A New Heating Control Method for Effective Hyperthermia Treatment of a Brain Tumor Using the Resonant Cavity Applicator with a Segmented Dielectric Bolus

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Abstract : This paper describes a new heating control method of the proposed resonant cavity applicator for non-invasive brain tumor hyperthermia treatments. In the previous study, the resonant cavity applicator for treating brain tumors was proposed. In the present study, a dielectric bolus was used to control the heated location inside brain tumors. The dielectric bolus was divided into four sections filled with dielectric materials, such as water, and was attached to the human head inside the cavity. By changing the dielectric materials inside each section, the heated location could be controlled inside brain tumors. In this paper, first, the method for controlling the heated location with the dielectric bolus was presented. Second, two types of numerical models to calculate temperature distributions were described. First, we used a cylindrical phantom model for the basic study to check the ability of the proposed method. Second, we used a 3-D anatomical human head model which was reconstructed from 2-D medical images by using the 3-D computer aided design (CAD) software. Finally, the temperature profiles calculated by the 3-D finite element method (FEM) and heating experiments heated by the developed heating system were discussed. From the results of computer simulations and heating experiment with the agar phantom, it was confirmed that the results of the computer simulations were in close agreement with the results of the heating experiments with an error of 10% or less. Next, we calculated the temperature distribution of the 3-D anatomical human head model that takes into account the cooling effect of blood flow. The proposed heating method covered approximately 97% of the brain tumor size without an undesirable hotspot. From these results, it was found that the proposed heating control method is useful for effective hyperthermia treatments.

Key Words : resonant cavity applicator, brain tumor, dielectric bolus, temperature distribution, 3-D FEM

Introduction

As a human brain is protected by a skull, it is difficult to heat deep seated brain tumors non-invasively. In the clinic, the radio frequency (RF) interstitial hyperthermia system, which has a needle electrode to heat malignant brain tumors invasively, is used^{1,2)}. This heating system has advantages and disadvantages. One of the advantages is that a direct and local heated area around the needle is possible. The disadvantages are the small heated area around the needle and its inherent invasiveness. In order to overcome these problems, we have already proposed resonant cavity applicator for non-invasive brain tumor hyperthermia treatments^{3–5)}. From the results of computer simulations and heating experiments with the agar phantom, it was found that the proposed resonant cavity applicator could heat deep regions of the agar phantom^{4,5)}. Furthermore, we found that the center region of a dog brain was heated up to 42.5°C without generating undesirable hotspots⁶⁾.

For effective and safe hyperthermia treatments, it is necessary to heat brain tumors locally without undesirable hotspots corresponding to the symptoms of the patient. In our previous study, by changing the electromagnetic heating modes inside the cavity, the heated area could be controlled. Generally, inside the resonant cavity, various electromagnetic heating modes are generated corresponding to the resonant frequencies. For the proposed resonant cavity, we could select two electromagnetic modes, which were called the TM_{010} -like mode and the TM_{012} -like mode, to heat the deep regions of the agar phantom. The resonant frequencies were approximately 130 MHz and 370 MHz, respectively⁷⁾. From the results of computer simulations and heating experiments using the developed heating system, it was found that the heated area inside the agar phantom when using the TM_{012} -like mode covers approximately 50% of the heated area than when using the TM_{010} -like mode^{7,8)}.

For controlling the heated area, a method was proposed^{9–11)}. In the proposed heating control method, the position of the human head inside the cavity was changed. From our computer simulations and heating experiments, it was found that the heated location inside the brain tumor could be controlled when using the TM_{010} -like mode. However, when using the TM_{012} -like mode, which could heat a smaller area than when using the TM_{010} -like mode, it was not easy to control the heated location inside the brain tumor¹²⁾. To overcome these problems, we proposed a heating control method using a dielectric bolus^{13–15)}. The dielectric bolus was filled with dielectric materials, such as pure water, saline water and so on. By changing the dielectric materials inside the bolus, the heated location inside the object could be changed. In the study using the dielectric bolus, we showed the effectiveness of the proposed heating control method with the TM_{010} -like mode for the basic study^{13–15)}.

In the present paper, we demonstrate the possibility of a new heating control method by changing the dielectric materials inside the bolus comprising four sections to control the heated location with the TM_{012} -like mode. First, the proposed heating control method is presented. Second, the two numerical models which are used in the present study are described. We constructed a cylindrical simple phantom model and a 3-D anatomical human head model which was reconstructed from 2-D medical images by using 3-D CAD software. Third, the calculated temperature distributions were presented. From these results, it was shown that the proposed heating control method is useful for effective hyperthermia treatments.

