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3D computational study of non-invasive patient-specific microwave hyperthermia treatment of breast cancer

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Abstract

Non-invasive microwave hyperthermia treatment of breast cancer is investigated using three-dimensional (3-D) numerical breast phantoms with anatomical and dielectric-properties realism. 3-D electromagnetic and thermal finite-difference time-domain simulations are used to evaluate the focusing and selective heating efficacy in four numerical breast phantoms with different breast tissue densities. Beamforming is used to design and focus the signals transmitted by an antenna array into the breast. We investigate the use of propagation models of varying fidelity and complexity in the design of the transmitted signals. An ideal propagation model that is exactly matched to the actual patient's breast is used to establish a best-performance baseline. Simpler patient-specific propagation models based on a homogeneous breast interior are also explored to evaluate the robustness of beamforming in practical clinical settings in which an ideal propagation model is not available. We also investigate the performance of the beamformer as a function of operating frequency and compare single-frequency and multiple-frequency focusing strategies. Our study suggests that beamforming is a robust method of non-invasively focusing microwave energy at a tumor site in breasts of varying volumes and breast tissue density.

Keywords

microwave hyperthermia; breast cancer treatment; breast hyperthermia; FDTD; numerical simulations

1. Introduction

Numerous studies have shown that hyperthermia (40-45°C, typically for 60 - 90 minutes) causes direct cytotoxicity due to heat damage (see, for example, Dewhurst et al. 2003, Lepock 2003) and increases sensitivity of cancer cells to radiation therapy and chemotherapy (see, for example, Vernon et al. 1996, Falk and Issels 2001, Lepock 2003, Jones et al. 2006, Kampinga 2006). The goal of hyperthermia cancer treatment is to achieve a temperature of approximately 40-45°C in a region which includes the tumor and a margin of healthy tissue while maintaining normal temperatures in surrounding tissue. The negative margin targeted by thermal therapy (Gianfelice et al. 2003, Cheng et al. 2008) is on the order of 1 cm. This practice is consistent with surgical resection protocols which typically involve the removal of a 1-cm negative margin in an attempt to reduce local recurrence rates (Veronesi et al. 1995, Singletary 2002, Schmitz et al. 2008, Luini et al. 2009). According to the American Cancer Society (American Cancer Society 2008), the most common stages of diagnosis of breast cancer are stages I and II, which include localized tumors from 1 mm to 5 cm in their largest dimensions. Volumes from 3 cm up to 9 cm in the largest dimension are

commonly targeted for treatment (Dooley et al. 2009). High-frequency (1 - 4 MHz) focused ultrasound hyperthermia creates a millimeter-size heating zone, thereby requiring multiple sonications in order to treat centimeter-size tumors (Malinen et al. 2005, Zippel and Papa 2005, Ho et al. 2007). Lower-frequency (1 kHz) ultrasound-based therapy has been explored recently (Bakker et al. 2009) as a means to achieve a larger heating zone with a single sonication. Focused microwave hyperthermia also offers promise for creating a centimeter-size heating zone from a single intended focal point.

Progress towards non-invasive microwave-induced thermal therapy of breast cancer has been made over the past decade. Fenn et al. (1999), Gardner et al. (2002), and Vargias et al. (2004) conducted clinical studies of an adaptive microwave phased array with an invasive electric-field feedback probe. The breast was compressed in order to immobilize the tissue and improve the coupling of microwave energy into the breast. The electric-field probe was used to adjust the phased array to achieve a focus at the treatment site. A more comprehensive review of these and other clinical studies was recently reported by Dooley et al. (2009). Theoretical studies of other focusing methods, such as time reversal (Guo et al. 2005, Kosmas et al. 2007), use of a deformable mirror (Arunachalam et al. 2007), and transmit beamforming (Converse et al. 2004, Converse et al. 2006), were conducted using computational electromagnetic (EM) and thermal simulations with two-dimensional (2-D) numerical breast phantoms of varying realism. While these techniques are intended to achieve focusing of microwave energy non-invasively, the theoretical performance demonstrations were successful in part because some degree of knowledge about the breast tissue configuration and dielectric properties was assumed to be available.

