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Thermal Simulation of Biological Tissues with Magnetite Microinsertions under Microwave Energy in Support of Chemo-Hyperthermal Delivery

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***Abstract* – This paper deals with the investigations of biological tissues with magnetite insertions through computer simulation and measurements in support of chemo-hyperthermal delivery. Modeling of microwave-thermal effects in tissues, under different clinical specifications, in relation with magnetic nano-assemblies features is taken into account to correlate the thermal effect of microwave with the thermal effect in the volume under irradiation. Simulation of the tissues was performed in CST Microwave Studio in the presence and absence of insertions. It has been observed that there is a very beneficial effect on the uniformity of the thermal effect in the tissue, in the presence of the inserts, due to the much better thermal conductivity of these materials beside the tissues.**

I. INTRODUCTION

Destruction (ablation) of local tumors is a minimally invasive method used to treat tumors in the liver, kidney, bone and lung [1], as an alternative for patients who have failed treatment with chemotherapy or radiotherapy. In the liver tumors, in some cases, ablation is considered as a first treatment option.

Most ablation systems consist of a generator and a device as a needle [2] that applying energy to the tissue in order to achieve a temperature higher than 60°C. It is also possible to achieve a lower temperature in order to obtain the necrosis of the tissue, but the required times are greater, due to the high temperature of the living organism's response. At temperatures above 60°C cell death is instantaneous. Although there are several ways to apply energy to the cell (radio frequency electromagnetic energy, laser, ultrasound) a preferred method is to use thermal effect of microwaves. The frequencies used are 915MHz and 2.45GHz, the center frequencies of two bands reserved ISM (Industrial, Scientific, Medical: ITU-R 5.138, 5.150, 5.280).

Thermal effect of microwaves in biological tissues will be studied and correlated with the use of magnetic micro insertions.

II. EXPERIMENTAL DETAILS

A. Dielectric modeling of human tissue

A first difficulty of electromagnetic analysis of the ablation phenomenon with microwaves is the modeling of tissues and in particular of the living tissue (in vivo). Tissues have a special dielectric behavior primarily due to the high content of water [3]. Tissues start from a very high relative permittivity (up to 10^6-10^7 at low frequencies) and suffer three dispersion phenomena (called α-dispersion, β-dispersion and γ-dispersion) [4] occurring at frequencies of hundreds of Hz, hundreds of kHz, respectively GHz, and lowering this permittivity at the working frequency of the microwave ablation methods.

In the case of biological tissues, various relaxation phenomena involved, requiring the use of more complex relationships to model this behavior. Extensive research conducted by Gabriel et. al. in 1996 [5],[6],[7], have imposed the dielectric relaxation of the tissue model in Equation 1, still valid model currently considered:

$$\hat{\varepsilon}(\omega) = \varepsilon_\infty + \sum_{n=1}^{4} \frac{\Delta\varepsilon_n}{1 + (j \cdot \omega \cdot \tau)^{1-\alpha}} + \frac{\sigma_j}{j \cdot \omega \cdot \varepsilon_0} \qquad (1)$$

This model can be used to determine any frequency relative permittivity and conductivity of the tissue, according to equation (2):

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$$\hat{\varepsilon}(\omega) = \varepsilon_r + \frac{\sigma}{j \cdot \omega \varepsilon_0} \qquad (2)$$

Typical parameter values obtained for different tissues are tabled and can be identified in [8], [9]. In this paper tissues were modeling based on equations (1)-(2).

The parameters used for the tissues are given in Table 1, and the results of modeling, specifying the values at interest frequencies, are showed in figures 1-4.

Table 1. Parameters of the dielectric model of tissues

Parameters/ Tissues	Bone	Kidney	Liver	Lung
ε_{inf}	2.5	4	4	2.5
Δ_1	10	47	39	18
τ_1 (ps)	13.263	7.958	8.842	7.958
α_1	0.2	0.1	0.1	0.1
Δ_2	180	3500	6000	500
τ_2 (ns)	79.577	198.944	530.516	63.662
α_2	0.2	0.22	0.2	0.1
sig	0.02	0.05	0.02	0.03
Δ_3	$5x10^3$	$25x10^4$	$5x10^4$	$25x10^4$
τ_3 (μs)	159.155	79.577	22.736	159.155
α_3	0.2	0.22	0.2	0.2
Δ_4	10^5	$3x10^8$	$3x10^7$	$4x10^7$
τ_4 (ms)	15.915	4.547	15.915	7.958
α_4	0	0	0.05	0

It should be noted that the measurements/modeling of Gabriel et al. [5], [6], [7] were confirmed as correct by subsequent studies as date [10], current research aiming to determine the variation of parameters with the age [11], [12], the sex of the patient or supplement the initial list of other organs [8].

