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Study of a Brain Hyperthermia System providing also Passive Brain Temperature Monitoring

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Abstract— **A newly developed system for deep brain hyperthermia able to provide also passive measurements of temperature distributions inside the human body and especially the brain, is presented in this paper. The proposed system able to comprise both therapeutic and diagnostic modules operates in a totally non-invasive contactless way based on the use of an ellipsoidal conductive wall cavity to achieve beamforming and focusing on the areas under treatment and temperature monitoring. The performance of the system's diagnostic module designed and developed for brain imaging, has been previously studied in phantom, animal and human tests illustrating promising results. In the present paper theoretical analysis of the therapeutic module designed for hyperthermia treatment, elicited during simulation performance, exhibit the system's focusing attributes. Moreover, initial phantom experimental results verify the proof of concept. Taking into consideration the present initial theoretical and experimental study and the great advantage of the proposed brain hyperthermia system of being non invasive and with a very acceptable cost, it is concluded that further research is required in order to explore its potentials at becoming a part of the standard treatment protocol of brain malignancy in the future.**

I. Introduction

Hyperthermia also called thermal therapy or thermotherapy, is a type of cancer treatment mainly under study in clinical trials and not widely available. During hyperthermia sessions body tissues are exposed to high temperatures resulting in damaging cancer cells, usually with minimal injury to healthy tissue [1], [2]. Research has shown that by killing cancer cells and damaging proteins and structures within cells, hyperthermia may shrink tumors [3]. Several methods of hyperthermia have been under study the past few years, including local, regional, and whole-body hyperthermia [1]-[8].

The length of treatment and cell and tissue characteristics in conjunction with the temperature distribution achieved during a hyperthermia session, determine the effectiveness of the treatment [1], [3]. A very crucial part of the hyperthermia methodology is the temperature monitoring of the tumor and surrounding tissue, in order to ensure the desired heating of the relevant areas [4]-[6]. In practice, this monitoring procedure is invasive (insertion of thermometric devices into the treatment area) and performed using local anesthesia.

Specifically, regarding the use of hyperthermia for the treatment of brain tumors, the methodology has long been known to improve the results of other treatments for brain tumors. Heating a tumor to a temperature between 42^{o}C-45^{o}C can enhance the effects of both chemotherapy and radiation therapy [7], [8]. The advantage of heating the suffering brain region is that hyperthermic toxic effects are independent of cell-cycle phase. The main difficulty in the therapeutic application of this modality has been the lack of an effective mode of application. Various experiments involving whole body and whole or half brain hyperthermia have been accompanied by unacceptable cerebral oedema. The only method that has been employed with good results, until now, is invasive, interstitial microwave hyperthermia [4]-[6]. This is normally performed in conjunction with interstitial brachytherapy and uses the same, stereotactically implanted, tubes for access by microwave antennae. The problem with interstitial hyperthermia is that it requires transcranial implantation of guiding tubes into the tumor (average 3). Each implantation has 1% risk of hemorrhage or infection. Also the tubes remain for only a short time – effectively preventing repeated treatments. (Repeated hyperthermia, unlike radiotherapy, does not lead to a cumulative toxic effect) [4]-[6].

In the present paper a new non-invasive method for inducing focal brain hyperthermia providing also non-invasive real-time temperature monitoring of the areas under treatment, is described. The proposed system is based on a Microwave Radiometry Imaging System (MiRaIS), developed in the Microwave and Fiber Optics Laboratory of the National Technical University of Athens, the past six years [9]-[14]. The operating principle of both the therapeutic (hyperthermia) and the diagnostic (temperature monitoring) modules of the system, is based on the use of an ellipsoidal conductive wall cavity for beamforming and focusing on the brain areas of interest.

The present paper is organized as follows: a description of the proposed methodology in conjunction with a theoretical simulation study exhibiting the system focusing

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properties at various operating frequencies are herein presented. Following, phantom experimental results performed in the framework of the present research, verifying theory and proof of concept are in detail described. The paper concludes with a discussion section including the assessment of theoretical and experimental results and finally, with the overall conclusions section.