The objective of this 3-D numerical study is to evaluate the sensitivity and robustness of non-invasive transmit beamforming for hyperthermia treatment of localized breast tumors for future clinical implementation. Transmit beamforming involves passing microwave signals through a set of filters which are designed to compensate for dispersive propagation effects in the interior of the breast so that, ideally, the transmitted signal from each antenna adds coherently at the treatment location and incoherently elsewhere. The efficacy of transmit beamforming depends on the quality of the assumed propagation model used in the design of the filters. The propagation model describes the one-way propagation effects from each antenna to the target location. In this numerical study, we investigate the use of propagation models of varying complexity and fidelity in the design of the beamformer; that is we investigate the use of patient-specific information under the assumption that the exact knowledge about the patient's breast may not be available.

The performance of microwave beamforming is assessed within the frequency range of 1 - 5 GHz. This frequency range is higher than the operating frequencies of most clinical applicators, which generally operate at a frequency within the 100 - 1000 MHz band (see, for example, Vernon et al. 1996, Van der Zee et al. 2002). We are interested in higher frequencies because they offer better resolution for the treatment of cm-size lesions ($\lambda \sim 4.3$ cm at 1 GHz and $\lambda \sim 0.90$ cm at 5 GHz, where λ is the wavelength in glandular tissue) and adequate penetration through breast tissue ($\delta_{\text{fat}} \sim 20.2$ cm, $\delta_{\text{glandular}} \sim 4.2$ cm at 1 GHz and $\delta_{\text{fat}} \sim 5.5$ cm, $\delta_{\text{glandular}} \sim 0.85$ cm at 5 GHz, where δ is the depth at which the amplitude of an electromagnetic plane wave is attenuated by $1/e$).

This numerical study represents significant advances over past studies (Converse et al. 2004, Converse et al. 2006) in terms of the realism of the testbeds used. The 2-D phantoms used in past studies underestimated the degree of dielectric heterogeneity of breast tissue and overestimated the dielectric contrast between normal and malignant breast tissue — both of which overly simplified the challenge of selectively heating the tumor. In this study, we use three-dimensional (3-D) anatomically realistic numerical breast phantoms as our numerical

testbeds. The dielectric properties of the phantoms are obtained from the Wisconsin-Calgary large-scale dielectric spectroscopy study (Lazebnik et al. 2007a). We assume no contrast between normal fibroglandular and malignant tissue, instead of the ~10% contrast reported by Lazebnik et al. (2007b). This assumption eliminates the role of differential microwave power absorption in the selective heating of tumors, thereby creating a more challenging testbed wherein selective heating must be achieved solely by focusing.

2. Models and methods

Beamforming hyperthermia performance is evaluated in four virtual patients represented by numerical breast phantoms having different breast compositions. A patient-specific propagation model is constructed from 3-D finite-difference time-domain (FDTD) EM simulations of the numerical phantom and is used to design the beamformer signal set that is transmitted into the breast. Next, the hyperthermia performance of the beamformer signal set is evaluated by calculating heating potential and steady-state temperature distributions inside the breast using 3-D FDTD-EM and FDTD-thermal models.

2.1. Numerical testbeds

We utilize four anatomically realistic numerical breast phantoms derived from MRIs of patients with different breast compositions (Zastrow et al. 2008) as our virtual patients. The phantoms are digitized to $0.5 \text{ mm} \times 0.5 \text{ mm} \times 0.5 \text{ mm}$ resolution. The specific numerical phantoms chosen for this study include one example of each of the following four American College of Radiology categories of breast tissue density (D'Orsi et al. 2003): fatty, scattered fibroglandular, heterogeneously dense, and extremely dense. The phantoms capture natural variations not only in breast tissue density but also in breast shape and size across the general patient population. The tumors in the phantoms are embedded within normal fibroglandular tissue. We assume no dielectric properties contrast between the tumor and surrounding fibroglandular tissue. The lack of contrast in conductivity creates a worst-case selective heating scenario. This is a significant difference from the previous studies of Converse et al. (2004) and Converse et al. (2006), which assumed a high conductivity contrast between the desired focus (tumor) and the surrounding tissue.