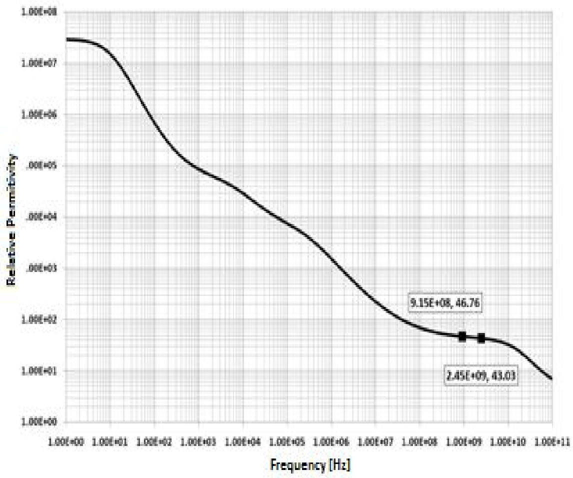

Fig. 1. Liver - Permittivity

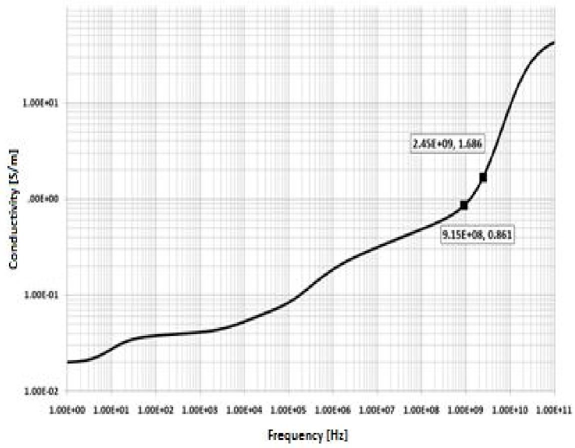

Fig. 2. Liver - Conductivity

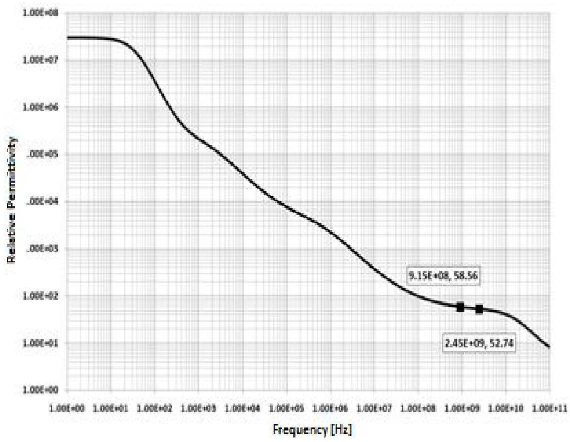

Fig. 3. Kidney - Permittivity

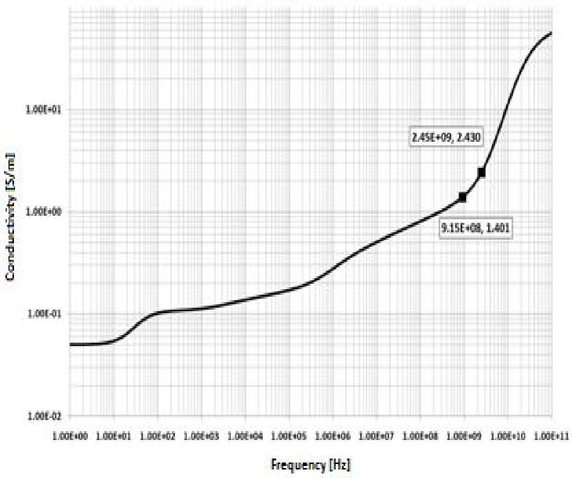

Fig. 4. Kidney - Conductivity

Modeling of equations (1)-(2) was performed in Excel, realizing in this way the Fig. 1-4 and the calculation in a sufficient number of points for modeling in CST.

