Feasibility Analysis of Theranostic Magnetic Scaffolds for Microwave Monitoring of Hyperthermia Treatment of Bone Tumors

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***Abstract*—Magnetic biomaterials are multifunctional tools currently under investigation as theranostic platforms for biomedical applications. They can be implanted in bone tissue after bone cancer resection to perform local interstitial hyperthermia treatment. Given the requirements of high quality treatment, the hyperthermia therapy should be performed monitoring the system temperature, to avoid hot spots and control the treatment outcome. It is known that the magnetic properties of such implants vary with temperature. It is hypotesized that the treatment dynamic could be monitored using a microwave monitoring system. The variation of the electromagnetic properties of the biological tissues and the magnetic implant during the therapy would result in a different propagation of the microwave signal. This work investigates the feasibility of using microwaves to non-invasively monitor hyperthermia treatments with a simplified monodimensional propagation model. The forward problem is solved to identify the working frequencies, the matching medium properties and study several candidate materials. By using the numerical solutions from nonlinear and multiphysics simulations of the bone tumor hyperthermia treatment using magnetic scaffolds, the microwave signal propagation dynamic is studied. From our feasibility analysis, we found that it is possible to correlate the average tumor temperature with significant (∼20 dB) variations in the transmission coefficient during a typical interstitial hyperthermia session using magnetic scaffolds. Our work brings together, for the first time, the electromagnetic material properties, the physio-pathology and physics of the hyperthermia treatment and the microwave propagation problem, thus paving the route for the development of an innovative theranostic system.**

***Index Terms*—Electromagnetic waves propagation, hyperthermia, magnetic biomaterials, microwave imaging, theranostic.**

I. Introduction

MAGNETIC biomaterials are smart, responsive and remotely-controllable devices thoroughly investigated for their multifunctional character in biomedical applications [1], [2], [3], [4], [5], [6], [7], [8], [9], [10], [11], [12]. Magnetic biomaterials can be synthesized by iron ion doping of bioceramics [7], [9], [10], [13], [14] or loading polymers with magnetic micro- or nanoparticles (MNPs) [15], [16], [17]. From a clinical perspective, the availability of such a large class of nanocomposites is appealing to manufacture prosthetic implants which would open novel therapeutic modalities [1], [2], [3], [4], [5], [6], [7], [8], [9], [10], [11], [12]. The advantages of implanting a so-called magnetic scaffold (MagS) are several. When a static or very low frequency (up to hundreds of Hz) magnetic field (MF) is applied, the MagS acts as a mechanotrasnducer, stimulating surrounding tissues [4], [8], [18], [19]. On the other hand, MagS could be used to enhance the controlled delivery of magnetic drug carriers for tissue repair [20], [21], [22], while favoring the controlled seeding of magnetized cells [23], [24]. Furthermore, when a MagS is exposed to a MF working in the radiofrequency (RF - from hundreds of kHz to few MHz) [16], [25], [26], [27], [28] or microwaves (MW) bands [29], the magnetic phase embedded in the biomaterial dissipate heat, which can be used for therapeutic purposes. In particular, the temperature increase due to the electromagnetic (EM) heating can activate the release of chemoterapeutic drugs [30] or can be used to perform local interstitial hyperthermia treatment (IHT) [25], [26], [27], [28], [29].

IHT is very promising in the field of orthopaedic oncology [31], [32], [33]. Indeed, primary or secondary bone cancers are currently treated by surgical intervention and their resection leaves a tissue damage which requires a graft, i.e. a scaffold [34]. If the implant is manufactured using a magnetic biomaterial, it can be implanted in bone tissue after bone cancer resection to perform IHT against the potential residual cells and limiting the recurrence rate [25], [26], [27], [28], [35]. During IHT it

Manuscript received 21 February 2023; revised 17 May 2023; accepted 18 June 2023. Date of publication 3 July 2023; date of current version 22 November 2023. This work was supported by the European Union - NextGenerationEU through the Italian Ministry of University and Research under PNRR - M4C2-I1.3 Project PE_00000019 "HEAL ITALIA" to Alessandro Fanti CUP F53C22000750006 University of Cagliari. *(Corresponding author: Alessandro Fanti.)*

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Digital Object Identifier 10.1109/JERM.2023.3288741

is mandatory to monitor the temperature of both target and non-target tissues, to avoid unwanted hot (or cold) spots and control the temperature pattern to maximize the treatment outcome and provide a high quality treatment [36], [37]. In the case of interstitial treatment, especially for bone tumors, the thermometry is a rather complex process [38]. For instance, the implant of a temperature probe can lead to infection. In this framework, non-invasive, cost-effective, fast and reliable strategies for temperature control would be a significant tool for translating and enhancing the effectiveness of IHT with MagS. However, currently, from the analysis of the state of the art, there is lack of any of such monitoring tools.

