Challenging the Modeling of Magnetic Hyperthermia of Secondary Bone Tumors Using Magnetic Prosthetic Implants

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Abstract

Magnetic biomaterials are powerful multifunctional tools in theranostic. They can be remotely controlled by an external magnetic field. When a radiofrequency field is used, the magnetic nano- or microparticles embedded in the biomaterial dissipate heat, which can be used for therapeutic purposes. Hyperthermia treatment of deep-seated tumors, such as bone cancers, can extensively benefit from the use of such class of magnetic responsive biomaterials. Therefore, in this work it is presented the numerical analysis of the hyperthermia treatment of secondary bone tumors performed using a magnetic hydroxyapatite prosthesis.

1 Introduction

Hyperthermia (HT) is a thermal therapy which aim to raise the temperature of a target tissue in the range 42°C-44°C [1]. These high temperatures damage cell proteins, alter the DNA repair mechanisms, elicit the immune system response, produce free radicals, increase the blood flow and the sensitivity to chemoterapy and radiotherapy. For deep seated tumors, such as primary or secondary bone cancers, the interstitial local HT is an appealing clinical strategy. In the case of orthopedic oncology this adjuvant thermal treatment is performed using implanted object called thermo-seeds [1, 2]. When a bone tumor is present, the surgical intervention is immediately performed, as shown in Fig. 1. The resection leaves a gap in the bone. This surgical injury must be filled with a bone graft, i.e. a prosthesis. Considering that the tumor margins are not clear, some residual cells may be present in the surrounding of the surgical fracture. If a magnetic material is implanted to fill the gap, then, exposing the system to a radiofrequency (RF) magnetic field, the HT can be performed (Fig. 1). The heat dissipated by the so-called magnetic scaffold can be conducted to the neoplastic cells. This clinical strategy allows to perform radio- or chemotherapy against biological target such as Osteosarcoma, Fibrosarcoma or metastatic bone cancers [3, 4].

The research about thermo-seeds is active and it is mainly driven by nanomaterial science [5-7]. Typically, magnetic scaffolds are biomaterial which embed magnetic nanoparticles (e.g. iron oxide) or ceramics doped with Fe ions [5-7]. Indeed, the use biocompatible material which could operate for working frequency of several kHz is a preferable strategies, considering that the actually employed medical grade steel requires to operate at few MHz, thus causing unwanted and uncontrolled heating of non-target tissues by the current induced in them [2-4]. Of course, a quantification of the hyperthermia response and the actual performance in a realistic scenario should be pursued [8]. This implies the modeling of the coupled eletromagneto-thermal phenomena proper of the hyperthermia treatment.

Therefore, in this work a numerical and multiphysic model for the hyperthermia treatment of secondary bone tumors using magnetic prosthetic implants is presented.

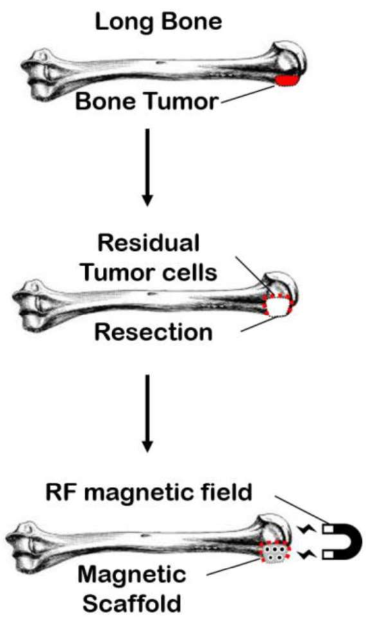

Figure 1. Rationale of the hyperthermia treatment against bone tumors using magnetic scaffolds as thermo-seeds.

