of $\Delta x = \Delta z = 0.01$ cm. The source excitation is set to be turned on slowly by using an exponential ramp function of $(1 - e^{-t/\tau})\sin(\omega t)$ with $\tau = 25 \cdot 2\pi/\omega$ to avoid exciting other frequency components.

To calculate the temperature distribution in tissue, we solve Pennes' bio-heat equation (BHE) [21]

$$C_p(\vec{r})\rho(\vec{r})\frac{\partial T(\vec{r})}{\partial t} = \nabla \cdot (K(\vec{r})\nabla T(\vec{r})) + A_0(\vec{r}) + Q(\vec{r}) - B(\vec{r})(T(\vec{r}) - T_B). \tag{3}$$

where Q is the electromagnetic power distribution, A_0 the metabolic heat production, B the heat exchange mechanism due to capillary blood perfusion, C_p the specific heat capacity, ρ the density, K the thermal conductivity, and T_B the blood temperature assumed to be a constant 37°C. In the calculation, all thermal parameters including capillary blood perfusion are defined following [22]. The initial temperature of biological tissues and water bolus is assumed to be 37°C.

2.2. Critical Source Interval for Joint Heating

Considering that the critical source interval is essentially determined by the focusing resolution of LHM in tissue, firstly in this section we may analyze it by applying two point sources or line sources in this new scheme.

Figure 2 depicts the normalized specific absorption rate (SAR) distribution and temperature distribution in tissue after 60 minutes heating with two identical sources of different source intervals $D = 0.5, 1.5, 2.5, 3.5, 4.5$ cm. In the simulation, the sources are deployed on a circle 2 cm away from the cylindrical LHM lens (i.e., $\sqrt{x^2 + z^2} = 11.5$ cm in Fig. 1), and have exact amplitude to acquire a highest temperature of 43°C in tissue.

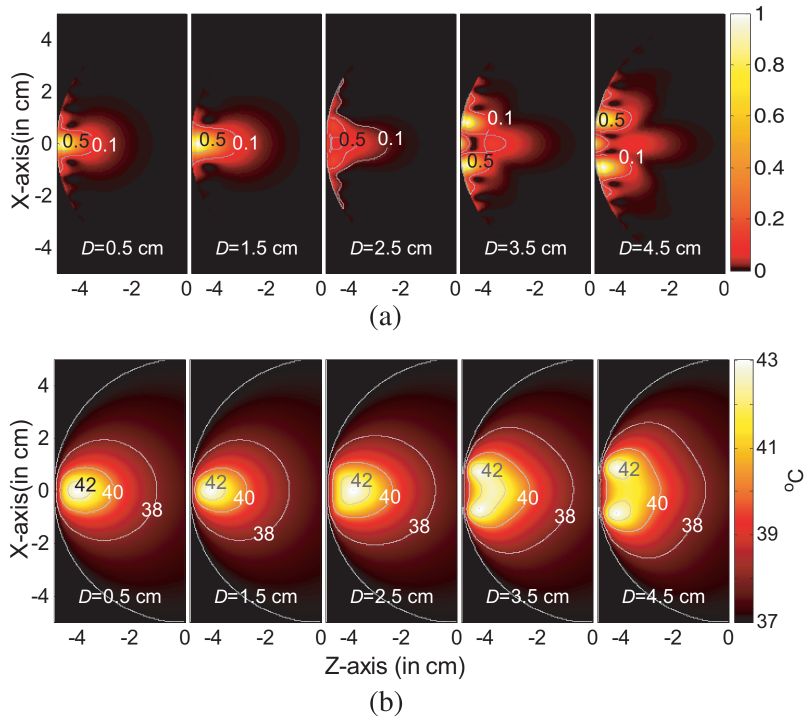

Figure 2. (a) Normalized SAR and (b) temperature distributions in tissue for different source intervals of $D = 0.5$, 1.5, 2.5, 3.5, 4.5 cm, respectively.