Figure 1 depicts the four virtual patients used in this study. The patient is assumed to be in a prone position with three 8-element conformal arrays surrounding the breast as shown in Figure 1 by the circles. The arrays are placed at elevations $x = x_f$ and $x = x_f \pm 1.5 \text{ cm}$, where x_f represents the x-coordinate of the desired focus. Figure 2 illustrates coronal cuts at $x = x_f$ through the four phantoms. The focus location for each patient is marked with a cross-hair. The desired focus is chosen to be located in fibroglandular tissue in each phantom at a depth at least 2 cm from the skin and not near the chestwall. The array elements are vertically directed electric current sources. Each element is excited with the corresponding beamformer output signal. Forced-air cooling of 20°C is assumed in the environment surrounding the breast. The optimal antennas, array configuration, and coupling medium for clinical hyperthermia experiments may differ from those employed in this study. For example, these omnidirectional antennas are too inefficient for a clinical hyperthermia system, but suffice to evaluate focusing performance. Also, hyperthermia performance may be further improved with the use of an optimized array configuration and an optimal choice of coupling medium between the antennas and the breast.

2.2. Beamformer design

The beamformer consists of a finite-impulse response (FIR) filter in each antenna channel. The filters are designed to focus microwave energy at the target region by adjusting the frequency-dependent amplitude and phase of transmitted signals. Let $H_n(\omega)$, $n = 1, \dots, N$ be

the frequency response of the FIR filter for the n th channel, and let $T_n(\omega, \mathbf{r}_f)$ represent the frequency-dependent one-way propagation from the n th source to the target location $\mathbf{r}_f$. The beamformer design objective is to maximize the fraction of the total transmitted power delivered to the target location $\mathbf{r}_f$. This is expressed mathematically as

$$\max_{H_n(\omega)} \frac{\int \left| \sum_{n=1}^N H_n(\omega) T_n(\omega, \mathbf{r}_f) \right|^2 d\omega}{\int \sum_{n=1}^N |H_n(\omega)|^2 d\omega} \quad (1)$$

We solve (1) by writing $H_n(\omega) = \sum_{k=1}^{M-1} h_n[k] e^{-j\omega k T_s}$, where $h_n[k]$, $k = 0, 1, \dots, M-1$ are the FIR filter coefficients in the n th channel and T_s is the sampling interval. The FIR filter coefficients are then obtained by solving an eigenproblem as in Haykin (2002). After the FIR filter coefficients are determined, the transmitted signal at each channel is then obtained by passing a desired input signal through the filter,

$$Y_n(\omega) = H_n(\omega) I(\omega) \quad (2)$$

where $I(\omega)$ is the input signal spectrum. Previous studies used a simple analytical propagation model to obtain $T_n(\omega, \mathbf{r}_f)$ (see, for example, Converse et al. 2004). In this study we use FDTD simulations to accurately identify $T_n(\omega, \mathbf{r}_f)$ for each propagation model.

Four types of propagation models — one heterogeneous and three homogeneous — are constructed for each patient. The heterogeneous model assumes that full knowledge of the patient's breast is available, including not only the breast shape and interior tissue structure, but also the spatially varying tissue dielectric properties. This knowledge permits us to construct a propagation model that corresponds to the true propagation characteristics of the patient's breast. Thus, Figure 1 depicts not only the numerical phantoms but also the heterogeneous propagation models for the four patients. The range of dielectric properties for heterogeneous propagation models is illustrated in Figures 3(a) and 3(b). Each of the three homogeneous propagation models is constructed under the assumption that the knowledge of the breast shape and the skin thickness is available. The interior properties are either patient-specific average properties or one of two different patient-independent properties. The patient-specific average properties are obtained by spatially averaging the true properties of each patient; we denote this propagation model as “homogeneous-average.” Since we consider four specific patients in this study, one from each of four classes of breast density, we have four examples of homogeneous-average models. The “homogeneous-low” propagation model consists of patient-independent median adipose properties reported in the Wisconsin-Calgary study (Lazebnik et al. 2007a) while the “homogeneous-high” propagation model consists of patient-independent properties that are equal to 3.5 times the median adipose properties. Figures 3(c) and 3(d) illustrate the wideband dielectric properties of the interior breast tissue for the three homogeneous propagation models.

2.3. Performance evaluation methods

The four distinct propagation models described in Section 2.2 are used to design the beamformer for each of the four virtual patients. This results in a total of 16 different pairings between patients and propagation models. A transmit signal set is calculated for each case and hyperthermia performance is evaluated for both wideband operation (1-5 GHz, 10% power bandwidth) and narrowband operation at seven different frequencies

evenly spaced between 1 and 4 GHz. This results in 128 simulated hyperthermia experiments.