Recently, noticeable developments have been made in magnetic resonance imaging (MRI)-guided hyperthermia [39]. Despite MagS have been tested for in vivo MRI to assess bone healing, vascular ingrowth and implant integration by quantifying the transverse relaxation times (T_2) changes [40], [41], [42], [43], and even though their safe and compatible use in MRI was assessed [43], given the realtively high cost of MRI, to date no studies about MRI-guided IHT with MagS exist. Magnetic particle imaging (MPI) [44], [45], [46] was proposed as methodology for assessing the temperature during magnetic fluid hyperthermia (MFH) with promising results [46]. However, it has never been investigated as a monitoring modality for the IHT of bone tumors using MagS. As a matter of fact, the theranostic potential of MagS is largely underestimated. Hence, there is room for investigating the feasibility of innovative diagnostic modalities which use MagS as core element.

Among the many biomedical applications of microwave (MW) diagnostic imaging [47], [48], [49], its use in the framework of thermal therapy looks promising, due to its capability of being a non-invasive, cost effective, fast and reliable strategy [50], [51], [52]. In particular, MW imaging is an approach under investigation for tissues temperature monitoring during hyperthermia [53] and ablation [54]. The working idea is to perform qualitative [50], [55], [56], [57] or quantitative MW imaging [47], [58], [59], [60], [61], [62], [63] considering the beginning of the treatment as the reference configuration and then assessing, in a differential way, the spatial and temporal changes of the dielectric contrast due to the tissues temperature variation during the hyperthermia [53]. This principle could be applied to the IHT of bone tumors with MagS.

To this goal, the true theranostic character of MagS could be fruitfully exploited relying on the presence of the magnetic phase (i.e., micro-particles or MNPs) in the biomaterials. Indeed, MNPs were already considered as powerful contrast agents and scatterers to enhance the performances of MW imaging of breast tumors [64], [65], [66], [67], [68], [69]. Considering this literature works, and knowing that the magnetic properties of MagS vary with temperature during IHT [25], [26], [70], we envisage that having a magnetic scatterer in the system, located around the target area, could lead to an effective monitoring of the IHT dynamics using a MW monitoring system. In other words, during the IHT with MagS, the magnetic and dielectric properties would vary during the therapy. However, this very first proposal and working hypothesis has never been tested. Given that the inverse-problem formulation for MW imaging with magnetic materials demands for specific and complex formulation [64], [65], [66], [67], [68], [69], [71], there is need of collecting and rationalizing all the primary data about the geometry, the material properties, the physio-pathology, the treatment physics and possible operative conditions of the scenario of IHT with MagS. When MW imaging is applied to a new field, it is usual to investigate the problem in a simplified geometry and propagation scenario, to determine if and which type of matching medium would be required to avoid significant reflections of the impinging MW signal, and to determine a suitable range of operative frequencies [54], [72]. This information will be fundamental for the design of antennas, but also for the setup of validation experiments and the manufacturing of tissue phantoms [73]. Therefore, to assess the theranostic potential of MagS, in this work the feasibility of using MW imaging for the monitoring of IHT with MagS is preliminary analyzed.

TABLE I
PARAMETERS OF THE SIMPLIFIED GEOMETRY FOR THE PROPAGATION PROBLEM

	Thickness (mm)	**Var. Name**
Skin	1.5	d_s
Fat	10	d_f
Muscle	45	d_m
Bone	2	d_b
Tumor	0.5	d_t
Fracture gap	0.3	d_{fr}

