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Microwave thermal ablation: Effects of tissue properties variations on predictive models for treatment planning

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ABSTRACT

Microwave thermal ablation (MTA) therapy for cancer treatments relies on the absorption of electromagnetic energy at microwave frequencies to induce a very high and localized temperature increase, which causes an irreversible thermal damage in the target zone. Treatment planning in MTA is based on experimental observations of ablation zones in *ex vivo* tissue, while predicting the treatment outcomes could be greatly improved by reliable numerical models. In this work, a fully dynamical simulation model is exploited to look at effects of temperature-dependent variations in the dielectric and thermal properties of the targeted tissue on the prediction of the temperature increase and the extension of the thermally coagulated zone. In particular, the influence of measurement uncertainty of tissue parameters on the numerical results is investigated. Numerical data were compared with data from MTA experiments performed on *ex vivo* bovine liver tissue at 2.45 GHz, with a power of 60 W applied for 10 min. By including in the simulation model an uncertainty budget (CI = 95%) of ±25% in the properties of the tissue due to inaccuracy of measurements, numerical results were achieved in the range of experimental data. Obtained results also showed that the specific heat especially influences the extension of the thermally coagulated zone, with an increase of 27% in length and 7% in diameter when a variation of −25% is considered with respect to the value of the reference simulation model.

1. Introduction

Microwave thermal ablation (MTA) procedures for the treatment of pathologic tissues rely on the generation of very high temperatures (55–60 °C at minimum) in the target zone owing to the absorption of electromagnetic energy at microwave (MW) frequencies (typically 915 MHz or 2.45 GHz). At temperatures of about 55–60 °C and above, an almost instantaneous cell death is achieved; at lower temperatures coagulation can be induced heating the tissue for a longer time, e.g., at 50 °C less than 5 min are needed to obtain irreversible cellular injury, whereas at least 60 min are needed at 46 °C [1,2]. MTA has remarkably developed in the last years, showing many promising advantages over surgical techniques for local treatment of soft-tissue pathologies, e.g. tumours. These advantages are mainly linked to the limited invasiveness of the applicators, which are typically interstitial antennas inserted into the body percutaneously or following natural paths (e.g. veins or orifices) up to the target area [3].

In tumours ablation procedures, treatment planning is based on the proper insertion of the antenna into the targeted tumour while avoiding vascular structures, usually exploiting image-guidance techniques, as well as on the MW power (with intensities up to 100 W) to be radiated and the duration (typically about 5–20 min) needed to achieve an ablated zone (also named thermal lesion) that is sufficiently wide to cover all the cancerous tissue plus a 5–10 mm safety margin of surrounding healthy tissue [2]. Nevertheless, there are still open issues under investigation related to the changes in the physical properties of tissues, both during the procedure and for inter-patient variability, and to the presence of very complex phenomena as, e.g., the shrinkage of the tissue [4–6]. These gaps in knowledge in predictive simulations weaken the reliability of the technique, delaying model-based treatment planning integration within the clinical workflow. On the other hand, a full understanding of the changes in the physical properties of tissues during MTA procedures, and of their influence on MTA outcomes, would allow obtaining more reproducible and reliable results.

Heating influences the dielectric properties of tissues causing irreversible structural changes. In particular, in a temperature range of 60–80 °C, protein denaturation occurs [7,8], while as the temperature approaches 100 °C the water content in the tissue drops due

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to the generation of vapour and to the diffusion of water from the treated cells [9]. These structural modifications lead to changes in both the dielectric and thermal properties of the tissue, followed by a change of the electromagnetic power deposition, of the heat conduction within the tissue, and eventually of the size and shape of the induced thermal lesion [10–13].

Most studies devoted to the thermal variation of dielectric properties are based on *ex vivo* tissue samples because of the difficulty of performing *in vivo* measurements. In particular, with reference to MTA, an irreversible decrease of the permittivity and electric conductivity at high temperatures, which can reach or exceed 100 °C close to the antenna, was demonstrated at 2.45 GHz in *ex vivo* bovine liver tissue [7–14]. Differences between *ex vivo* and *in vivo* measurements of the dielectric properties of tissues, as well as between normal and pathologic tissues, are still an open issue. As an example, in O'Rourke et al. [15] significantly higher values of dielectric properties (up to 43%) were measured *in vivo* with respect to *ex vivo* cases; likewise, significantly higher values (up to 30%) of dielectric properties were measured in malignant with respect to normal tissues. At the same time, variations within the natural inhomogeneity of each tissue were taken from Peyman et al. [16] for the *in vivo* versus the *ex vivo* cases at room temperature, while significant differences were confirmed between the dielectric properties of normal and malignant tissues, depending on the pathologic state [16].