2 In Silico Test of the Hyperthermia Effectiveness

A simplified 2D-axysimmetric geometry is selected to represent the geometry of a human arm [9], as shown in Fig. 2. It is supposed that the bone tumor affects a long bone and it was set in an intra-cortical region. The case of a single thermo-seed with radius r_{sc} 5 mm is considered, and the surrounding tissues are a surgical gap (r_{fr}=0.3 mm), the residual bone tumor margin (r_t=1 mm), the

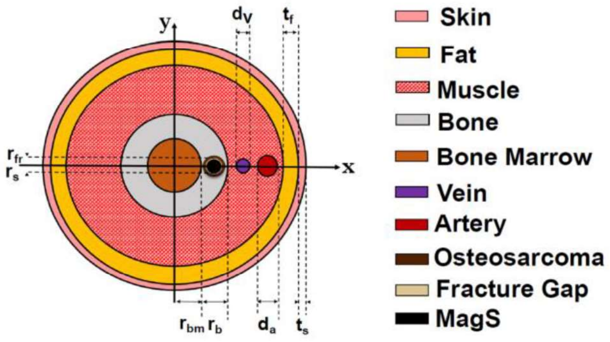

Figure 2. Geometry for the in silico evaluation of the hyperthermia treatment of magnetic biomaterials.

healthy bone tissue (r_b=10 mm), the skeletal muscle (rm=30 mm), the fat (rf=10 mm) and, finally, the skin (rb=1 mm). The brachial and radial artery are modeled as found in [9].

At the time t=0, given a uniform initial temperature distribution, the solution of Maxwell's equation in the frequency domain is performed assuming that the magnetic phase in the magnetic hydroxyapatite scaffold is uniformly distributed and has the properties reported in [7-9]. The source of magnetic field is assumed to be a pair of Helmholtz coils with a number of turns N, an exciting current, I, and radius a = 8 cm. The electromagnetic problem is solved in the frequency domain to compute the power deposited in the tissues. The biological system is supposed to be exposed to a non-uniform magnetic field, which can cause unwanted heating to non-target tissues due to the conduction currents which arise by the presence of the induced electric field. The dielectric properties of all tissues are taken form [9].

With the knowledge of the power losses due to the scaffold and the tissues, the Pennes Bio-Heat equation is solved in the time domain and the temperature is found. The PDE for the temperature is subject to continuity condition and to a Neumann boundary condition at the skin interface.

Considering that both the electromagnetic (EM) and thermal properties can be assumed to be temperature dependent [9], the EM problem is solved with the retrieved temperature field, then the thermal equation are computed again with the new power losses, and so on, until the final time is reached. The temperature dependence of the thermal properties are retrieved from [9]. This chopped solution is ensured by the rather different dynamic of the electromagnetic and the thermal fields (tenths of ms vs hundreds of ms). More details about the resolution scheme can be found in [9].

The problem for the geometry in Fig. 2 is solved using the commercial Finite Element Method software Comsol Multiphysics (Comsol Inc., Burlington MA). In particular, the AC/DC and the Bioheat Transfer module were used.

3 Results

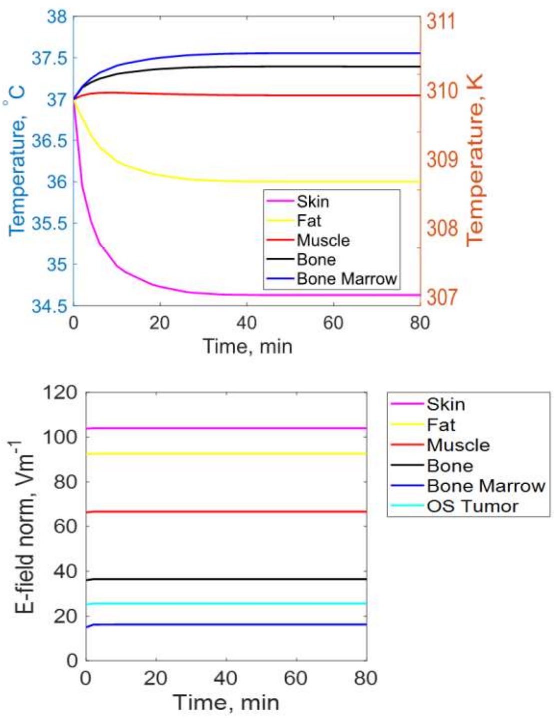

Figure 3. a) Time evolution of the average temepraturein the non-target tissues. b). Average values of the electric field norm in the non-target tissues.