II. SYSTEM GEOMETRY

Bone tumors can affect several body sites, mainly limbs [74], [75], [76]. In this framework, we envisage herein a MW monitoring system composed of transmitting (TX) and receiving (RX) antennas deployed around a human limb (e.g., an arm), modeled as a cylindrical structure, which extends indefinitely along the z-direction, as shown in Fig. 1(a). However, the propagation analysis of a cylindrical geometry can be complicated, with loss of physical insights, thus hampering the fundamental understanding of material properties role, and how IHT dynamics impact on the MW propagation. Hence, as a preliminary investigation, we further simplify the anatomical problem by relying on the 2D surface phantom model proposed in [26] and investigate a planar case, focusing on the white straight line depicted in Fig. 1(a) Therefore, the geometry is assumed to be a planar, multilayered structure composed of $N = 8$ layers, as presented in Fig. 1(b). The layers of biological tissues are skin, fat, muscle, bone, a generic bone tumor (e.g., FS and OS) and the fracture gap. Two semi-infinite media are considered, i.e., a matching medium (MM), having an unknown relative permittivity $\epsilon_m \in [\epsilon_0, 80]$, and an implanted MagS. The matching medium is assumed to be lossless, given that this contribution is negligible [62], [72]. The thicknesses and physical sizes of the tissue layers are taken from the case study reported in [26] and provided in Table I.

III. PROPAGATION MODEL

The propagation medium is assumed to be homogeneous and indefinite in the zy-plane. A planar, linearly polarized, time-harmonic transverse-magnetic (TM) wave is impinging on the system shown in Fig. 1(b), traveling along the x-direction. The

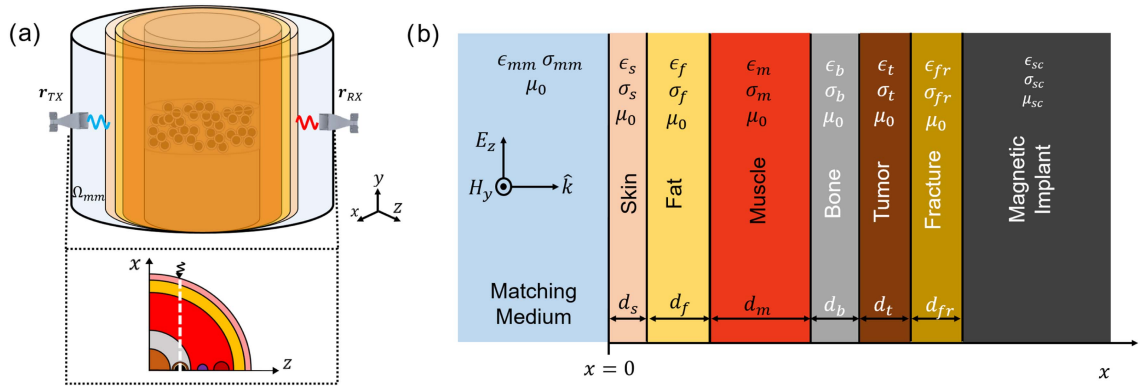

Fig. 1. (a) Envisioned system and schematic description of the simplified imaging problem. (b) Mono-dimensional layered model for a transverse magnetic (TM), linearly polarized plane wave impinging on a multilayer structure composed of skin, fat, muscle, tumor and fracture tissue and a MagS, assumed as semi-infinite medium.

media are characterized by a relative complex permittivity ϵ_i, an electrical conductivity σ_i (S/m) and permeability μ_i (in H/m), for $i = 1, 2, \ldots, N$. All tissues are assumed to be non-magnetic ($\mu_i = \mu_0$, for $i = 1, 2, \ldots, N-1$).

The system shown in Fig. 1(b) is analyzed by using the wave-amplitude transmission matrix (WATM) method [54], [72], [77], [78]. By knowing the amplitude of the propagating and reflected electric field along the x-axis at the first layer, $E_{x+}^{(1)}$ and $E_{x-}^{(1)}$, respectively, the multilayered structure can be fully described by

$$\begin{bmatrix} E_{x+}^{(1)} \\ E_{x-}^{(1)} \end{bmatrix} = [M_1][T_1][M_2][T_2]\ldots[T_{N-1}][M_{N-1}] \begin{bmatrix} E_{x+}^{(N)} \\ 0 \end{bmatrix} . \quad (1)$$

The matrix M_i accounts for the EM wave in the i-th medium as a function of the MW signal in the $(i+1)$-th medium, so that

$$M_i = \frac{Z_i - Z_{i+1}}{Z_i + Z_{i+1}} \begin{bmatrix} 1 & \frac{2Z_i}{Z_i+Z_{i+1}} \\ \frac{2Z_i}{Z_i+Z_{i+1}} & 1 \end{bmatrix} , \quad (2)$$

where the wave impedance of the i-th medium (Z_i) is $Z_i = \sqrt{\frac{\mu_i}{\epsilon_i}}$. Then, the propagation in the i-th layer is described by the transmission matrix T_i, defined as