II. MATERIALS AND METHODS

A. Description of the proposed system

The proposed focused deep brain hyperthermia system consists of an ellipsoidal cavity with an opening aperture to host the human head to receive the focused brain hyperthermia (Fig.1). The ellipsoidal cavity is axis-symmetric with 1.5m length of large axis and 1.2m length of small axis. It is an exact replica of the ellipsoidal cavity of the Microwave Radiometry Imaging System (MiRaIS) [9]-[14], previously mentioned. The new cavity though has been cut transversally to the major axis, at a distance of 5cm of the focal plane (having currently a length of large horizontal-axis 1.25m) and the subtracted shell is currently not being used (Fig. 2). This action has been taken in order to have better access in the interior of the cavity, ensuring easier positioning and monitoring during experimental procedure. It is demonstrated in the following section through theoretical analysis that the system's focusing properties are not affected by this alteration compared to those achieved using the whole cavity volume.

a b

Fig. 1. a. Conductive wall cavity of Hyperthermia System b. Magnetron generator providing microwave energy of 200W at the frequency of 2450 MHz

Each irradiation is performed by placing the area of interest (of a phantom at present) on one focal area, while the transmitting dipole antenna is placed on the other geometrical focus of the ellipsoid (Fig. 2). Hence, the ellipsoidal cavity is excited by a dipole antenna while it is foreseen that in the future the human head should be placed properly on the conjugate focus with the aim to achieve focusing on the area under treatment. Each irradiation will be followed by the respective temperature monitoring of the heated area, using the microwave radiometry methodology with the same ellipsoidal setup, as it has been described in the past [9]-[14]. It has been provisioned by constructing an opening on the top of the cavity to insert the receiving radiometric antenna inside the cavity while current research work by our group aims at optimizing the combination of therapeutic and diagnostic techniques in one module (e.g. use of the same antenna-applicator for heating and measuring after implementing appropriate cooling of the receiver).

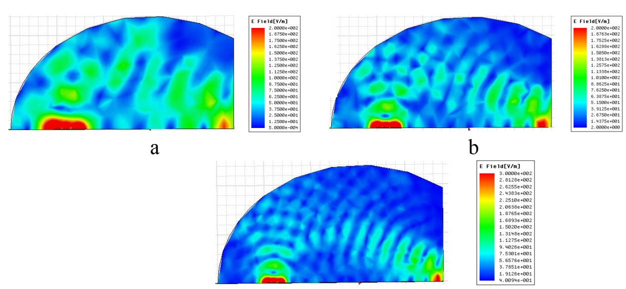
Fig. 2. Front view of the conductive wall cavity of the proposed Brain Hyperthermia System

At present the energy for heating is provided by a magnetron generator operating at 2450MHz with microwave energy of 200W, connected to the dipole antenna (Fig. 1b).

B. Theoretical Analysis using a FEM simulation methodology

During the past few years extensive electromagnetic analysis has been performed by our group using both semi-analytical methods based on Green's function theory and a FEM simulation tool [9]-[14]. The previous theoretical results show that focusing can be achieved in the brain areas of interest with a variety of dimensions of the focusing region and penetration depths related to the operation frequencies used [9]-[14].

In the present paper, the focusing properties of the new ellipsoidal conductive wall cavity having the above mentioned large opening at the focal plane are examined at three operating frequencies: 1GHz, 1.5GHz and 2GHz. Initially, the focusing properties of the system are studied through simulations of the cavity-dipole antenna setup without the presence of the human head model. In Figs. 3a, 3b and 3c the field distribution inside the ellipsoidal is depicted at 1GHz, 1.5GHz and 2GHz, respectively. It is well observed that focusing on the ellipsoid's geometrical focal point is achieved regardless of the large opening and the conductive wall cavity part missing. These results are totally compliant with numerical and simulation results obtained in the past using the entire ellipsoidal setup [9]-[14].



a b c

Fig. 3. Ellipsoid focusing properties at a. 1GHz b. 1.5GHz and c. at 2GHz

Following, the same configuration has been used but with the presence of a spherical human head model, with its center placed at the ellipsoid's focal point. The model is double layered comprising two types of head tissues; the inner sphere of 9cm of radius, representing average brain tissue whereas the outer spherical shell has a radius of 10cm, representing the skull tissue, all having the respective conductivity and permittivity values [15] at the various operation frequencies.

