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ORIGINAL ARTICLE

Microwaves for breast cancer treatments



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KEYWORDS

Hyperthermia; APA; COMSOL MULTIPHYSICS **Abstract** Hyperthermia is potentially an effective method for the treatment of cancer, especially breast cancer tumors. One of the most attractive attributes of hyperthermia is the possibility of providing therapeutic benefit noninvasively, minimizing side effects. To be effective, a hyperthermia treatment must selectively heat the cancerous tissue, elevating the temperature in the tumor without exposing healthy tissue to excessive temperature elevations. In this paper, a suggested simple model of Annular Phased Array (APA) using eight half wavelength linear dipoles is presented. New software (COMSOL MULTIPHYSICS) is used to calculate the temperature distribution inside a model of a three layered breast (skin, breast tissue, and tumor). In addition, the effect of changing the amplitude and phases of the array elements on the temperature distributions and the conditions on the values of the phases are demonstrated in order to achieve the objective of hyperthermia for breast tumor treatment.

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1. Introduction

Breast cancer is a 'multi-factorial' disease, a term describing a condition that is believed to have resulted from the interaction of genetic factors, with environmental factor, or factors. Available techniques for treating breast cancer often introduce strong side effects. The most common treatment is surgical treatment such as mastectomy, a radical approach which comes down to removing the entire breast, or lumpectomy, where only part of the breast is removed. Ablative therapies such as radiation therapy and chemotherapy that cause cellular damage are also common. In the thermal treatment of cancer, the tissue temperature is raised in order to kill the malignant tissue. The thermal treatment of cancer has a lot of potential, since it can offer a noninvasive treatment with low side effects. Therefore, further development of this approach deserves attention [1].

In oncology, the term 'hyperthermia' refers to the treatment of malignant diseases by administering heat in various ways [2]. The objective of hyperthermia treatment of cancer is to raise the temperature in the tumor volume above 42–43 °C for a sufficient period of time while preserving normal physiological temperatures (well below 42 °C) in the surrounding tissue. One of the persisting challenges in achieving this objective with noninvasive electromagnetic (EM) hyperthermia treatment is focusing EM power in the cancerous tissue while avoiding the introduction of auxiliary foci in normal tissue.

In the microwave frequency range, energy is coupled into tissues through waveguides or antennas (applicators) that emit microwaves. The shorter wavelengths of microwaves, as compared to RF, provide the capability to direct and focus the energy into tissues by direct radiation from a small applicator [2].

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The challenge in focused microwave ablation is to avoid heating the healthy tissue while heating the tumor. The relatively high conductivity of tumor tissue increases the local heating potential, and thus high temperature gradients can be obtained. However, healthy glandular tissue and skin tissue also possess a high conductivity, which implies that secondary (unwanted) hot spots may appear there. Hot spots in the healthy tissue result in undesired side effects such as extra pain, burns and blisters. Also, these hot spots deteriorate the system efficiency. Several techniques that focus EM energy at a tumor have been developed in the past. A more flexible approach for focusing EM energy is the use of a phased array system. The resulting power distribution can be steered by adjusting the amplitude and phase of each array element. This type of applicator has already been used in EM systems and at RF. It is shown that a phased array can be used to adaptively steer nulls at pre-assigned areas of the target body, while heating the part that contains the tumor. However, thermal ablation is not possible at these frequencies since the focal spot includes a large part of the body [2-7].

The problem of radiation of EM waves by an antenna in a given environment is essentially that of solving Maxwell's equations subject to the boundary conditions introduced by both the radiating antenna and its environment. Techniques to solve radiation problems can be divided into two broad classes: frequency domain and time domain. In the past, frequency domain techniques have been widely used to analyze antenna radiation. Also, a time domain method, the finite-difference time-domain (FDTD), is applied to model and predict antenna radiation. In this technique the physical space is split into elementary elements that must be smaller than both the shortest wavelength of interest and the smallest details of the geometry of the objects to be placed within the part of space of interest [8].