$$T_i = \begin{bmatrix} e^{k_i d_i} & 0 \\ 0 & e^{-k_i d_i} \end{bmatrix} , \quad (3)$$

being the wavenumber $k_i = \sqrt{\mu_i \epsilon_i}$. By relying on the fact that the electric field is continuous at the interface between the i-th and the $(i+1)$-th layers, and considering that the field amplitude can be computed considering the forward and backward propagating waves, it is possible to write the following system

$$\begin{bmatrix} E_{x+}^{(1)} \\ E_{x-}^{(1)} \end{bmatrix} = \begin{bmatrix} \zeta & \xi \\ \gamma & \delta \end{bmatrix} \begin{bmatrix} E_{x+}^{(N)} \\ 0 \end{bmatrix} . \quad (4)$$

From (4), the total reflection and transmission can be found considering that the generic reflection coefficient, Γ, at the i-th interface $\Gamma_i = \frac{E_{i-}}{E_{i+}}$ must satisfy the recursion [77]

$$\Gamma_i = \frac{\frac{Z_i - Z_{i+1}}{Z_i + Z_{i+1}} + \Gamma_{i+1} e^{-2k_i d_i}}{1 + \frac{Z_i - Z_{i+1}}{Z_i + Z_{i+1}} \Gamma_{i+1} e^{-2k_i d_i}} . \quad (5)$$

With (5) is possible to evaluate the reflection of the i-th layer.

The WATM method have been implemented in Matlab 2021a (The MathWorks Inc., Boston USA). The propagation is studied for $f \in [0.1, 10]$ GHz to find MM properties which ensure an effective signal transmission, while determining the operative bandwidth to use MWI as tool for monitoring the IHT of bone tumors with MagS.

IV. Non-Linear Multiphysics Simulations of Hyperthermia Treatment With MagS and Impact on MW Propagation

Once the MM properties and the working frequencies are selected, we developed a new methodology to study if MWI can be used to monitor the IHT of bone tumors with MagS. We simulated the IHT with MagS and modeled the influence on the propagation problem.

To simulate the IHT of bone tumors with MagS, the spatio-temporal evolution of the temperature field ($T(\mathbf{r}, t)$) during the IHT was computed using a multiphysics non-linear model developed in the commercial Finite Element Software (FEM) COMSOL v5.5 (Comsol Inc., Burlingthon, MA, USA) [26]. In brief, for the geometry shown in Fig. 1(a), with tissue thicknesses reported in Table I, Maxwell's equations are solved in the frequency domain, considering the coupling with the Pennes' Bio-Heat equation (PBHE), as described in [26], [27]. The EM and thermal properties of tissue and MagS are assumed to vary with the system temperature. By assuming a steady-state temperature distribution $T(\mathbf{r}, t_0) = T_b = 37$ °C), under the boundary condition of air-skin convective heat transfer ($T_{air} = 22$ °C), a magnetic field of 300 kHz and 15 mT amplitude is applied, so that the biological tissues and the MagS dissipate heat. The total dissipated EM power (Q_{EM}, in W $\cdot$ m^{-3}) is used as source term in the PBHE and the new temperature distribution is found. The EM properties are updated, Q_{EM} is computed, PBHE is solved

Fig. 2. Proposed approach for studying, in silico, the feasibility of using microwaves for monitoring the hyperthermia treatment of bone tumors using magnetic scaffolds.

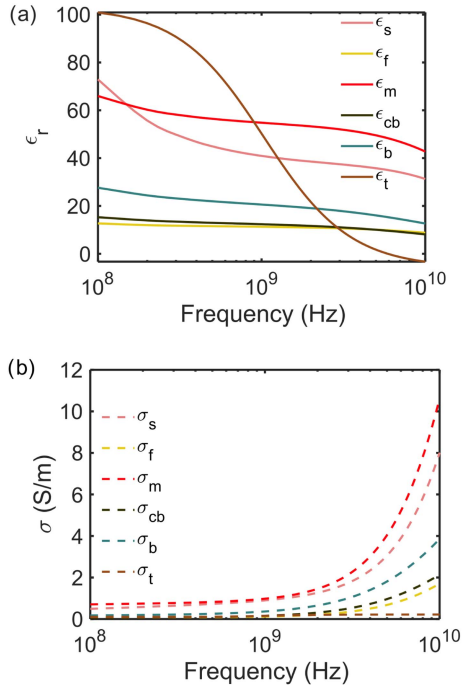

Fig. 3. (a) Relative dielectric permittivity ϵ_r of the tissues for the layered phantom. (b) Electrical conductivity σ (S/m) of the tissues for the layered phantom.

again, and the resolution scheme stops at the end of the treatment, for $t = 80$ min.