The computational domain of the FDTD-EM model comprises a uniform spatial grid of cubic Yee cells. The grid cell size of $\Delta x = \Delta y = \Delta z = 0.5$ mm provides a grid sampling density of $N_\lambda \sim 18$ in glandular tissue at 5 GHz. Uniaxial perfectly matched layer (UPML) absorbing boundary conditions are used to terminate the computational domain. Materials dispersion is incorporated into the FDTD model via the auxiliary differential equation method (Taflöv and Hagness 2005). A Courant factor of $S = 0.5$ is chosen to ensure stability. The distribution of the heating potential, Q [W/m³], inside the numerical breast phantoms is evaluated for wideband operation using the FDTD-computed time-domain field quantities as follows:

$$Q_{i,j,k} = R \sum_{n=0}^{n_{\max}} (\vec{E}_{i,j,k}^n \cdot \vec{J}_{i,j,k}^n) \Delta t \quad [\text{W/m}^3] \quad (3)$$

Here i, j, k are the computational grid indices, R is the assumed pulse repetition rate, t is the FDTD timestep, $\vec{E}$ and $\vec{J}$ are the time-domain electric field and total current density vectors, respectively, and $n_{\max}$ is the maximum timestep in the simulation. Similarly, Q is evaluated for narrowband operation using the following expression:

$$Q_{i,j,k} = \frac{1}{T} \sum_{n=n_{\max}-n_{\text{period}}}^{n_{\max}} (\vec{E}_{i,j,k}^n \cdot \vec{J}_{i,j,k}^n) \Delta t \quad [\text{W/m}^3] \quad (4)$$

where T is the period of the transmitted signal and n_{period} is the number of time steps in one period. The simulations are executed until steady-state field interactions are established. In both (3) and (4), we use the six-field-component averaging approach described in Caputa et al. (1999).

A 3-D FDTD-thermal model based on the Pennes bio-heat equation (Pennes 1948) is used to obtain the steady temperature profile in the numerical breast phantoms.

$$C_p(\mathbf{r}) \rho(\mathbf{r}) \frac{\partial T(\mathbf{r})}{\partial t} = \nabla \cdot (K(\mathbf{r}) \nabla T(\mathbf{r})) + A_0(\mathbf{r}) + Q(\mathbf{r}) - B(\mathbf{r}) (T(\mathbf{r}) - T_b) \quad [\text{W/m}^3] \quad (5)$$

The tissue-dependent thermal parameters, C_p , ρ , K , A_0 , B , are the specific heat, density, thermal conductivity, metabolic heat generation, and capillary blood perfusion coefficient, respectively. The blood perfusion coefficient for each tissue is assumed to be time-independent and is assigned its basal value. We assume that T_b , the blood temperature, is constant and equal to the body's core temperature of 37°C. Q is the heating potential computed by the FDTD-EM model. We assign the thermal properties of fat and muscle to the parameters for fatty and fibroglandular breast tissue, respectively. The thermal properties of fatty breast tissue and skin used in the thermal model are the same values found in Converse et al. (2006). The thermal properties of fibroglandular breast tissue and muscle chest wall are the same as the thermal properties of muscle listed in Gosalia et al. (2004). The thermal properties are summarized in Table 1. A convective heat boundary condition is employed at the skin-air interface with a convection coefficient of $h = 5$ [W/m²/°C] — a value appropriate for natural convection or low-flow forced convection of air (Seagrave 1971). The FDTD implementation of (5) and the convective heat boundary condition follows the method described in Bernardi et al. (2003). The grid resolution of the FDTD-

thermal model is identical to that used in the FDTD-EM model. The FDTD-thermal simulations are executed until the steady-state temperature is reached.

The relative amplitude and phase of each signal to be transmitted into the breast is obtained from (2). However, the absolute amplitude across the array — that is, the input power required to achieve the desired temperature — is not determined by the beamformer design process. Therefore, our strategy is to conduct an FDTD-EM simulation using the beamformer signal set obtained from (2) and compute the heating potential. Then we conduct several FDTD thermal simulations using scaled versions of the heating potential as the source to determine the amplitude factor that achieves a steady-state temperature at the desired focus, $\mathbf{r}_f$, of $45 \pm 0.15^\circ\text{C}$. Finally the steady-state temperature distribution is reported for the appropriately scaled transmitted signal set.