Obviously, as the results are acquired in the scheme with a flat lens, both the SAR distribution and the 42°C region expand as the source interval increases. Therefore, it is possible to apply this new scheme to acquire a larger heating area by deploying more sources with proper source interval.

In [17], we demonstrated that the critical source interval can be defined according to the 50% SAR contours, because the 42°C heating zone and 50% SAR contour zones almost at the same source intervals start to split into two separate contours. If we deploy multiple sources for conformal hyperthermia, the interval between two neighboring sources should be less than the critical source interval to make sure that a contiguous 42°C heating zone can be acquired in tissue. Obviously, to realize such deployment, the minimum edge size of the practical antennas applied in this system should be smaller than the critical source interval.

Similarly, based on these principles, we define critical source interval of this scheme to be 3.5 cm because at this source interval the 50% SAR contour zones start to split into three separate contours, and the 42°C heating zone begins to deform measurably. Obviously, the critical source interval of this scheme is nearly three times of that defined in the scheme based on a flat LHM lens. In other words, the size limitation on practical antennas to realize joint heating is greatly relaxed in this scheme.

2.3. Source Interval for Practical Antennas

To demonstrate the critical source interval when practical antennas are applied in this scheme, we consider a LHM-based hyperthermia system as depicted in Fig. 3, in which open rectangular waveguides are used to emit microwave.

As the scheme presented in [17], open waveguides are set in coupling medium (water) with broad wall parallel to x-axis, and filled with dielectric the same as the coupling medium (water) and operate in the dominant mode. And the dimensions of the waveguide are $0.7\,\text{cm} \times 1.4\,\text{cm}$. Interval between the two open waveguides (viz., D in Fig. 3) is defined as the distance between the two waveguide center axes.

Firstly, we consider that only one open waveguide is set with the z-axis as its center axis to study the SAR distribution in tissue for an open waveguide irradiation. Fig. 4 shows SAR distribution in xoz-plane and yoz-plane in tissue. Obviously, a focusing spot is acquired in tissue beneath the waveguide aperture. Similar to the situation for flat LHM lens based scheme, due to the contribution of each point source on the aperture (emitting secondary wave by Huygens' principle), the heating spot has a larger size than that generated by a single point source. Therefore, hyperthermia with practical antennas allow a larger critical source interval if compared to that with point or line sources.

Then we deploy two open waveguides behind the lens as shown in Fig. 3 to study the critical source interval. In this simulation, the two waveguides are set to have the same aperture-lens distance of

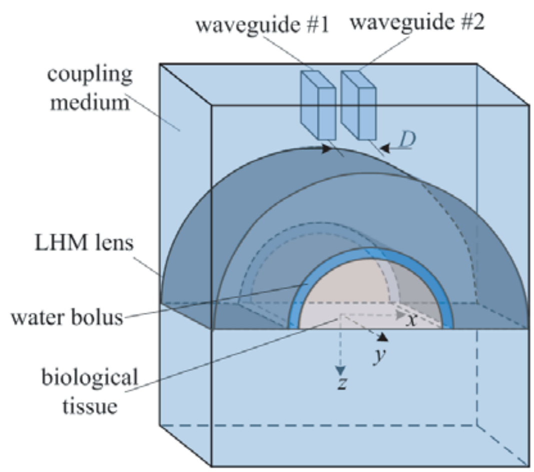

Figure 3. Hyperthermia with two open rectangular waveguides.

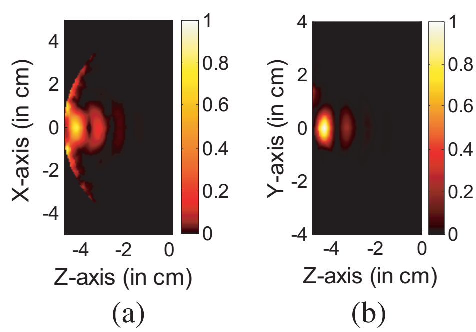

Figure 4. SAR distribution in tissue. (a) xoz-section plane, (b) yoz-section plane.