To study how IHT impact on MW propagation, we followed the approach summarized in Fig. 2. We solved the PBHE with our nonlinear, multiphysics model to derive the thermal distributions ($T(\mathbf{r}, t)$) in the MagS and biological tissues (Fig. 1(b)), and then compute the average values ($T(t)$). We used the simulated results to compute, for each time step of the simulated IHT, the variation of the scaffolds and tissue EM properties and solve the MW propagation problem for each time step. In detail, we compute a $\Gamma(t, T)$ and investigated the differences in the transmission coefficient with respect to the initial time $t = 0$ and uniform temperature distribution ($T = T_b \ \forall \ x$), which is assumed as reference configuration for the imaging problem, i.e.

$$\Delta[1 - |\Gamma|^2] = [1 - |\Gamma(t = 0, T_b)|^2] - [1 - |\Gamma(t, T)|^2] \,. \quad (6)$$

V. Material Properties

A. Biological Tissues

The properties of the skin, fat and muscle tissues (Fig. 1) at $T_b = 37\,^{\circ}$C are taken from [79] and given in Fig. 3. The properties of the fracture gap are assumed to be the volume-weighted average of blood and bone EM properties [80]. The fracture gap is assumed to be in the inflamed state [25], [26] and its EM properties are reported in Fig. 3. As regards the bone tumors, the EM properties in the kHz range can be found [25], [26], but in the literature there is lack of ex vivo or in vivo characterization of the MW dielectric permittivity of bone tumors [81], [82], [83]. Anyway, the mouse tumor data reported in [81] offers different staging and were used in this study. The variation of the dielectric properties of biological tissues with T is assumed to be linear through coefficients K_ϵ and K_σ [25], [26], [84]

$$\frac{\epsilon(T)}{\epsilon_{T_0}} = (1 + K_\epsilon \Delta T)$$
$$\frac{\sigma(T)}{\sigma_{T_0}} = (1 + K_\sigma \Delta T) \,. \quad (7)$$

B. Magnetic Scaffolds

The characterization of MagS at MW is not available in the literature, but a complete characterization of magneto-dielectric composite MW-absorbing materials can be found. In principle, some of them could be used for IHT of bone tumors. However, the biocompatibility and the feasibility of using these materials as MagS must be considered. We selected three different composite ferromagnetic biomaterials characterized at MW. In particular, among the magneto-dielectrics, the NiFe-PE (Ni $_{81}$ Fe$_{19}$ poly-ethylene), with a 40% loading of μm-sized spherical inclusions, was considered [85]. The 30% Fe-PLA, manufactured with a two-step mixture process, from [86] was selected. Finally, the Fe-PLA from Proto-Pasta, recently characterized by a dedicated broadband method [87] was also considered. This latter materials was also experimentally characterized for the IHT of bone tumors [28]. The MagS EM properties are given in Fig. 4.

The modeling of the temperature variation of the three MagS is more challenging. A characterization of these materials as a function of the temperature have not been carried out yet. We assume that the variation of the dielectric properties of MagS are negligible during the IHT, whilst the magnetic properties are assumed to be variable during the IHT of bone tumors. We hypothesize that the temperature increase in the MagS is far from the Curie-Weiss temperature of the material, so that

$$T_C \gg T \,, \quad (8)$$

and the material retains its natural ferromagnetism and the magnetic phase does not change [88]. This is a reasonable assumption since magnetite, iron, nickel and their alloys presents T_C of several hundreds of °C: for μm-sized iron $T_C = 700\,^{\circ}$C, whilst for NiFe permalloy particles $T_C \simeq 500\,^{\circ}$C [88]. In this