The temperature of the non-target tissues during 80 min of HT was monitored in order to account if any potential damage or unwanted overheating could occur. The curves for the skin, fat, muscle, bone and bone marrow layers are reported in Fig. 3. These curves are obtained in the case of a non-uniform magnetic field produced by a pair of Helmholtz coils, in a way different from [8, 9]. This interesting case for the non-target tissue was monitored by considering the temperature on the tissues of the geometry in Fig. 3.a. It can be notice that the highest temperature values occur in bone and bone marrow, i.e. nearby the magnetic scaffold, whilst in the other tissues the temperature levels are lower and approximately equal to the value of 37°C. Of course, observing the average value of the electric field norm in tissues over time, shown in Fig. 3.b, the levels are almost constant and decrease from the skin to the tumor, coherently to the distribution in the coil system. Furthermore, it is worth noting that the skin layer can exchange heat with air by natural convection and irradiation, and therefore, its temperature decreases, trying to equilibrate with the surroundings. Furthermore, the action of the brachial artery and vein is evident, since the muscle tissue is Fig. 3.a.

As regards the temperature distribution in the surroundings of the implanted thermo-seed, in Fig. 4 it is presented the temperature profile along the x-axis at the final time t = 80 min. Since the dielectric losses are much lower than the power deposited by the magnetic phase contained in the prosthetic implant, the heating is very local, i.e. the temperature gradient is steep between the

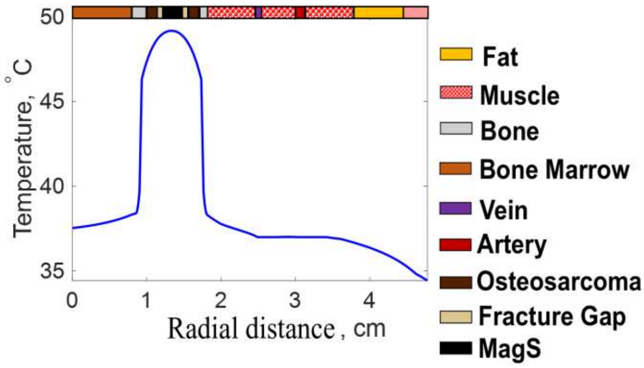

Figure 4. Spatial dependence (x-direction) of temperature at t=80 min. The effect of the MagS is local. The other tissues are in safe condition at the end of the treatment. (Color legend: Pink = Skin, Yellow = Fat, Red and white dots = Muscle, Grey = Bone, Light Brown = Bone Marrow, Violet = Vein, Red = Artery, Dark Brown = Osteosarcoma, Cream = Fracture Gap, Black = Magnetic Scaffold - MagS.).

scaffold and the healthy bone tissue. As a consequence, the temperature in the area containing the residual cells of the metastatic cancer reaches and overcome the therapeutic value of 42°C. For the magnetic hydroxyapatite implant considered in this work, the average temperature in the area of residua tumor cells is 44°C and this steady state value is reached after about 15 min of exposure, implying a heating rate of about 2.93 °C/min. These findings indicate that the

4 Conclusions and Future Perspectives

A multiphysic and non-linear model is employed to cope with the study and the planning of the hyperthermia treatment of secondary bone tumors employing magnetic prosthetic implants as thermo-seeds. The geometry of a human arm is considered, the temperature dependence and the coupling of magnetic, electric and thermal properties is considered to evaluate the treatment outcome when a magnetic hydroxyapatite scaffold is used [7-9]. The induced electric field, the temperature profile and dynamic are evaluated in both the target and non-target tissues. The local action of the thermo-seed and its effectiveness are verified.

With the proposed numerical framework it would be possible to develop an optimization strategy for the design of the inductor to be exploited to perform an accurate and controllable hyperthermia treatment. Moreover, the proposed model can be further extended to include the dependence of the magnetic susceptibilities of the scaffolds on the amplitude of the applied magnetic field. This modification could allow to study the design of the magnetic field source to focus the heating on a more local region, by including a tunable field free region [10, 11].

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