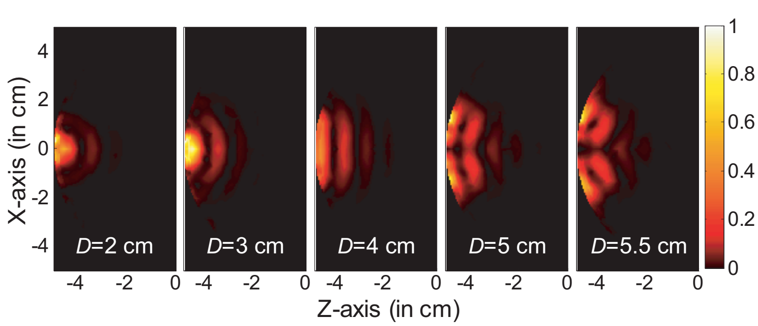

Figure 5. SAR distribution in xoz-plane in tissue when two open rectangular waveguides are set with different intervals $D = 2.0$, 3.0, 4.0, 5.0, and 5.5 cm, respectively, in narrow wall direction.

2.0 cm (i.e., waveguide apertures position satisfying $\sqrt{x^2 + z^2} = 11.5$), but different waveguide intervals of $D = 2.0$, 3.0, 4.0, 5.0, 5.5 cm, respectively. Fig. 4 shows the SAR distribution in the xoz-plane in tissue. By evaluating the 50% SAR contours in Fig. 5, it is found that that the critical source interval in the narrow wall direction is approximately 5 cm, which is several times larger than that for the applicator with a flat LHM lens.

3. METHODS TO ACQUIRE TILTED HEATING ZONE

In [17], it is demonstrated that in the hyperthermia scheme based on a flat LHM lens, only by adjusting the source-to lens distance or changing the phases of microwave sources, the tumors with different inclinations in tissue can be heated effectively. Considering that the cylindrical LHM lens has similar focus property to flat lens, we believe that the same way can be used in the new hyperthermia scheme. So in this section we still investigate the method to tune heating zone in tissue for hyperthermia with joint heating from two aspects.

3.1. Effects of Source-to-Lens Distance

Due to the focusing character of a cylindrical LHM lens, the focusing depth in tissue of a microwave source would be closely related to source-to-lens distance. Therefore, it could be feasible by adjusting the source-to-lens distance to tune the heating zone in tissue.

For demonstration, firstly we consider that two line sources in phase are deployed behind the lens. Fig. 6 depicts the effects of source-to-lens distance on hyperthermia with two line sources after 60 minutes heating. In the simulation, the two sources have a lateral source interval of 3.0 cm, i.e., $|x_1 - x_2| = 3.0$. Source #2 is fixed at $S_2(-1.5, -11.4)$, while source #1 is set at different positions of $S_1(1.5, -11.1)$, $S_1(1.5, -10.8)$, $S_1(1.5, -10.5)$, and $S_1(1.5, -10.2)$, respectively. This means that source #1 has different source-to-lens distances (i.e., different z_1).