3. Results

We quantify the selective heating efficacy of transmit beamforming using several thermal metrics defined as follows:

- i. V_{43} (cm^3): the volume of breast tissue with temperature greater than 43°C .
- ii. r (mm): the radial distance from $\mathbf{r}_f$ to the location of peak breast interior temperature.
- iii. t_{skin} ($^\circ\text{C}$): peak skin temperature.
- iv. t_{breast} ($^\circ\text{C}$): peak breast interior temperature.

Our goal is to induce therapeutic heating in a volume of tissue roughly on the order of 1 cm^3 . This is considered to be a small volume in the context of microwave hyperthermia. In addition to a small V_{43} , we consider accurate focusing (small r), a low peak skin temperature (low t_{skin}), and a peak breast interior temperature close to the temperature at $\mathbf{r}_f$ ($t_{\text{breast}} \approx 45^\circ\text{C}$) to be desirable. For each patient, the hyperthermia experiments are evaluated for four distinct propagation models used in beamformer design: heterogeneous, homogeneous-average, homogeneous-low, and homogeneous-high. For each propagation model, we consider beamforming performance under seven different cases of narrowband operation and under wideband operation. Beamforming performance for the 32 experiments performed on each of the four patients is reported in two stages to streamline the presentation. In Section 3.1, we consider performance as a function of operating frequency, while in Section 3.2 we consider performance as a function of the propagation model used in beamformer design.

3.1. Performance as a function of operating frequency

Figure 4 illustrates the narrowband performance trends for the four patients as a function of operating frequency, in terms of the thermal metrics defined above. Results are shown for the case where a heterogeneous propagation model is used to design the transmit signal set. The trends indicate that for each patient, there exists an operating frequency at which the narrowband beamformer achieves a desirable outcome. This optimal frequency depends upon the physical structure and tissue composition of the breast.

The results in Figure 4 indicate that in the fatty breast, the smallest V_{43} ($\sim 1.6 \text{ cm}^3$), and the smallest r ($\sim 1.4 \text{ mm}$) are achieved at the operating frequency of 3.0 GHz. The peak temperatures in the skin and the breast interior increase slightly at operating frequencies greater than 3.0 GHz. The operating frequency for the scattered fibroglandular breast with minimum V_{43} ($\sim 0.4 \text{ cm}^3$) is 4.0 GHz while minimum r ($\sim 1.0 \text{ mm}$) occurs at 1.0 GHz. However, the peak skin temperature reaches an unsafe value ($t_{\text{skin}} \sim 45^\circ\text{C}$) at 1.0 GHz.

Therefore, the optimal operating frequency for the scattered fibroglandular breast is 4.0 GHz. For these two low density breasts (fatty and scattered fibroglandular), the results presented in Figure 4 show small variations in the heating zone size and focusing accuracy over the frequency range of interest.

In contrast, the performance trends presented in Figure 4 for the heterogeneously dense breast and extremely dense breast show significant variations in the heating efficacy over the frequency range of interest. The narrowband frequency for the heterogeneously dense breast with minimum V_{43} ($\sim 1.4 \text{ cm}^3$) and r ($\sim 2.1 \text{ mm}$) is 1.5 GHz. For the extremely dense breast, the best performance is also observed at an operating frequency of 1.5 GHz, which yields the smallest V_{43} ($\sim 1.6 \text{ cm}^3$) and the smallest r ($\sim 1.2 \text{ mm}$). For these two high density breasts (heterogeneously dense and extremely dense), the results presented in Figure 4 show the peak skin and the peak breast interior temperatures increasing rapidly for operating frequencies greater than 2.0 GHz. Poor focusing accuracy, indicated by $r > 10 \text{ mm}$, occurs at operating frequencies greater than 3.0 GHz.

Figures 5-8 present the normalized EM heating potential and steady-state temperature distributions as a function of operating frequency for patients with fatty and extremely dense breasts. Figures 5 and 6 depict $Q(r)$ normalized to $Q(\mathbf{r}_f)$, and the corresponding steady-state temperature distribution, respectively, in the coronal plane containing $\mathbf{r}_f$ for the fatty breast. The normalized Q of 0 dB corresponds to a specific absorption rate of 181, 305, 340, and 348 W/kg in Figures 5(a), 5(b), 5(c), and 5(d), respectively. Figures 7 and 8 depict similar information for the extremely dense breast. The specific absorption rates corresponding to a normalized Q of 0 dB in Figures 7(a), 7(b), 7(c), and 7(d) are 141, 218, 215, and 118 W/kg, respectively. Detailed discussion of these results is provided in Section 4.