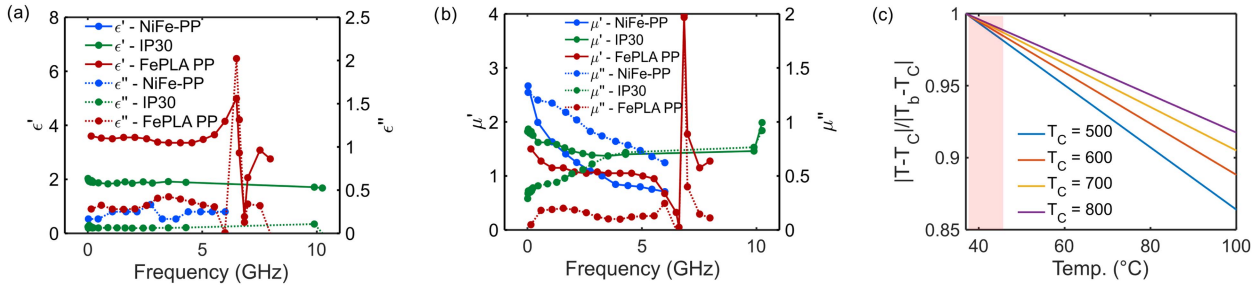

Fig. 4. (a) Complex dielectric permittivity: real (ϵ') and imaginary (ϵ'') parts of the magneto-dielectric scaffolds. (b) Complex magnetic permeability: real (μ') and imaginary (μ'') parts of the magneto-dielectric scaffolds. (c) Coefficient for the variation of the magnetic properties as a function of temperature. The dependence from the Curie temperature of the materials is highlighted.

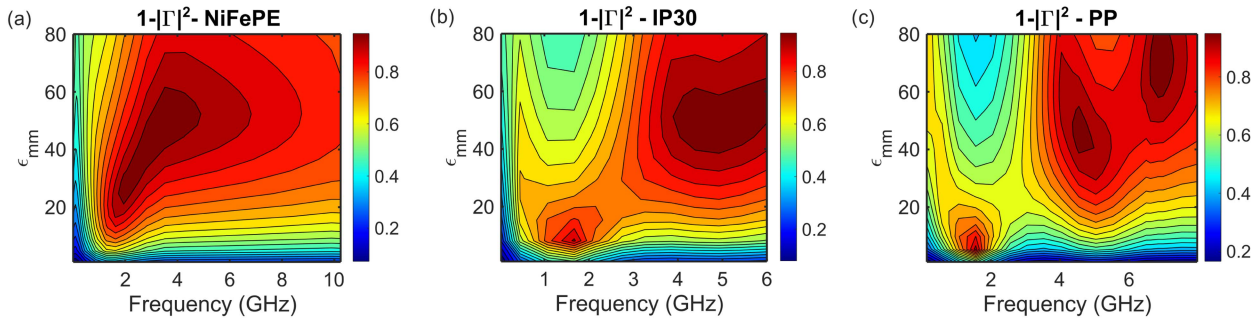

Fig. 5. (a) Transmission coefficient as a function of frequency (f) and the properties of the matching medium (ϵ_{mm}) for the NiFe-PE scaffold. (b) Transmission coefficient as a function of frequency (f) and the properties of the matching medium (ϵ_{mm}) for the IP30 Fe-PLA. (c) Transmission coefficient as a function of frequency (f) and the properties of the matching medium (ϵ_{mm}) for the Proto-Pasta MagS. The transmission is evaluated a the matching medium-skin interface.

framework, relying on the classical mean-field theory of ferromagnets, the MagS magnetization is assumed to decreases as temperature increases ($M_{sc} \propto \frac{1}{T}$) [88], whilst the magnetic permeability follows the following relationship [88]

$$\mu(T) \simeq 1 + \frac{C_{cw}}{|T - T_C|}. \tag{9}$$

where C_{cw} is the material specific Curie constant. Under the assumption of (8), we can linearize (9) by considering the ratio of $\mu(T)$ and $\mu(T_b)$, so that

$$\mu(T) \simeq \frac{|T - T_C|}{|T_b - T_C|}\mu(T_b). \tag{10}$$

The variation coefficient, for different values of T_C is shown in Fig. 4(c). It can be noticed that, in the range of temperature typical of hyperthermia (41–45 °C), the variation of the MagS properties is relatively narrow (∼2.5%). However, as reported in [22], [25], [26], [27], [28], [29], the MagS temperature can lie in the range 50–70 °C. Therefore, the complex magnetic permeability can reduce of up to ∼10% of the initial value.