B. Thermal modeling of biological tissues

The model of thermal analysis used in CST Studio Suite is built in respect to the characteristics of biological tissues in vivo. The equation used in CST to calculate the temperature variations is (3):

$$\rho \cdot C \cdot \frac{\partial T}{\partial t} = \nabla (K \cdot \nabla T) + \rho_S \cdot C_S \cdot \omega_S \cdot (T_S - T) + Q_{met} + \rho \cdot SAR \quad (3)$$

where involved the thermal parameters of tissue, especially of the blood (index s) and various heat sources encountered. The dynamic term (the left side of the equation) depends on heat dissipation of the thermal conduction, dissipation by blood flow (at a different temperature - typically 37 °C T_s), on the metabolic generation of heat, and the amount of energy received by the microwave irradiation.

The dependent term on SAR (Specific Absorption Rate) is defined in [13] as derived function of time of the incremental energy (dW) absorbed by (dissipated in) the mass element (dm) contained in the elementary volume (dV) of known density (ρ). SAR is measured in W / kg.

$$SAR = \frac{d}{dt}\left(\frac{dW}{dm}\right) = \frac{d}{dt}\left(\frac{dW}{\rho \cdot dV}\right) \quad (4)$$

III. SIMULATION AND RESULTS

A. Boundary conditions

The boundary conditions used (Fig. 5) were designed to investigate the interaction of a plane wave with the considered sample.

The plane wave characteristics generation of the electromagnetic field has been determined by the choice of electrical wall (x_{min} and x_{max}) and magnetic wall (y_{min} and y_{max}) conditions. Conditions for input and output ports are called "open", corresponding to the placement of an interface that allows the entry and the exit of the energy without reflection. Details of these conditions can be found in [14] and [15], and the effect, by limiting the number of modes 1, is the generation of a configuration of field -type plane wave.

These conditions, by limiting the number of modes to 1, generate a field configuration - plane wave type (Fig. 5).

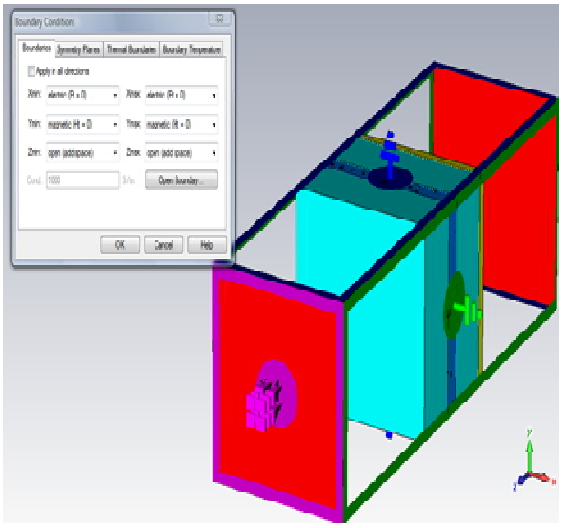

Fig. 5. Boundary conditions

The simulation was performed on a PC with 8GB RAM and a dual-core processor (3GHz). In general, in time domain the simulator is used for analysis, and in frequency domain the simulator is used for measuring the results due to much higher resource needs (to calculate a frequency point with this simulator requires a memory of 5.5GB and 6 hours). The convergence was chosen for a total of 23 sampling cells for one wavelength (corresponding to 4 GHz, the maximum frequency analyzed).

The insertion material was magnetite in two concentrations 0.05% and 0.25%.

B. Thermal modeling of biological tissues

CST has the possibility to use electrical power due to electromagnetic analysis to estimate the temperature rise in the volumes studied (in this case, the tissue subjected to microwave irradiation). This method has been applied first in the absence of the inserts to obtain the results shown in Fig. 3.

The initial temperature was set at 310.1K (37°C), the same temperature of the blood flowing through the tissue by removing the heat. Energy input corresponds to a power of 4W amplitude (2W actual value) on the surface of the input port, so to one illumination with $2W/cm^2$ density, temperature should be adjusted accordingly to higher wave power. The boundary conditions were chosen to exterior insulation.

For the case of using insertions were kept the same conditions (external temperature of 310.1K and lighting with $2W/m^2$ density). The results are showed in figures 6-8.