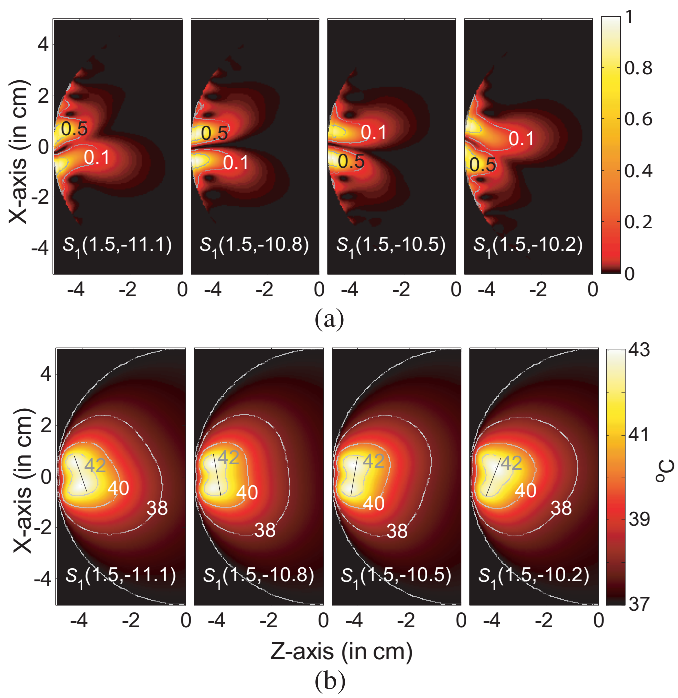

Figure 6. (a) Normalized SAR distribution and (b) temperature distribution in tissue by fixing source #2 at $S_2(-1.5, -11.4)$ and setting source #1 at different positions of $S_1(1.5, -11.1)$, $S_1(1.5, -10.8)$, $S_1(1.5, -10.5)$, and $S_1(1.5, -10.2)$, respectively. The dashed line in temperature distribution is defined by linking the two peak-temperature points.

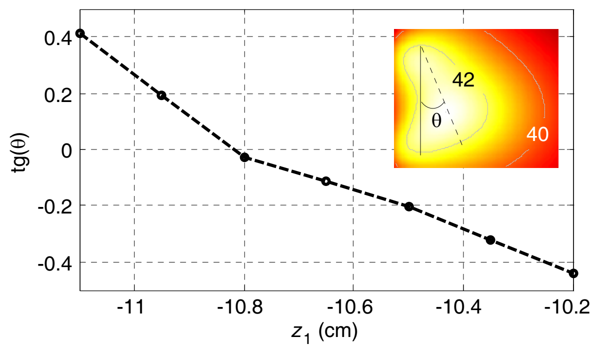

Figure 7. Inclination of effective heating zone in tissue with different source-to-lens distances of source #1, as source #2 is set at $S_2(-1.5, -11.4)$.

It is shown in Fig. 6 that the line linking the two peak-temperature points in heating zone rotates clockwise as source #1 moves towards the lens. By further calculation, the inclination of heating zone (characterized by an angle θ) with respect to source-to-lens distance (indicated by different z_1) is shown in Fig. 7. We can see while source #1 moves 0.9 cm towards the lens, the tangent value of the angle θ deceases form about 0.41 to -0.44. This means the heating rotates clockwise about 180°. Therefore, it is convenient by adjusting the source-to-lens distance to acquire a tilted heating zone of different inclinations.

3.2. Effects of Microwave Phase

It is stated that in this hyperthermia scheme neighboring source intervals should be smaller than critical source interval to make sure that the microwaves emitted from two neighboring sources join sufficiently. In this situation, microwaves emitted from neighboring sources will interfere with each other in the joint heating zone. As a result, it is possible to modify the heating pattern in tissue by adjusting the phases of microwave sources.

Figure 8 shows the effects of phase difference on joint hyperthermia. In the calculation, two line sources with the same amplitude are deployed at $S_1(1.5, -11.4)$ and $S_2(-1.5, -11.4)$, respectively, which results in a typical source-to-lens distance of 2 cm and a source interval of 3.0 cm. As the phase of source #2 is fixed as a reference phase, the phase of source #1 is set with different leading values of $d_p = 0.2\pi$, 0.4π, 0.6π, 0.8π, and π, respectively.

Figure 8 exhibits that the heating zone rotates clockwise as d_p increases. The inclination of heating zone indicated by an angle θ with respect to different leading phases of source #1 is shown in Fig. 9.

By comparison, we can see from Fig. 6, Fig. 7, Fig. 8, Fig. 9 that adjusting source-to-lens distance and source phase acquires almost the same performance in adjusting the tilted heating zone. The only difference is that the rotation due to phase adjustment is restricted within the joint heating region, as the rotation due to source-to-lens distance adjustment has the potential to extend a bit deeper into tissue.