Concerning thermal properties of tissues, a limited number of studies are available in the literature. Some works were devoted to the measurement of the temperature dependence of specific heat and thermal conductivity up to about 80–90 °C, while measurements up to 80 °C showed a reversible behaviour in thermal properties changes [17,18], and measurements up to 90 °C resulted in irreversible changes (i.e. the altered measured value was mostly maintained also when the tissue was allowed to cool down [17–19]). Experimental variations on measured data of tissue thermal properties up to 10% can be found in the literature [20–22], whereas some studies have reported thermal conductivity values of core and peripheral tumours resected from humans and animal models to be as much as 20% higher than healthy liver tissue [23,24]. Rossmann and Haemmerich [25] reported a summary of published research on temperature-dependent thermal properties of biological tissues, evidencing that no data could be found to demonstrate variation of thermal properties *in vivo* versus *ex vivo*.

To reduce the uncertainties related to MTA treatment procedures and to improve the reliability of clinical protocols, the development of predictive models could be very helpful. To this purpose, an accurate knowledge of the properties of tissues at MW frequencies and their temperature-dependent changes is crucial; moreover, the possibility to account for their possible variations related to differences either inter-individual or between normal and malignant tissues would enable reliable pre-treatment planning. Some papers presented sensitivity studies to evaluate the effect of variations of both thermal and electrical properties of tissues on the prediction of the ablation zone dimensions in computational models of radiofrequency [20,21] or MW [22,23] ablation. In particular, Sebek et al. [22] performed an in-depth numerical study considering the influence of variations in electrical and thermal properties of tissues, obtained from literature data, on antenna matching as well as on the shape and dimension of the thermally ablated area. Deshazer et al. [23] considered different types of liver tissue, i.e. healthy, cirrhotic, tumour, and numerically investigated the differences in the obtained thermal lesion. Both papers found that blood perfusion influences the dimension of the thermally ablated area, albeit in [23] no influence on the outcomes was obtained when differences in blood perfusion between tumour and healthy liver were studied. Finally, a significant influence of the electric conductivity was reported [23].

In this paper, a fully dynamical multi-physics simulation model was considered [26], looking at the effects of variations in the properties of the tissue, for the prediction of the temperature increase in the zone of ablation and the extension of the ablated area. Variations were obtained from the evaluation of uncertainty in experimental studies devoted to the measurements of dielectric and thermal properties of tissues, also accounting for human inter-variability. Numerical results were compared with data from MTA experiments performed on *ex vivo* bovine liver tissue at 2.45 GHz, with a power of 60 W applied for 10 min. The aim of this work is to investigate the influence of dielectric and thermal parameters on the temperature increase obtained in the tissue close to the radiating antenna, and, correspondingly, on the maximum dimensions of the thermally ablated area. The achieved results would allow researchers to know the dielectric and/or thermal parameter that mostly condition MTA outcomes. In particular, comparing numerical with experimental data on the temperature increase close to the radiating antenna allows looking at the physical phenomena underlying the ablation procedure, and pushing for new experimental studies for their characterisation.

2. Methods and models

2.1. Variations in tissue properties and uncertainty budget

Possible sources of variations in the properties of the tissue during MTA procedures depend on the changes in the physical characteristics with increasing temperature, on the uncertainty of measurement including the experimental variability and the instrumental accuracy, as well as on the state of the tissue (e.g. inter-individual variability, malignant vs. normal tissues, different pathologic state). Dielectric measurements at MW frequencies are typically carried out using an open-ended coaxial probe connected to a vector network analyser [27]. Reported typical accuracy of the measurement technique at room temperature is between 5% and 10% [11], which corresponds to a standard uncertainty less than 5.8% (assuming the normalization factor $\sqrt{3}$ of rectangular distribution). Inter-individual variation of dielectric data on each normal tissue sample can be up to 10%; similar inter-individual variation was observed for measurements carried out on tumour samples [15,16]. Concerning the uncertainty in dielectric measurements performed at increasing temperatures during MTA procedures, uncertainties less than 3.75% and 4.5% were experimentally assessed for relative permittivity and electric conductivity, respectively, carried out on *ex vivo* bovine liver [11].

The uncertainty budget in measuring dielectric properties of tissues during MTA procedures at 2.45 GHz can therefore be evaluated through the combined expanded uncertainty (CEU), accounting for the above-mentioned sources of uncertainty and variability. Table 1 reports the different sources of uncertainties and calculates the CEU (confidence interval CI = 95%) according to the following formula:

$$CEU = 2 \cdot \sqrt{(EU)^2 + (MT)^2 + (EV)^2} \quad (1)$$

where *EU* is the experimental standard uncertainty of measurements, *MT* is the standard uncertainty related to the accuracy of the measurement technique, and *EV* is the standard uncertainty associated to the state of the tissue.

Limited data are available in the literature with reference to measurements of thermal properties and the related variations in biological tissues. Measurements are typically carried out using the transient line heat source technique [27], which allows an accuracy of 10% over the 20–90 °C temperature range [19]. Yet, contact resistance may form between the heated sensor and the tissue into which the sensor is inserted. This is likely to occur at higher temperatures where significant water loss and protein denaturation

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