VI. Results

To evaluate the feasibility of using MW to monitor the IHT of bone tumors using MagS, we performed a novel analysis based on a monodimensional propagation model for the geometry shown in Fig. 1(b). We investigated the transmission coefficient over the frequency range 0.1–10 GHz by varying the dielectric properties of the MM, and considering three different magneto-dielectric as candidates MagS. At $t = 0$ and $T(\mathbf{r}) = T_b$, the transmission maps are shown in Fig. 5. Given the contrast between the biological tissues (Fig. 3) and the MW response of the MagS (Fig. 4), the transmission coefficients are not identical for the MagS under study. In detail, from Fig. 5(a), for the NiFe-PE MagS high level of transmission are achieved if $\epsilon_{mm} \in [20, 80]$ is used, for $f \in [2, 5]$ GHz. Different conclusions can be sought for the two iron-filled PLA MagS. The dispersion of IP30 and PP magneto-dielectrics are not identical, as can be verified from Fig. 4(a) and (b). For IP30 and the PP MagS, a region with high transmission ($1 - |\Gamma|^2 \simeq 0.8$) can be found at ∼ 2.45 GHz and $\epsilon_{mm} \simeq 20$. Other maxima in the transmission can be achieved for $\epsilon_{mm} > 40$ and $f > 4$ GHz. By analyzing Fig. 5, we can set $\epsilon_{mm} = 40$ and achieve suitable MW propagation for all the MagS.

The MW propagation for the proposed model could be used to study, for the first time, if significant differences in the transmitted/reflected MW signal during IHT of bone tumors arise. For $\epsilon_{mm} = 40$, the variations of the transmission coefficient during a simulated IHT were investigated. The findings are reported in Fig. 6(a)–(c). Few frequency spots offer a significant variation in the transmission during the treatment time. The IP30 and PP MagS exhibit a similar response. Hence, forecasting the development of a MW system, we will focus more on the industrial, scientific and medical (ISM) frequencies of 434 and 915 MHz, 2.45 and 5.8 GHz. Also, given that MW monitoring would be carried out in a differential scenario, the evaluation

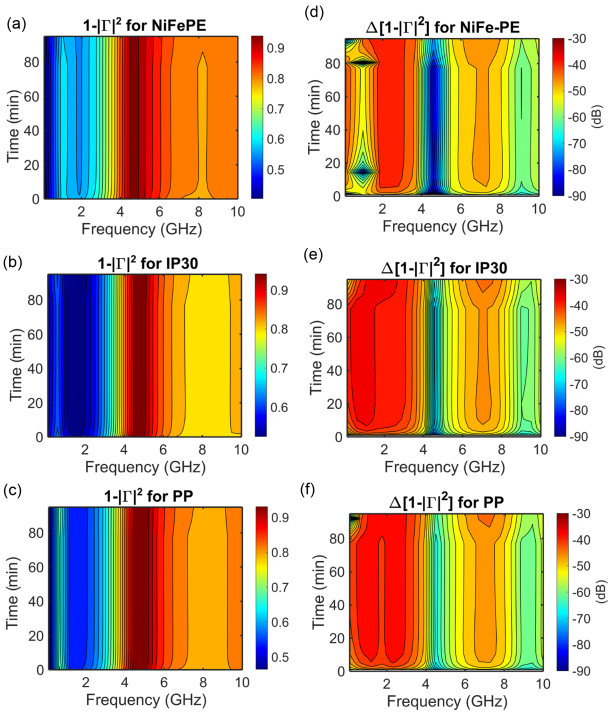

Fig. 6. Transmission coefficient at the matching medium-skin interface, for $\epsilon_{mm} = 40$, as a function of treatment time and frequency, for the (a) NiFe-PE magneto dielectric implant, (b) IP30 magnetic scaffold and (c) PP magnetic PLA. Differential transmission coefficient, in dB, evaluated at the initial time $t = 0$ and during the treatment for the (d) NiFe-PE magneto dielectric implant, (e) IP30 magnetic scaffold and (f) PP magnetic PLA.

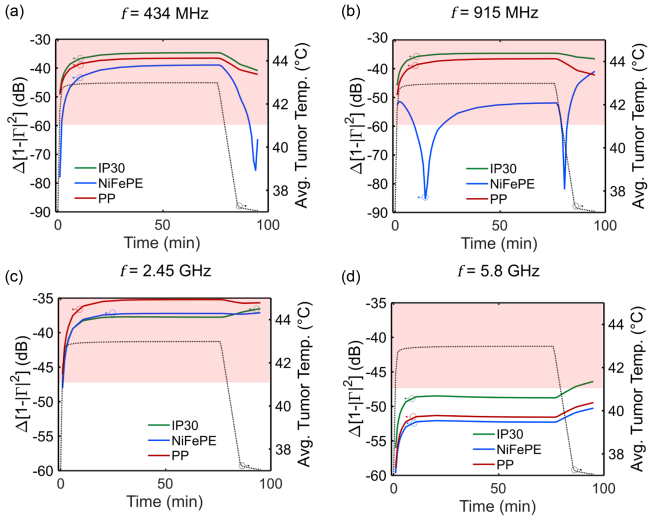

Fig. 7. Difference in the transmission coefficient evaluated at $t = 0$ and during the simulated hyperthermia treatment: (a) as a function of treatment time (in dB), and (b) as a function of tumor temperature (in dB).