To study the effects of microwave phase to the hyperthermia performance with practical antennas applied as shown in Fig. 3, we consider that two open waveguide apertures are centered at $S_1(1.5, -11.4)$ and $S_2(-1.5, -11.4)$. Fig. 10 shows the SAR distribution in tissue for open waveguide #1 excited with a leading phase of $d_p = 0.2\pi$, 0.4π, 0.6π, 0.8π, and π, respectively, compared to open waveguide #2. As marked in Fig. 10, we find that the inclination of heating zone can be effectively modified by adjusting the phase of antenna excitation.

In conclusion, adjustment of the phase of sources may acquire tilted heating zone with different inclinations, thus it can be very useful as the substitute for adjustment of source-lens distance, especially when the adjustment of source-to-lens distance is not convenient.

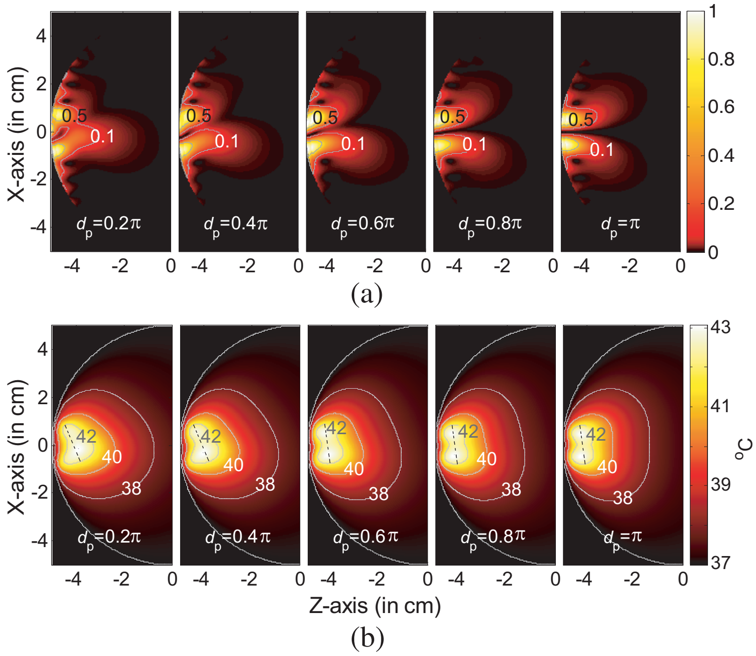

Figure 8. (a) Normalized SAR distribution and (b) temperature distributions in tissue after 60 minutes heating for source #1 of leading phase of $d_p = 0.2\pi$, 0.4π, 0.6π, 0.8π, and π, respectively.

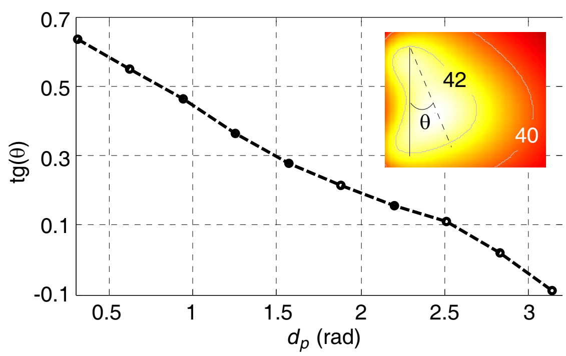

Figure 9. Inclination of heating zone with different leading phases of source #1, as two sources are set at $S_1(1.5, -11.4)$ and $S_2(-1.5, -11.4)$, respectively.

4. CONFORMAL HYPERTHERMIA OF LARGE TUMOR

To demonstrate hyperthermia from two neighboring microwave sources, we have investigated the critical source interval of two adjacent sources and the methods to tune heating zone pattern in tissue. Based on these analyses, we believe that conformal hyperthermia of tilted superficial tumor can be realized by deploying multiple sources (*phase centers of antennas in practice*) of source intervals less than critical source interval, properly setting the phase of source and source-to-lens distance.

For thorough illustration of the proposed conformal hyperthermia scheme, we set 7 microwave sources in phase behind the LHM lens, i.e., $n = 7$ in Fig. 1.