The results presented in Figure 9 compare steady-state temperature distributions for wideband excitation and the optimal narrowband frequency in fatty and extremely dense breasts. We observe that narrowband excitation at the optimal frequency results in slightly better selective heating performance in the extremely dense breast and comparable performance in the fatty breast. The similarity between wideband and optimal narrowband performance in the fatty breast is evident by comparing the steady-state temperature distributions shown in Figures 9(a) and 9(b). For the extremely dense breast, the performance with wideband excitation (Figure 9(c)) is poorer than that with the optimum narrowband excitation of 1.5 GHz (Figure 9(d)); namely, the treatment region obtained with wideband excitation is skewed from $\mathbf{r}_f$. The skin temperature remains below 30°C for both excitations.

3.2. Performance as a function of propagation model complexity

In this section, we report the selective heating performance as a function of propagation model assumed in the design of the beamformer. We begin by reporting the performance of the narrowband beamformer at the optimal operating frequency. The optimal operating frequency varies within a given patient, depending on the propagation model used in the beamformer design. The bar graphs in Figure 10 illustrate the best achievable performance in each pairing of patient and propagation model. The heterogeneous model generally provides the best overall performance. The metrics V_{43} and r are more sensitive to propagation model choice than t_{skin} and t_{breast} .

Figure 11 illustrates the performance of the wideband beamformer in each pairing of patient and propagation model. The performance trends of the wideband beamformer for the four patients follow the narrowband performance trends. For the fatty and scattered fibroglandular breasts, the performance is comparable across the four propagation models while for the patients with more heterogeneous breast tissue (heterogeneously dense and

extremely dense), the use of patient-specific propagation models (heterogeneous or homogeneous-average) generally provides better selective heating in the breast.

In order to separate the effects of heterogeneity and misestimation of tissue properties, we consider a virtual patient with homogeneous breast tissue. We assume wideband operation and construct seven homogeneous propagation models: correct properties and $\pm 25\%$, $\pm 50\%$, and $\pm 75\%$ misestimation of properties. The results are summarized in Table 2. The performance is found to degrade more rapidly with underestimation of properties than with overestimation.

4. Discussion

We first consider the performance of transmit beamforming as a function of narrowband operating frequency for fatty and extremely dense breasts. The EM heating potential in the interior of the fatty breast shown in Figure 5 is highest in the fibroconnective/glandular tissue region (see Figure 2(a) for tissue distribution), while absorption in the fatty region is minimal. These results are consistent with the differences in effective conductivity between fat and fibroglandular tissue. Absorption in the fatty region is only slightly elevated at higher frequencies. The elevated absorption in the fatty region at 4.0 GHz, illustrated in Figure 5(d), leads to a skewed treatment region in the direction of the elevated absorption region, as shown in Figure 6(d). The skin remains cool due to the 20°C forced air cooling over the range of frequencies considered. The treatment volume size (V_{43}) spans the range of 1.6-5.5 cm³.

In contrast, the heating zone size varies considerably with excitation frequency for the extremely dense breast as shown in Figures 7 and 8. The treatment region is skewed and grossly enlarged at the higher operating frequencies. Note that V_{43} spans a wider range (1.6-25.7 cm³) in extremely dense breast tissue than in fatty tissue. This is a direct consequence of the presence of a greater amount of fibroconnective/glandular tissue (see Figure 2(d) for tissue distribution).

Next we consider the selective heating performance as a function of the propagation model assumed in the design of the beamformer for the fatty and extremely dense breasts. We limit the discussion to these two patients as they represent the least and most challenging testbeds, respectively, for selective heating. For both patients, we observe a slight decrease in the heating zone volume when patient-specific propagation models (heterogeneous or homogeneous-average) are used in the beamformer design. The performance in the fatty breast is comparable for the three homogeneous propagation models as shown in Figures 10 and 11. The best achievable V_{43} in the fatty breast ranges from 1.6 cm³ to 3.1 cm³ in the narrowband case and 1.9 cm³ to 3.1 cm³ in the wideband case, in spite of the fact that the homogeneous-high ϵ_r (dashed line in Figure 3(c)) overestimates the average ϵ_r of the patient by a large margin. Therefore, the results indicate that transmit beamforming is able to accommodate the overestimation of the average ϵ_r introduced in the homogeneous-high propagation model for this patient.