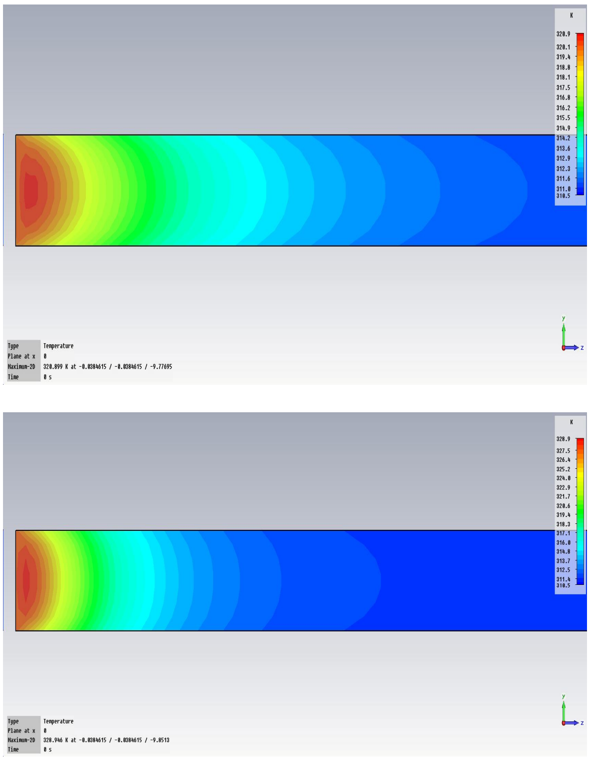

Fig. 6. Tissue temperature at 915MHz and 2.45 GHz without insertions

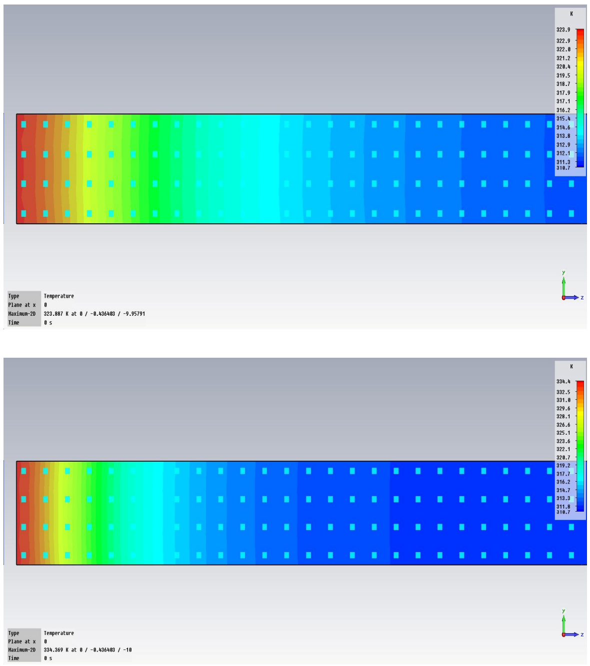

Fig. 7. Tissue temperature at 915MHz and 2.45 GHz with 0.05% magnetite (Fe_2O_3) insertions

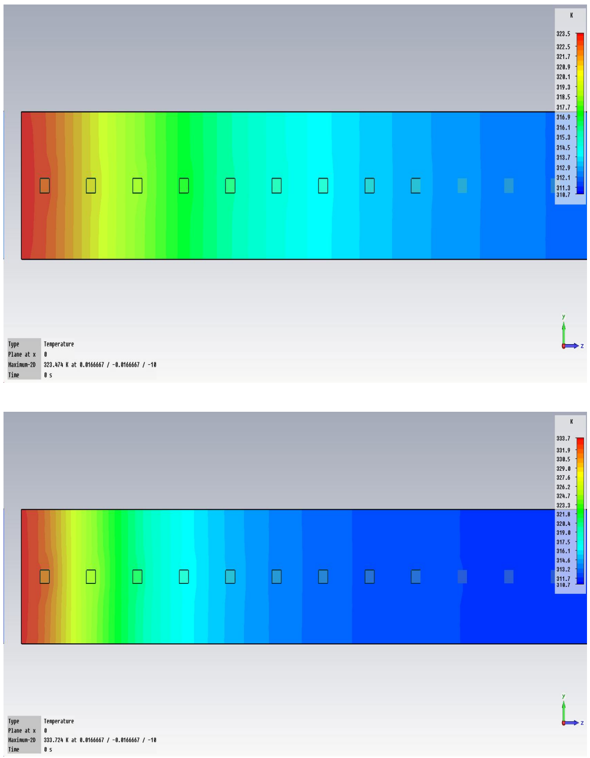

Fig. 8. Tissue temperature at 915MHz and 2.45 GHz with 0.25% magnetite (Fe_2O_3) "tunnel" insertions

It has been observed that there is a very beneficial effect on the uniformity of the thermal effect in the tissue, in the presence of the inserts, due to the much better thermal conductivity of these materials beside the tissues. Also in equal lighting conditions ($2W/cm^2$) noted a slight increase of maximum temperature 334.3K (tissue with magnetic insertions) beside the 328.9K (normal tissue). This increase in maximum 5.4 °C, is exactly the desired effect by applying microwave process for liver tumors control, based on microwave activation of functionalized nanostructures subendothelial immobilized.