Materials and method

Proposed heating control method with dielectric bolus

Fig. 1 shows an illustration of the proposed heating control method for the resonant cavity applicator. A human head was placed in the gap between the inner electrodes and was heated by electromagnetic fields stimulated inside the cavity without physical contact between the surface of the human head and the applicator. In the proposed method, the dielectric bolus, which was filled with a dielectric material such as water, was attached to the human head inside the cavity. The bolus was divided into four sections. By changing the electrical properties of each section, the heated location inside the brain tumor could be controlled.

Fig. 1. Illustration of the proposed new method with segmented dielectric bolus.

The tissue temperature (T) in a human head heated by electromagnetic energy can be calculated by equations (1)-(6) :

$$\nabla^2 \mathbf{E} + k^2 \mathbf{E} = 0 \quad (1)$$

$$k^2 = \omega^2 \mu \left(\varepsilon - j \frac{\sigma}{\omega} \right) \quad (2)$$

$$W_h = \frac{1}{2} \sigma |\mathbf{E}|^2 \quad (3)$$

$$\rho c \frac{\partial T}{\partial t} = \nabla \kappa \cdot \nabla T + W_h - W_c + W_m \quad (4)$$

$$W_c = (F\rho)_{\text{tissue}} \times (\rho c)_{\text{blood}} \times (T - T_b) \quad (5)$$

$$W_m = W_{m0}(1.1)^{\Delta T} \quad (6)$$

where $\mathbf{E}$ is the electric field vector, ω is the radial frequency, μ is the magnetic permeability, ε is the dielectric constant, σ is the electrical conductivity, ρ is the volume density of the tissue, c is the specific heat of the tissue, κ is the thermal conductivity, W_h is the heating energy, W_c is the cooling energy from blood flow, F is the blood flow rate, T_b is the blood temperature, W_m is the metabolic heat generation and W_{m0} is the basal metabolic heat generation rate. In $\Delta T = T - T_{M0}$, T_{M0} is the basal metabolic temperature. In equation (6), the metabolic heat generation W_m was assumed to increase 10 percent of W_{m0} depending on the temperature increase (ΔT)¹⁶⁾. Also, in equation (5), the blood flow rate F was assumed to increase as follows¹⁷⁾ :

$$F = \begin{cases} F_{ba} & (T < 39^\circ\text{C}) \\ F_{ba} \{ 1 + 0.8(T_{\text{tissue}} - 39) \} & (39^\circ\text{C} < T < 44^\circ\text{C}) \\ 5F_{ba} & (T > 44^\circ\text{C}) \end{cases} \quad (7)$$

where F_{ba} is the basal blood flow rate. Equations (1) and (4) could be solved numerically with the FEM⁴⁾.

Fig. 2 shows an algorithm for calculating temperature distribution with blood flow. In computer simulations, the commercial FEM software, JMAG-Studio (Tokyo, JSOL Co., Ltd.), does not have the function to take into account blood flow when calculating cooling energy. This function to calculate blood flow was described within the dotted line in Fig. 2^{14,16)}. In the developed process, heating power W_{hi} was recalculated for each time step “i” in the FEM calculation. The value of $W_{h(i+1)}$ in the new step was calculated from the value of W_h and W_{ci} in the last step¹⁶⁾.

Fig. 2. Algorithm for calculating temperature distribution with blood flow.

Simple cylindrical head model

Fig. 3 shows a computer simulation model for calculating temperature distributions. Fig. 3a presents the FEM model which was comprised of 261,269 elements. In the FEM calculation, the calculation area is divided into the finite area which is called an “element” shown in

Fig. 3. Computer simulation model for calculating temperature distributions. *a*, FEM model. *b*, Detailed view of phantom and segmented dielectric bolus model.

Fig. 3a. The cavity was 500 mm in diameter and 1,000 mm in height. To concentrate the heating energy inside the phantom, inner electrodes placed inside the cavity were used. These inner electrodes were 100 mm in diameter and 400 mm in height. A detailed view of the phantom and bolus model was shown in Fig. 3b. The dielectric bolus was attached to the phantom and was divided into four sections. The phantom was 180 mm in diameter and 130 mm in height. The physical parameters used in the computer

simulations are listed in Table I¹⁵⁾. The four sections of the bolus were filled with one of two liquids, which we call β and γ . We performed four tests, referred to as “Test 1” - “Test 4” in Table I, using different combinations of β and γ to fill the four sections of the bolus. In Table I, σ is the electrical conductivity, ϵ_r is the relative permittivity, κ is the thermal conductivity, c is the specific heat of the tissue and ρ is the volume density of the tissue.