In contrast, the average ϵ_r of the extremely dense breast is close to the homogeneous-high ϵ_r (dashed line in Figure 3(c)) while the homogeneous-low ϵ_r (solid line in Figure 3(c)) significantly underestimates the average ϵ_r . Figures 10 and 11 show that the best achievable V_{43} ranges from 1.5 cm³ to 2.2 cm³ in the narrowband case and 3.0 cm³ to 4.6 cm³ in the wideband case for the heterogeneous, homogeneous-average and homogeneous-high propagation models. However, the use of homogeneous-low propagation model in the beamformer design leads to a larger heating zone, causing the best achievable V_{43} to increase to 4.3 cm³ and 13.8 cm³ in the narrowband and wideband cases, respectively.

Therefore, transmit beamforming is relatively sensitive to underestimation of average ϵ_r in this patient.

The results in Table 2 show that selective heating efficacy in a homogeneous phantom is also much more sensitive to underestimation of ϵ_r than to overestimation. Hence, we conclude that the sensitivity of transmit beamforming to underestimation of the average ϵ_r is not limited to scenarios with a high degree of heterogeneity, as in the extremely dense breast. These results indicate that overestimation of the average ϵ_r used in the beamformer design is preferable to underestimation.

5. Summary and conclusions

This study illustrates the potential of non-invasive patient-specific microwave hyperthermia treatment via transmit beamforming with assumed knowledge of the breast shape. 3-D anatomically realistic numerical breast phantoms with accurate dielectric properties of normal breast tissue were used as our testbeds. We have assumed that there is no conductivity contrast between malignant and normal fibroglandular tissue in order to create the most challenging selective focusing scenarios. Focus locations were chosen to be in fibroglandular tissue, at least 2 cm from the skin surface, and away from the chestwall. We have investigated the performance of transmit beamforming for patients with widely varying breast tissue density. Treatment regions as small as 1-2 cm in size were achieved within the breasts considered in the study. We have explored the use of patient-specific propagation models of varying complexity. Use of propagation models with patient-specific dielectric properties improves the focusing efficacy of beamforming — particularly in dense breasts. Complete patient-specific knowledge such as interior tissue structure, and the dielectric properties of breast tissue, is not needed to obtain selective heating for effective hyperthermia treatment as long as appropriate homogeneous properties of the breast are chosen for the propagation model. In general, the performance of microwave hyperthermia via transmit beamforming is more sensitive to underestimation of properties in the propagation model than overestimation. Lastly, the study also indicates that for each patient, there exists a narrowband frequency at which focusing is optimum and slightly better than that obtained with wideband focusing. The promising results obtained here suggest that future work involving experiments with physical phantoms is warranted.

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Figure 1.

Cutaway view showing the relative permittivity distribution at 5 GHz in each of four 3-D numerical breast phantoms used as performance testbeds. The desired focus is indicated by a cross-hair and the 24 antenna locations are marked by small circles. The phantoms are representative of all four categories of breast tissue density. (a) Fatty. (b) Scattered fibroglandular. (c) Heterogeneously dense. (d) Extremely dense. (Original figures in colour)

Figure 2.

Relative permittivity distribution in the coronal cross-section containing the desired focus (indicated by a cross-hair) in each of the phantoms of Figure 1. The antenna locations at elevation $x = x_f$ (noted in the upper right corner of each image) are indicated by 'o' markers. (a) Fatty. (b) Scattered fibroglandular. (c) Heterogeneously dense. (d) Extremely dense.

Figure 3.

(a) Relative permittivity as a function of frequency for representative voxels in the heterogeneous propagation model. (b) Effective conductivity as a function of frequency corresponding to the data shown in (a). (c) Relative permittivity as a function of frequency in the homogeneous-low, homogeneous-high, and homogeneous-average propagation models. (d) Effective conductivity as a function of frequency corresponding to the data shown in (c). (Original figures in colour)

Figure 4. Selective heating efficacy quantified in terms of four thermal metrics for the four virtual patients, as a function of frequency. Results are shown for the case where a heterogeneous propagation model is used to design the transmit signal set. (a) Volume of breast tissue with temperature greater than 43°C. (b) Distance from the desired focus to peak breast interior temperature. (c) Peak skin temperature (°C). (d) Peak breast interior temperature (°C).