IV. CONCLUSIONS

From the tests carried out, it can be seen that the penetration field/electromagnetic energy within the tissue can be controlled by different concentrations of magnetite insertions. The depth of penetration remains determined by the wavelength used, and is recommended to not be reduced excessively because with increase of the wavelength occurs the increase to very high values of permittivity, following, the low frequency waves penetrate deeper, but are more less effective.

The optimal variant of electromagnetic energy application remains to design a specific antenna to dissipate the energy in desired region.

There is a very beneficial effect on the uniformity of the thermal effect in the tissue, in the presence of the inserts, due to the much better thermal conductivity of these materials beside the tissues. Also in equal lighting conditions (2W/cm2) noted a slight increase of maximum temperature 334.3K (tissue with magnetic insertions) beside the 328.9K (normal tissue). This increase in maximum 5.4 °C, is exactly the desired effect by applying microwave process for liver tumors control, based on microwave activation of functionalized nanostructures subendothelial immobilized.

V. ACKNOWLEDGEMENT

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REFERENCES

[1] E.M. Knavel, C.L. Brace, "Tumor Ablation: Common Modalities and General Practices", Techniques in Vascular and Interventional Radiology, Volume 16, Issue 4, December 2013, Pages 192–200

[2] T. Seki, "Microwave Coagulation Therapy for Liver Tumors în Tumor Ablation", Principles and Practice, ISBN: 978-0-387-95539-1, Springer, 2005, pp 218-227

[3] RD. Adey: "Tissue interactions with non-ionizing electromagnetic fields". Physiol Rev 1981; 6: 435-514.

[4] U. Kaatze, "The dielectric properties of water in its different states of interaction", Journal of Solution Chemistry, November 1997, Volume 26, Issue 11, pp 1049-1112

[5] C. Gabriel, S. Gabriel, E. Corthout, "The dielectric properties of biological tissues: I. Literature survey". Phys Med Biol. 1996 Nov;41(11):2231-49

[6] S. Gabriel, RW. Lau, C. Gabriel, "The dielectric properties of biological tissues: II. Measurements in the frequency range 10 Hz to 20 GHz"., Phys Med Biol. 1996 Nov;41(11):2251-69.

[7] S. Gabriel, R.W. Lau, C. Gabriel, "The dielectric properties of biological tissues: III. Parametric models for the dielectric spectrum of tissues", Phys Med Biol. 1996 Nov;41(11):2271-93

[8] Foundation for Research on Information Technologies in Society, Zurich, Switzerland, http://www.itis.ethz.ch/itis-for-health/tissue-properties/downloads/ , accesat la 25.11.2013

[9] Institute for Applied Physics, Florence, Italy, http://niremf.ifac.cnr.it/, accesat la 25.11.2013

[10] D. Miklavčič, N. Pavšelj, F. Hart, "Electric Properties of Tissues, capitol în Wiley Encyclopedia of Biomedical Engineering", John Wiley & Sons, 2006

[11] A. Peyman, C. Gabriel, EH. Grant, G. Vermeeren, L. Martens, "Variation of the dielectric properties of tissues with age: the effect on the values of SAR in children when exposed to walkie-talkie devices", Phys Med Biol. 2009 Jan 21;54(2):227-41.

[12] A. Peyman, "Dielectric properties of tissues; variation with age and their relevance in exposure of children to electromagnetic fields; state of knowledge", Prog Biophys Mol Biol. 2011 Dec;107(3):434-8

[13] IEEE Std C95.1™-2005, "IEEE Standard for Safety Levels with Respect to Human Exposure to Radio Frequency Electromagnetic Fields, 3 kHz to 300 GHz", 2005

[14] CST GmbH, Application Note, Photonic Crystal Simulation, Article ID: 296, 2007 - http://www.cst.com

[15] R. Ciobanu, R.F. Damian, I. Casian Botez, "Electromagnetic Characterization of chiral auxetic metamaterials for EMC applications", Computer Standards & Interfaces, Volume 32, Issue 3, March 2010, Pages 101-10