Table I. Physical parameters used in the computer simulations.

	Case of the dielectric bolus			
	Test 1	Test 2	Test 3	Test 4
Phantom	α			
Segmented bolus A	β	β	β	β
Segmented bolus B	γ	β	β	β
Segmented bolus C	γ	γ	β	β
Segmented bolus D	γ	γ	γ	β

α : $\sigma=0.6[\text{S/m}]$, $\epsilon_r=75.0$, $\kappa=0.6 [\text{W/m } ^\circ\text{C}]$, $c=4,200[\text{J/kg } ^\circ\text{C}]$, $\rho=1,000[\text{kg/m}^3]$,
 β : $\sigma=0.0[\text{S/m}]$, $\epsilon_r=75.0$, $\kappa=0.6 [\text{W/m } ^\circ\text{C}]$, $c=4,200[\text{J/kg } ^\circ\text{C}]$, $\rho=1,000[\text{kg/m}^3]$,
 γ : $\sigma=0.0[\text{S/m}]$, $\epsilon_r=1.0$, $\kappa=0.025[\text{W/m } ^\circ\text{C}]$, $c=1,010[\text{J/kg } ^\circ\text{C}]$, $\rho=1.165[\text{kg/m}^3]$

Experimental conditions for heating the agar phantom

Fig. 4 shows a photograph of the setup of the developed heating system. This heating system consists of a cavity, an amplifier and an impedance matching unit as shown in Fig. 4a. The agar phantom was 180 mm in diameter and 130 mm in height. The dielectric bolus was made of agar and was attached to the agar phantom as shown in Fig. 4b. In the experiments, the heating power was set to 30 W, the heating time was 60 min and the “Test 2” bolus listed in Table I was used.

Fig. 4. Heating system setup. *a*, Cavity heating system. *b*, Agar phantom and segmented dielectric bolus.

Anatomical human model for calculating temperature distribution with blood flow

Fig. 5 shows an anatomical human head model which was reconstructed from 2-D medical images¹⁶⁾. Fig. 5a presents a detailed view of the anatomical model. As shown in Fig. 5a, the model consists of several tissues, such as muscle, skull, eye ball, eye

Fig. 5. Anatomical human head model. *a*, Detailed view of anatomical human head model. *b*, Cross-sectional view through tumor. *c*, Cross-sectional view through eyeball.

lens, brain, brain tumor and so on. Fig. 5b and 5c show two horizontal cross-section views through the brain tumor and eye ball, respectively. Fig. 6 shows a 3-D FEM model for calculating temperature distribution with blood flow. The cavity was 500 mm in diameter and 1,000 mm in height. The electrodes inside the cavity were 100 mm in diameter and 380 mm in height. The total number of elements was 2,363,726.

In the computer simulations, it is necessary to consider the frequency dependencies of the electric properties as shown in Table II^[18,19]. The thermal properties of several tissues are listed in

Fig. 6. FEM model.

Table II. Electrical properties of tissues at 300 MHz.

Tissue	σ [S/m]	ϵ_r	ρ [kg/m ³]
Bone	0.027	5.759	1,810
CSF	2.225	72.734	1,010
Eye ball	1.518	69.017	1,000
Gray matter	0.692	60.022	1,030
Heart	0.904	69.307	1,040
Inner ear	1.518	69.017	1,010
Kidney	1.022	70.485	1,000
Lens	0.648	48.951	1,050
Liver	0.610	53.512	1,000
Lung	0.000	1.000	1.165
Muscle	0.771	58.201	1,040
Pancreas	0.851	62.448	1,000
Spleen	0.969	66.491	1,000
Stomach	0.972	68.711	1,000
Tumor	0.771	58.201	1,040
Ventricle	2.225	72.734	1,010
White matter	0.413	43.776	1,030
Segmented bolus A	0.00	20	1,000
Segmented bolus B	0.00	20	1,000
Segmented bolus C	0.00	1.0	1.165
Segmented bolus D	0.00	1.0	1.165

Table III. Thermal properties of tissues.