Figure 5. Normalized EM heating potential (coronal cross-section) resulting from narrowband focusing at different operating frequencies, for a patient with fatty breast composition (see Figures 1(a) and 2(a)). Results are shown for the case where a heterogeneous (exact) propagation model is used in the beamformer design. The contour lines indicate -10 dB contours. (a) 1 GHz. (b) 2 GHz. (c) 3 GHz. (d) 4 GHz.

Figure 6. Steady-state temperature distribution (coronal cross-section) corresponding to the heating potential of the fatty breast shown in Figure 5. (a) 1 GHz. (b) 2 GHz. (c) 3 GHz. (d) 4 GHz.

Figure 7. Normalized EM heating potential (coronal cross-section) resulting from narrowband focusing at different operating frequencies, for a patient with extremely dense breast composition (see Figures 1(d) and 2(d)). Results are shown for the case where a heterogeneous (exact) propagation model is used in the beamformer design. The contour lines indicate -10 dB contours. (a) 1 GHz. (b) 2 GHz. (c) 3 GHz. (d) 4 GHz.

Figure 8. Steady-state temperature distribution (coronal cross-section) corresponding to the heating potential of the extremely dense breast shown in Figure 7. (a) 1 GHz. (b) 2 GHz. (c) 3 GHz. (d) 4 GHz.

Figure 9.

Comparison of steady-state temperature distributions (coronal cross-section) resulting from wideband focusing and narrowband focusing at the optimum frequency. Results are shown for the case where the heterogeneous (exact) propagation model is used in the beamformer design. (a) wideband (fatty). (b) optimum narrowband (fatty, 3.0 GHz). (c) wideband (extremely dense). (d) optimum narrowband (extremely dense, 1.5 GHz).

Figure 10.

The best achievable selective heating efficacy of narrowband operation quantified in terms of four thermal metrics for the four patients (fatty, scattered fibroglandular, heterogeneously dense, extremely dense), as a function of propagation model complexity used in the beamformer design (heterogeneous, homogeneous-average, homogeneous-low, homogeneous-high). The results are shown at the optimal narrowband frequency of each pairing of patient and propagation model. (a) Volume of breast tissue with temperature greater than 43°C. (b) Distance from the desired focus to peak breast interior temperature. (c) Peak skin temperature (°C). (d) Peak breast interior temperature (°C).

Figure 11.

Selective heating efficacy of wideband operation quantified in terms of four thermal metrics for the four patients (fatty, scattered fibroglandular, heterogeneously dense, extremely dense), as a function of propagation model complexity used in the beamformer design (heterogeneous, homogeneous-average, homogeneous-low, homogeneous-high). The results are shown for each pairing of patient and propagation model. (a) Volume of breast tissue with temperature greater than 43°C. (b) Distance from the desired focus to peak breast interior temperature. (c) Peak skin temperature (°C). (d) Peak breast interior temperature (°C).

Table 1

Thermal properties used in the FDTD-thermal model

Tissue	C_p [J/kg ^o C]	ρ [kg/m ³]	K [W/m ^o C]	A_0 [W/m ³]	B [W/m ^{3/°C}]
skin	3765	1085	0.397	1620	5929
fatty tissue	2279	1069	0.306	350	2229
fibroglandular tissue and muscle (chest- wall)	3600	1050	0.5	690	2700

Table 2

Selective heating efficacy quantified in terms of four thermal metrics evaluated for a numerical phantom with homogeneous breast tissue. Homogeneous propagation models are used in the wideband beamformer design. The performance is evaluated as a function of dielectric properties mismatch with respect to the true properties of the breast. A negative (positive) percentage mismatch refers to the case in which the propagation model underestimates (overestimates) the dielectric properties

% mismatch	V_{43} (cm ³)	r (mm)	t_{skin} (°C)	t_{breast} (°C)
-75%	6.89	2.01	32.40	46.54
-50%	5.00	1.66	32.38	46.36
-25%	3.87	1.37	32.24	46.09
0%	3.47	1.35	32.29	45.96
+25%	3.41	1.39	32.66	45.92
+50%	3.46	1.43	33.27	45.87
+75%	3.67	1.49	33.94	45.92