To acquire a heating zone shallow in the middle and deep at the two sides, according to the results depicted in Fig. 6, we properly adjust the position of the sources and finally deploy them at $S_1(4.5, -10.4)$, $S_2(3, -10.9)$, $S_3(1.5, -11.4)$, $S_4(0, -11.5)$, $S_5(-1.5, -11.4)$, $S_6(-3, -10.9)$ and $S_7(-4.5, -10.4)$, respectively. Then after 60 minutes heating by using these sources a 42°C heating

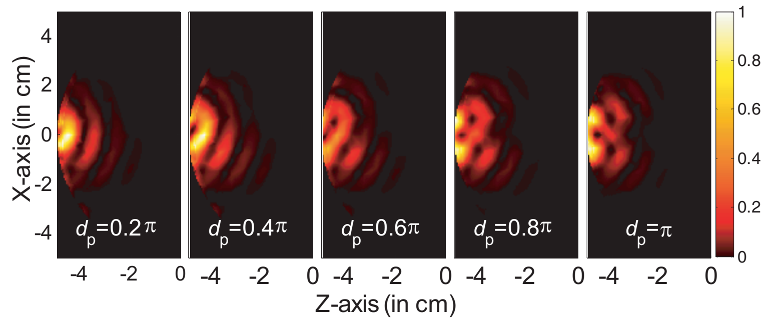

Figure 10. Inclination of heating zone of hyperthermia with two open waveguides of different leading phases in waveguide #1.

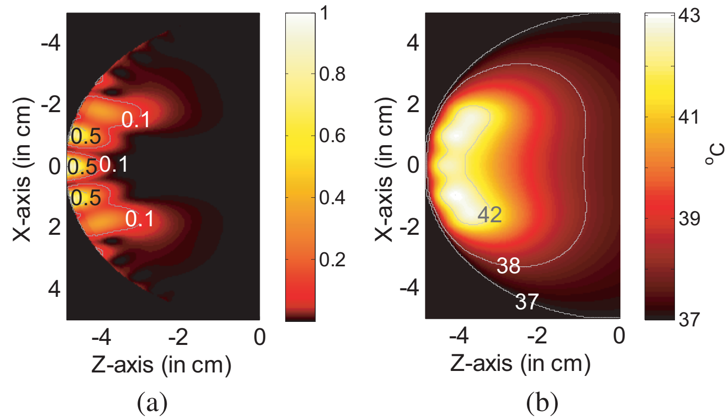

Figure 11. (a) Normalized SAR and (b) temperature distributions in tissue for conformal hyperthermia with 6 sources.

zone with expected pattern extends continuously almost 4 cm laterally and 1 cm longitudinally in tissue as shown in Fig. 11 is acquired. Owing to the special focusing performance of cylindrical LHM lens depicted in [18], the 42°C heating zone acquired in this calculation is smaller than that obtained with 6 sources depicted in [17]. It is also demonstrated that in the proposed hyperthermia scheme with a cylindrical LHM lens, the sources deployed in a relatively large region can be gathered in tissue to perform joint heating. Therefore, it is still feasible by deploying multiple sources in a relatively large region to heat a large tumor in tissue.

5. CONCLUSION

In conclusion, conformal hyperthermia with cylindrical LHM lens applicator can be acquired by joint heating of multiple sources. By deploying multiple microwave sources in a specific array larger than the heating zone, and properly adjusting the source-to-lens distance or phases of sources to adjust the inclination of heating zone, a heating zone better fit to large superficial tumor can be generated.

Compared to the applicator with a flat LHM lens, this new applicator with a cylindrical LHM lens should be more useful for hyperthermia treatment of large superficial tumor occurring in cylindrical tissue, such as neck, leg, etc. Owing to the similar shape, the cylindrical LHM lens can well fit to the tissue, so make it easier to generate a heating zone better fit to tumor. In addition, owing to the special focusing mechanism of cylindrical LHM lens, a larger critical source interval is defined in this new applicator. This means that the size limitation on practical antennas to realize joint heating is greatly relaxed in this scheme.

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