The perfectly matched layer, PML, is a new technique developed for the simulation of free space with FDTD method. For solving interaction problems with the finite-difference method, various techniques have been used in the past to absorb the outgoing waves, such as the matched layer [9], which consisted of surrounding the computational domain with an absorbing medium whose impedance matches that of free space, or the one-way approximation of the wave equation [10-13]. To obtain satisfactory solutions, it is well known that these absorbing boundaries must be set at some distance from the scattering structure with the result that most of the computational domain is a surrounding vacuum.

The EM phased array has the potential to overcome many of the difficulties associated with noninvasive hyperthermia, and is more effective if the driving amplitudes and phases of the array are carefully selected. A variety of approaches have been suggested to determine the optimal driving signals of phased arrays for hyperthermia. Perhaps the simplest approach is the phase-conjugate focusing scheme, in which the driving signals are chosen so that the EM radiation from each radiator interferes constructively at the desired focal spot. A major drawback of this approach is that it makes no provision for the reduction of hot spots. A more flexible approach to selecting optimal phased-array driving signals is to maximize the power deposition at the tumor site over the surrounding healthy tissues site. It has been shown that this approach can indeed focus a phased array in the presence of EM inhomogeneities without inducing hot spots [14-16].

 Table 1
 Electrical and thermal properties of skin, breast, and tumor at 6 GHz [21,22].

Tissue	Density (kg/m ³)	Relative permittivity	Thermal conductivity (W/m K)	Electric conductivity (S/m)
Skin	1200	39	0.5	1.1
Breast	1020	4.49	0.37	0.59
Tumor	1000	50	0.5	4

Table 2	The dipol	les parameters.
	Inc appor	co parameters.

Parameter	Value
Wavelength (λ)	5 cm
Arm length $(\lambda/2)$	2.5 cm
Radius of the dipole	0.125 cm
Gap size	0.5 mm



Figure 1 The developed breast model with the applied PML in COMSOL.

Numerous investigations have been conducted over the past several decades to explore and evaluate methods of focusing EM energy using arrays that transmit amplitude- and phase-adjusted narrowband (NB) signals. In contrast, until very recently, less attention has been given to the possibility of using multiple-frequency or ultra-wideband (UWB) signals.

The use of a multi-antenna array offers the opportunity for transmitting signals that constructively interfere at a desired location and, thus, provide selective heating. Constructive interference is obtained with NB (single-frequency) focusing methods [17], by adjusting the amplitude and phase of a sinusoidal signal in each antenna channel to compensate for the expected radial spreading and time delay incurred when the signal propagates from the antenna to the target focal point. In [18], the UWB approach uses a space–time beam-former



Figure 2 The temperature distribution of the breast for all dipoles amplitudes (a) 10 V, (b) 15 V, (c) 18 V, and (d) 20 V.



Figure 3 The arrangement of each dipole phase.

to implement frequency-dependent amplitude and phase adjustments in each channel. Thus, analogous to NB methods, UWB methods also exploit constructive/destructive interference in space. However, an UWB approach further exploits incoherent combining of power across frequency and space.

In [19], a computational study comparing the performance of NB microwave hyperthermia for breast cancer treatment with a recently proposed UWB approach is presented using anatomically realistic numerical breast phantoms containing a 2-mm-diameter tumor.

From this study, it is observed the disadvantages of UWB for breast cancer treatment. First, the design of UWB transmit focusing is more complex than NB design. Second, UWB focusing yields higher absorbed power near the surface of the breast. The results show that NB focusing performs reasonably well when the excitation frequency is optimized. In this paper, a special case of NB (single frequency) is used.

Table 3Different phases trials

Trial no.	Φ_1	Φ_2	Φ_3	Φ_4	Φ_5	Φ_6	Φ_7	Φ_8
1	0	0	0	0	0	0	0	0
2	0	5	10	15	20	25	30	35
3	0	10	20	30	40	50	60	70
4	0	20	40	60	80	100	120	140
5	0	20	30	40	50	60	70	80
6	0	30	40	50	60	70	80	90
7	0	40	50	60	70	80	90	100
8	0	-40	-50	60	70	80	90	100
9	90	100	0	-40	-50	60	70	80
10	70	80	90	100	0	-40	-50	60
11	-50	60	70	80	90	100	0	-40
12	0	-60	-50	60	70	80	90	100
13	0	-80	-50	60	70	80	90	100
14	0	-100	-50	60	70	80	90	100
15	0	-120	-50	60	70	80	90	100
16	90	100	0	-100	-50	60	70	80
17	70	80	90	100	0	-100	-50	60
18	-50	60	70	80	90	100	0	-100
19	0	-80	-30	40	50	60	70	80
20	0	-90	-40	50	60	70	80	90
21	0	-120	-70	80	90	100	110	120