Tissue	κ [W/m °C]	c [J/kg °C]	$F_{ba} \times 10^{-6}$ [m ³ /kg s]	W_{m0} [W/m ³]
Bone	0.39	1,300	0.19	610
CSF	0.62	4,000	3.95	7,100
Eye ball	0.59	3,932	0.00	0.0
Gray matter	1.13	3,675	11.18	7,100
Heart	0.54	3,720	15.00	9,600
Inner ear	0.56	3,900	0.00	0.0
Kidney	0.54	4,000	43.55	48,000
Lens	0.4	3,664	0.00	0.0
Liver	0.51	3,700	16.78	12,000
Lung	0.025	1,010	0.00	0.0
Muscle	0.53	3,546	8.20	480
Pancreas	0.52	4,000	9.08	7,300
Spleen	0.54	3,900	19.03	15,000
Stomach	0.53	3,553	6.23	5,200
Tumor	0.5	3,437	0.87	7,100
Ventricle	0.62	4,000	3.95	7,100
White matter	0.5	3,621	3.95	7,100
Segmented bolus A	0.6	4,200	—	—
Segmented bolus B	0.6	4,200	—	—
Segmented bolus C	0.025	1,010	—	—
Segmented bolus D	0.025	1,010	—	—

Fig. 7. Temperature distribution calculated by FEM. *a*, without dielectric bolus. *b*, with “Test 2” bolus.

Table III^{20–25}). The initial body surface temperature was 33°C and the body temperature was 37°C. The water (25°C) inside the bolus was circulated⁴⁾.

Results

Calculation and experimental heating results of using the simple cylindrical model

To evaluate the proposed method for heating the targeted tumor, computer simulation and experimental heating results using a simple cylindrical model were described.

Fig. 7 shows the calculated temperature distributions using the “Test 2” bolus listed in Table I. In Figs. 7a and 7b, hotspots were generated inside the phantom without undesirable hotspots. In Fig. 7, which is a result of the FEM calculation, the distance the hotspot moved from the center of the phantom

was 78 mm along the x-axis and 30 mm along the z-axis. Fig. 8 shows a comparison of the calculated E field both without the dielectric bolus and with the “Test 2” bolus. Fig. 9 shows the temperature distribution heated by the developed heating system. In Fig. 9, which is a result of the heating experiment, the distance the hotspot moved from the center of the agar phantom was 83 mm along the x-axis and 34 mm along the z-axis. Therefore, the result of the heating experiment was supported by the FEM calculations.

Fig. 10 shows the domain of the heated volume which moved inside the phantom. In Fig. 10, the “x” marks presented the center of the hotspot locations. Each domain (57 mm×75 mm×86 mm) for “Test 1” - “Test 4” overlaps with each other and is useful for treating various tumors.

Fig. 8. Calculated E field inside agar phantom. *a*, without dielectric bolus. *b*, with “Test 2” bolus.

Fig. 9. Temperature distributions heated by proposed system. *a*, without dielectric bolus. *b*, with “Test 2” bolus.

Fig. 10. Heated area (over 42°C) for experiments inside phantom.

Temperature distribution using the anatomical human head model

A 3-D anatomical human head model, as shown in Fig. 5, was used to demonstrate the possibility of clinical application.

Fig. 11 shows the calculated temperature distribution without the dielectric bolus. From Fig. 11a, the maximum temperature was shown at the neck region. It is not easy to heat the brain tumor by moving the position of the head^{12,26)}. On the other hand, from Fig. 11b, it could be seen that the brain tumor, which was the targeted area, was not heated to 42-43°C. Therefore, it is not easy to concentrate the heating energy on the brain tumor without the dielectric bolus.

Fig. 12 shows the calculated temperature distribution with the proposed dielectric bolus. From Fig. 12a, it was found that the brain tumor was heated to 42-43°C along the center profiles of the human head without any hotspots. Fig. 12b shows the temperature distribution through the center of the brain tumor. In Fig. 12b, the brain tumor was heated to the maximum temperature 43.3°C.

Fig. 13 shows the normalized temperature distribution through the center of the brain tumor. The normalized temperature T_N was given by the following equation :

Fig. 11. Temperature distribution without the bolus. *a*, A-A' section. *b*, B-B' section.

Fig. 12. Temperature distribution with the bolus. *a*, A-A' section. *b*, B-B' section.

Fig. 13. Normalized temperature distribution through the center of the brain tumor.

$$T_N = \frac{(T - T_{\min})}{(T_{\max} - T_{\min})} \quad (8)$$

where $T_{\min}$ is the minimum temperature and $T_{\max}$ is the maximum temperature inside the brain tumor.