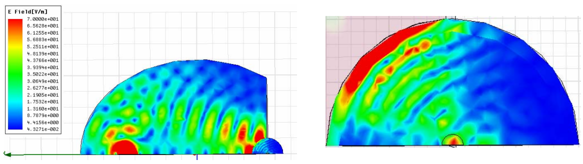


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Fig. 4. a. Electric field distribution inside the ellipsoidal in the presence of a head model at 1.5GHz (center head on focus) b. Magnification of head model

In Figs. 4 and 5 the electric field distribution in the presence of the human head model is depicted. Focusing on the head center is achieved at the lower frequency since the penetration depth is quite large. At 2GHz the penetration depth is of the order of 3.5cm. Once again the results are similar to those obtained in the past [9]-[14].

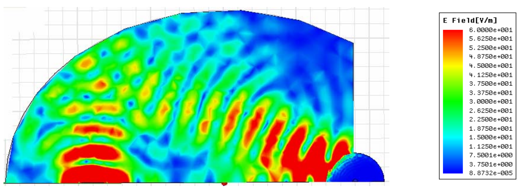

Fig. 5. Electric field distribution inside the ellipsoidal in the presence of a head model at 2GHz (center head placed on focus).

Another important aspect of the present analysis is the focusing sensitivity of the system –in respect to the energy merged on the ellipsoid's focus- when moving the center of the human head model from the ellipsoid's geometrical focus. The results of the simulation performed at 1GHz when the head center is moved 5cm away from the focus towards the ellipsoid center are shown in Fig.6. A small shift of the merged energy from the focal area is observed; the maximum electric field was expected to be observed on the right circle marker of Fig. 6b, where the ellipsoid's focal point is placed, whereas the left marker denotes the head center.

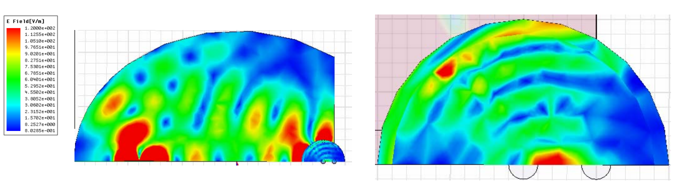

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Fig.6. a. Electric field distribution @1GHz (head center placed 5cm away from focus) b. Magnification of head model

This phenomenon is mainly attributed to the spherical geometry of the head model and the penetration depth in conjunction with the resonance phenomena generated in the inhomogeneous spherical head model. In the case in which the head center is moved to a larger distance from the focus (e.g. 20cm), the peak of the electric field distribution is observed at the focal point regardless of the diffraction or scattering caused by the presence of the human head model (Fig. 7).

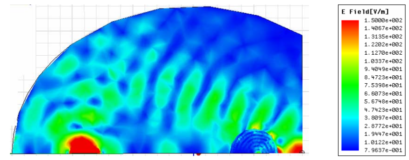

Fig. 7. Electric field distribution @1.5GHz (head center placed 20cm away from focus)

Finally, by moving the head center 5cm from the focus area at higher operating frequencies (e.g. 2GHz) the maximum electric field is observed towards the focal area but with lower penetration depth, as expected (Fig. 8).