The organization of the paper is as follows. Section 2 describes generating a 3D breast model with eight half wavelength dipoles. Section 3 shows the experimental results.

2. Generating a 3D breast model with eight half wavelength dipoles

The breast model was developed using COMSOL MULTIPHYSICS 4.3 [20], which is presented as a 5 cm wide and 5 cm high cone (prone configuration). The breast volume consists of breast skin and remaining volume consisting of breast fatty tissues. In the simulations the skin thickness is ignored. The tumor is presented as 8 mm diameter sphere. The skin, breast tissue, and the tumor electrical and thermal properties at the operating frequency 6 GHz are shown in Table 1. The developed breast model was simulated placing eight half wavelength dipoles 3 mm away from the breast.

Eight half wavelength linear dipoles of transverse electromagnetic (TEM) mode operating at 6 GHz were distributed around the breast. Each port has an input voltage V, and phase angle ϕ . A PML layer of 2.5 cm thickness is applied to the model. The dipoles parameters are shown in Table 2. The complete model of the breast, tumor, the eight half wavelength dipoles, and the applied PML is shown in Fig. 1.

The distribution of temperature inside the biological medium is obtained by solving the following bio-heat transfer equation (BHTE):

$$\rho C_{\rm P} \frac{\partial T}{\partial t} + \nabla \cdot (-k \nabla T) = \rho_b C_b \omega_b (T_b - T) + Q_{\rm met} \tag{1}$$

where ρ_b is 1025 kg/m³, C_b is 3639 J/kg k, ω_b is 0.0036 1/s, and $Q_{\text{met}} = 0$.



Figure 4 Temperature distribution when all phases assigned a zero phase value.

3. Results

In this section, the effect of different values of amplitudes and phases to reach the desired hyperthermia temperature and to control the heating area will be shown.

3.1. The effect of changing amplitudes

The goal is to find the best amplitude value in order to reach desired hyperthermia temperature. First each dipole is assigned an amplitude voltage equal to 10 V and the maximum temperature obtained is 38.6 °C, as shown in Fig. 2a; then, when each dipole is assigned an amplitude voltage equal to



Figure 5 Temperature distribution of the breast for different phase shift values, (a) at 5° phase shift, (b) at 10° phase shift, (c) at 20° phase shift.

Figure 6 Temperature distribution of the breast when using negative values to two of the phases in the first quarter $[\Phi_2 = -40^\circ, \Phi_3 = -50^\circ].$

15 V, the maximum temperature obtained is 40.5 °C, as shown in Fig. 2b, while when each dipole is assigned an amplitude voltage equal to 18 V, the maximum temperature equals 42 °C, as shown in Fig. 2c.

Finally, it is found that each dipole needs 20 V to produce maximum temperature close to 43 °C, which is the required maximum temperature for hyperthermia, as shown in Fig. 2d.

3.2. The effect of changing phases

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In this section, with taking all amplitudes equal to 20 V, a number of trials are achieved in order to find the values of each dipole phase needed to heat a certain area of the breast.

The eight dipole phases are from Φ_1 to Φ_8 , and are arranged as shown below in Fig. 3. In order to demonstrate the effect of phases on steering the heat area, the breast is divided into four quarters as shown in that figure. The central phases of each quarter are $(\Phi_2, \Phi_4, \Phi_6, \Phi_8)$. Table 3 shows the different phase values that have been tried.

When all phases were assigned a zero value, the heated area with a maximum temperature of 43 °C was at the center of the breast, while the temperature is kept at 38 °C on the surface of the breast due to the bolus as shown in Fig. 4. In Fig. 5 the effect of choosing different phase shift values of (5°, 10°, and 20°) between two adjacent dipoles starting from Φ_2 on the temperature distribution of the breast is shown. Fig. 5(a) shows when 5° phase shift is used, a very small change from the all zero valued phases, and the maximum temperature still concentrated at the center of the breast.