Fig. 14 shows cross-sectional views of the heated area at the brain tumor and eye ball levels. In Fig. 14a, the brain tumor was heated to 42–43.3°C, and the desired maximum temperature was generated inside the brain tumor. In Fig. 14b, the temperature inside the eye ball was under 37°C. Therefore, it was found that the brain tumor was heated to 42–43.3°C without undesired hotspots using the proposed dielectric bolus.

Fig. 14. Temperature distributions with the bolus (cross-section).
a, C-C' section. *b*, D-D' section.

Discussion

In the present paper, we proposed a method for controlling the heated area inside the brain using a dielectric bolus filled with dielectric materials, such as water. First, the results of computer simulations and heating experiments using the cylindrical agar phantom were presented. In Fig. 7b and Fig. 9b, the resonant frequencies were 376.4 MHz and 360.2 MHz, respectively. The difference between these resonant frequencies was approximately 4%. In the heating experiments, the impedance matching operations were performed manually. If the matching operation was carried out with higher accuracy, the error between these resonant frequencies could be reduced. Because the quantity Q value increases for a higher resonant frequency⁷⁾. In Fig. 7b, the distance the hotspot moved from the center of the phantom in the computer simulation was 78 mm along the x-axis and 30 mm along the z-axis. On the other hand, the result of the heating experiment showed that the hotspot moved 83 mm along the x-axis and 34 mm along the z-axis, as shown in Fig. 9b. Comparing these results, the results of heating experiment agree with the results from the computer simulation with an error of 10% or less. As shown in Figs. 7 and 9, the hotspot moved from the center of the phantom toward the dielectric bolus. We demonstrated this fact by showing the calculated E fields in Fig. 8. Without the dielectric bolus, the E field is concentrated at the center of the agar phantom, as shown in Fig. 8a. On the other hand, in Fig. 8b, it is concentrated toward the dielectric bolus and the hotspot moved from the center of the phantom.

Next, the dielectric properties of each section was changed to control the hotspot. The volume of the heated area is (57 mm × 75 mm × 86 mm), as shown in Fig. 10. From these results, it was found that

by changing the dielectric materials inside each section, the hotspot moved to different locations inside the brain tumor. To demonstrate the possibility of clinical application, temperature distributions using the 3-D anatomical human head model were presented. In Fig. 11, the maximum temperature was reached inside the neck region when the dielectric bolus was not attached. On the other hand, in Fig. 12, when using the dielectric bolus, the hotspot occurred inside the brain tumor. The hotspot generated at the neck region in Fig. 11 was not present, because the hotspot moved to the upper region of the head due to attaching the dielectric bolus.

We discussed the temperature distribution inside the brain tumor in detail. The normalized temperature distribution through the center of the brain tumor is shown in Fig. 13. In Fig. 13, we compared the tumor size (α_1) to the heated region (α_2) over the normalized temperature value of 0.8. The brain tumor was heated to the maximum normalized temperature value of 1.0. The brain tumor was heated between the normalized temperature value of 0.8 and 1.0 without any undesirable hotspots. Here, the minimum temperature is 37°C and the maximum temperature is 43.3°C. In this case, the temperature rise is 6.3°C. Therefore, 42°C is approximately 80% of the possible temperature rise. The proposed heating method covers approximately 97% of the brain tumor.

Some researchers reported that temperature rise due to microwaves causes a cataractogenic disease^{27–29}. In Fig. 14b, when using the proposed cavity applicator with the dielectric bolus, undesirable hotspots due to microwaves did not significantly appear. The temperature inside the eye balls was 37°C or less. From these results, it is suggested that the proposed cavity applicator is a safe heating system for treating brain tumors.

In the present study, to demonstrate the possibility of the proposed heating control method, we calculated the temperature distributions using the blood flow rate inside tissues, as shown in equation (7), due to a lack of those data. Precise data for blood flow changes must be known to execute the numerical computation^{30,31}.

Conclusion

The present paper discusses a new heating control method for the proposed cavity applicator using a dielectric bolus. To evaluate the proposed heating control method, a simple cylindrical phantom model was used. The temperature distribution of the 3-D anatomical human head model that takes into account the cooling effect of blood flow was calculated by the FEM. From these results, it was confirmed that the proposed heating control method is useful for brain tumor hyperthermia treatments.

We are now planning to develop a new hyperthermia system which has the function to calculate the position and size of the brain tumor using an ultrasound imaging system.

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