of the figure of merit defined by (6) was investigated. The findings are reported in Fig. 6(d)–(f). For the three MagS large variations (at least ∼20–30 dB) occurs in some non-ISM bands, such as around 4–5 GHz. However, the permalloy material, exhibits significant changes in the MW signal levels at lower frequencies ($f < 2$ GHz). The two PLA-based implant show similar features, but with large magnitude differences, since the PP material has a wider dynamic range. With these information, we investigated the dynamic of the MW transmission at ISM bands versus the treatment time, and, also, tried to correlate this information with the IHT simulation results.

In Fig. 7 we report the relative changes in the transmission coefficient, at the first interfaces, over the treatment time, with superimposed the average tumor temperature (T_t) derived from the simulations. At the lowest frequency of 434 MHz (Fig. 7(a)), as T_t increases, the transmission coefficient increases of ∼15 dB for IP30 and PP MagS, and of more than 30 dB for the NiFePe case. As the external RF field is turned off and the biological system cools down, the transmission coefficient almost recovers its initial value, with a ∼1 min lag. In Fig. 7(a), we highlighted the therapeutic range of IHT (41–45 °C). Given the variations, we can hypothesize that an empirical threshold can be set to identify the target temperature changes. On the other hand, at 915 MHz differences in the material responses appear. For the case of a NiFe-PE MagS, abrupt changes (> 25 dB) at the peak temperature occurs (Fig. 7(b)). Differently, the curves for the IP30 and PP cases exhibit a ∼10 dB decrease as the IHT is terminated. For $f = 2.45$ GHz, the dynamic range of $\Delta[1 - |\Gamma|^2]$ reduces (see Fig. 7(c)). At the initial time ($t = 0$) the differences between the three MagS candidates is narrow. As the MagS and the tumor are heated, a ∼7–10 dB increase can be noticed (Fig. 7(c)). At $t = 80$ min, the PP scaffold exhibits a reduction in $\Delta[1 - |\Gamma|^2]$, whilst in the case of IP30 magneto-dielectric implant the figure of merit increases (±2 dB). The NiFe-PE retains an intermediate behavior. For the highest ISM frequency ($f = 5.8$ GHz), similar considerations holds, with lower differences between the materials, as shown in Fig. 7(c). The differences in the findings in Fig. 7(a) and (b) from that given in Fig. 7(c) and (d) can be due to the increased frequency and, then, to the reduced penetration depth, which results in a lower mark of the EM properties change due to the MagS heating.

VII. Discussion

Despite these promising results, our study has limitations and a discussion is in order. hese findings will be used to design and plan future experiments, in which more precise and comprehensive measures will be taken to explore the complexity of this theranostic application of MagS in IHT. The non-linear, ill-posed MW problem of finding the temperature variations of the EM contrast will be solved using qualitative [53], quantitative [62] or machine learning-based [89] methods.

A. Limitations

Given that a simplified case has been considered, the proposed analysis has to be extended to 2D or 3D cylindrical geometries to investigate the MW propagation in more detail.

VIII. Conclusion

We investigated the use of MW for monitoring the IHT of bone tumors using theranostic MagS. Using a monodimensional propagation model, after collecting and rationalizing material

properties and physio-pathological features, we identified suitable matching medium properties and the possible working frequencies. The IHT was simulated with a nonlinear multiphysics model with temperature-dependent EM properties and evaluated the MW signal variation during the therapy with three different MagS. Suitable MM properties to ensure adequate transmission can be found. Then, we analyzed the transmission spectrum as a function of the treatment time and evaluated the variation from the initial time for the major ISM bands. Significant changes in signal level were found and correlated to the tumor average temperature variation, thus positively answering to the feasibility of the MW monitoring.

ACKNOWLEDGMENT

The views and opinions expressed are those of the authors only and do not necessarily reflect those of the European Union or the European Commission. Neither the European Union nor the European Commission can be held responsible for them.

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Open Access funding provided by 'Università degli Studi di Cagliari' within the CRUI CARE Agreement