While when 10° phase shift is used the most heated area of the breast is in the first quarter, but also small areas from the rest of the breast were heated to the maximum temperature as shown below in Fig. 5(b). Now, when the phase shift is 20° , a worse result is obtained compared to the previous results as shown in Fig. 5(c). From the previous results, till now, it is observed that a 10° phase shift is the best phase shift value to be used compared to larger phase shift values. Next, our goal is to try to make the heating more focalized, so negative

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<mark>53</mark>37 ▼ 36.9310-3



Figure 7 Temperature distribution of the breast for different values of the central phase of the first quarter, (a) -40° , (b) -60° , (c) -80° , (d) -100° , (e) -120° .



Figure 8 Temperature distribution of the breast of the four quarters, (a) first quarter, (b) second quarter, (c) third quarter, and (d) the fourth quarter.

values will be assigned to two of the phases in the first quarter $[\Phi_2, \Phi_3]$ with $\Phi_1 = 0^\circ$, while positive values were given to the rest phases keeping a 10° phase shift between two adjacent dipoles to show its effect on the area been heated. In Fig. 6, $(\Phi_1 = 0^\circ, \Phi_2 = -40^\circ, \Phi_3 = -50^\circ)$, the maximum temperature was concentrated in the first quarter and a small portion of the second quarter.

In Fig. 7, five different values of Φ_2 [-40°, -60°, -80°, -100°, and -120°] will be compared in order to find the best value of Φ_2 to make the heating in the first quarter of the breast more focalized. From the shown figures, it is observed that when the central phase Φ_2 is equal to -100° the heat is more focalized in the first quarter than when it is equal to -40°, -60°, -80° or -120°. It can also be noticed that the value of the center phase in each quarter is a negative value and is equal to the largest positive value of the remaining phases which is in this case 100°. From the previous observations, the other quarters of the breast could be heated as shown in Fig. 8.

As noticed from the previous results that the value of the center phases in each quarter (Φ_2 , Φ_4 , Φ_6 , Φ_8) must be a negative value and must be equal to the largest positive value of the remaining phases, but it has been found that there is a limit for the largest positive value. In Fig. 9 different values for the largest positive phase larger and lower than 100° are tried. It has been observed that as long as the largest positive phase value is lower than or equal to 100° there is no hot spots compared to larger positive values than 100°.

4. Conclusions

The objective of hyperthermia treatment of cancer is to raise the temperature in the tumor volume above 42–43 °C for a sufficient period of time while preserving normal physiological



Figure 9 Temperature distribution of the breast when the largest positive value is as follows: (a) 80°, (b) 90°, (c) 100°, and (d) 120°.

temperatures (well below 42 °C) in the surrounding tissue. The APA has emerged as a popular alternative for the treatment of deep-seated tumor sites. For radiation from an APA to be focused at the tumor site without the formation of auxiliary foci ("hot-spots"), the driving phases and amplitudes of the array must be chosen carefully.

In this paper the effect of different values of the amplitudes and phases of the eight linear dipoles on the temperature distribution of the breast is shown. From all results, an observation was gained of how to choose the amplitudes and phases values to reach our objective. First, in order to heat any quarter of the breast to the desired maximum temperature (43 °C), the amplitudes of the eight dipoles must be equal to 20 V. Second, to focus the heat in any quarter of the breast, it is noticed that values of the three phases surrounding the quarter needed to be heated should be as follows: one should be assigned a zero value and the two phases following it should be assigned negative values equal to the largest positive value of the remaining phases. Third, the largest positive phase value must not be larger than 100° to reduce hot spots. Fourth, the remaining phases surrounding the rest of the breast must be kept with positive values and with 10° phase shifts.

5. Future works

In this paper NB (single frequency) focusing method is used. In future work, another types of antennas, such as rectangular microstrip patch antenna may be used in order to choose the best antenna for hyperthermia breast tumor treatments.

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