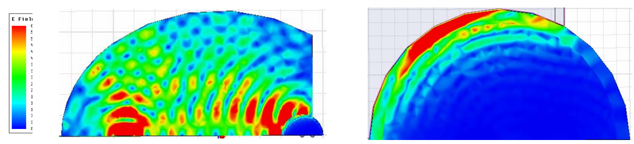

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Fig. 8. a. Electric field distribution @2GHz (head center placed 5cm away from focus) b. Magnification of human head model

III. Experimental Study: Procedure and Results

The performance of the system's diagnostic module designed and developed for brain imaging, has been previously studied in phantom, animal and human tests illustrating promising results [9]-[14]. In the framework of the present research the hyperthermia module, as described in section II.A, is tested through phantom experimentation. The phantom used is a cylindrical glass container (10cm height, radius of 6cm), filled with a gel based aqua saline solution, having the electromagnetic properties of average brain tissue at 2450MHz (Fig. 2). The latter is the operating frequency of the magnetron generator used to feed the radiating dipole antenna (Figs. 1, 2, 9).

a b

Fig. 9. a. Phantom placed on focal area and digital thermometer with measuring probe (side view) b. Ellipsoidal interior: phantom placed on focal area whereas dipole radiating antenna placed on second focus

The geometrical center of the container was placed at the ellipsoid's focus and the temperature of the phantom was measured before the heating procedure at a number of various arbitrary points in its whole volume and was found uniform. Following, the phantom volume under test-which is the area placed at the ellipsoid's focus- was electromagnetically heated for a time period of 3min. Then the temperature of the heated area was measured with the probe of a digital thermometer. The same procedure was performed three times. The temperature was found in the order of 1^oC higher than the one measured before the heating in a volume of approximately $8cm^3$ at the geometrical center of the phantom, all three times that the experiment was repeated. The results are presented in detail in Table I.

TABLE I
PHANTOM HYPERTHERMIA EXPERIMENTAL RESULTS

Experiment	Temperature before heating (C^o)		Temperature after 3min heating (C^o)	
	Phantom area under test	Surrounding phantom areas	Phantom area under test	Surrounding phantom areas
1st	17.3	16.5	18.3	16.5
2nd	17.6	16.8	18.5	16.7
3rd	18.1	16.5	19.3	16.8

IV. DISCUSSION

In the present paper the focusing properties of an ellipsoidal beamformer based hyperthermia system are investigated through a simulation and experimental study. The design and construction of the conductive wall cavity used for focusing on the areas of the human head under treatment is based on the MiRaIS, a microwave radiometry imaging system developed the past few years by our group [9]-[14]. A new cavity has been constructed actually being a replica of the one of the MiRaIS with a single difference: a larger opening at the ellipsoid's focal plane permitting the entrance of the human body inside the cavity in a horizontal (lying) position. Comparing the results of the simulation study of the focusing properties of the new cavity with the focusing properties exhibited by the whole one used in the past, compliance of results was found. Thus, from the simulation and numerical results it is concluded that in the range 1.3-3.5GHz imaging of the head model areas placed at the ellipsoid's focus is feasible with a variety of detection/penetration depths and change of the spatial resolution, depending on the frequency used. According to the numerical results the penetration depth varies from 1.8cm to 5cm while the spatial resolution (3dB focusing region) from 1cm to over 3cm [9]-[14].

Moreover the experiment of heating a specific 3D region of a phantom at 2450MHz performed in the framework of the present research has shown promising results; raise of 1^oC has been achieved in the region of interest (volume of $8cm^3$ approximately) while the temperature of the surroundings remained unchanged. In the near future further research work will aim at optimizing the system's focusing properties at various operation frequencies through theory and experiment, in order to improve both spatial resolution and penetration depth. The heating will be monitored through the microwave radiometry module of the system that has already been developed and tested.

V. CONCLUSION

In the present paper a brain hyperthermia system comprising also a passive brain temperature monitoring module has been presented. Simulation results and experiments reveal the system's potential as a possible future clinical tool. Since interstitial hyperthermia can double prognosis it is logical to assume that the proposed new method, if shown to be sufficiently accurate after further and in depth investigation, could also work. With the great advantage of being non invasive, which allows it to be repeated as often as necessary without significant risk and with an acceptable cost, it could possibly complement the treatment protocol of brain malignancy in the future.

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