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Investigation of physical properties of Fe$_3$O$_4$/Au-Ag@MoS$_2$ nanoparticles on heat distribution in cancerous liver tissue

Tina Seyedjamali$^{1,}$$^*$, Mohamadreza Kazem Farahzadi$^2$ and Hossein Arabi$^3$

$^1$Department of Physics, Iran University of Science and Technology, Narmak, Tehran 16846, Iran
$^2$Department of Radiation Medical Engineering, Science and Research Branch, Islamic Azad University, Tehran, Iran
$^3$Division of Nuclear Medicine and Molecular Imaging, Department of Medical Imaging, Geneva University Hospital, CH-1211 Geneva 4, Switzerland

$^*$Author to whom any correspondence should be addressed.
E-mail: tinaseyedjamali@gmail.com

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Abstract
Liver cancer has significantly grown in recent years, and thus its mortality rate has also increased since its symptoms appear to be in malignant stages and the treatment path at this stage is extremely challenging. New therapies based on producing heat in cancerous tissues have opened up a new way to treat cancer. This study investigated the treatment of liver cancer by the magnetic hyperthermia approach and nanoparticles (NPs) such as iron oxide (Fe$_3$O$_4$) core with gold (Au), silver (Ag) alloy shell, and molybdenum disulfide (MoS$_2$) coating. The optical properties of these NPs within the tumor, including the extinction coefficient and surface plasmon peak (SPR) as a function of size, structure, different compositions, and thickness, were also examined using the effective medium theory, followed by assessing the impact of temperature distribution through the analytical modeling of an alternating current magnetic field. The results demonstrated that NPs with a compound of Fe$_3$O$_4$ – Au$_{0.25}$Ag$_{0.75}$@MoS$_2$, a 3 nm thick cover of Au-Ag alloy, and two layers of MoS$_2$ have the best coefficient of extinction and SPR in the biological window. The Au-Ag alloy improved the extinction coefficient and simultaneously prevented the accumulation of magnetic NPs. Considering that the Au-Ag alloy alone cannot function within the range of biological windows, MoS$_2$ was used, which increased the extinction efficiency at higher wavelengths. The examination of the temperature distribution in the tumor for the proposed alloy compound indicated that after a short time from irradiation initiation, the tumor temperature reaches 45°C. Further, the temperature distribution within the tumor tissue reached its maximum value at the center of the tumor and decreased dramatically while getting away from the center. Finally, the use of magnetic hyperthermia enabled localized delivery of therapeutic doses to malignant tumors, thereby representing superior performance and efficiency over the photothermal method.

1. Introduction

Since the symptoms of liver cancer appear late in patients, the disease detection/diagnosis is normally achieved in advanced stages, and surgery alone may not be sufficient. Although much progress has been made in treating liver cancer, patients with malignant liver cancer have always had high mortality rates. In this respect, exploring new treatments can significantly affect the efficient management of this cancer. Cancer treatment only encompassed radiotherapy, chemotherapy, and surgery methods in previous decades. Radiation therapy uses high-energy rays to kill cancer cells. Drawbacks of this treatment include damage to healthy tissue, perforation of the colon, infertility, and the possibility of secondary cancer [1, 2]. The chemotherapy technique uses targeted substances; however, this method also has disadvantages as these carriers, though targeted, can also damage
other healthy cells in the bone marrow, gastrointestinal tract, and hair follicles [2, 3]. Finally, there are some limitations associated with the surgery treatment: the entire cancerous tissues cannot be removed depending on the tumors’ location [2]. In this regard, hyperthermia is one of the recently employed complementary methods in cancer treatment.

Since cancer cells are more sensitive to temperature, recent therapeutic initiatives have mostly relied on the heating characteristics of the tumor cells. Although the heating techniques alone are insufficient, they could effectively destroy cancerous tissues. Thus, they can be considered a complementary treatment [4, 5]. Hyperthermia is one of the minimally invasive therapies based on converting energy sources, including microwaves, radio waves, and ultrasound into heat. In this method, nanoparticles with high energy absorption and high light-to-heat conversion efficiency are used in the near-infrared (NIR) region [6]. In the hyperthermia technique, the temperature within the tumor commonly ranges from 41 to 45 °C. Sharma et al showed that when the temperature exceeds 46 °C (i.e., thermal erosion), it can effectively result in cell necrosis [7–9]. In the laser interstitial thermal therapy (LITT) technique proposed by Skandalaki et al, surgery is performed by implanting a laser catheter in the tissue that can produce the required local heat after injection of nanoparticles and localization. Therefore, it is an invasive method and may adversely affect healthy tissues [10].

Photodynamic therapy (PDT) is a technique that uses a light-sensitive substance and a laser to stimulate material in the tumor to produce activated oxygen and cure liver cancer. However, Hong Zhu et al showed that it has drawbacks such as severe damage to surrounding tissues. Since light absorbers in this method may accumulate in healthy liver tissue more than cancerous tissue, it may cause damage to healthy tissue. On the other hand, a high wavelength and power laser beam should be used in this method because the liver organ is located deep in the abdomen (in addition to its large volume). Thus, it is likely to cause side effects and damage healthy tissues [11].

When using hyperthermia as a treatment for cancer, it must have very low toxicity and the ability to heat up and kill cancerous tissue topically [12, 13]. In magnetic hyperthermia was proposed for deep lesions to address this limitation [14, 15]. Magnetic hyperthermia treatment (MHT) is a treatment that has far fewer side effects than chemotherapy and radiotherapy and, unlike other cancer treatments, can activate the immune system [16]. Besides, the abundance of blood vessels in the liver causes rapid heat loss, thereby reducing damage to healthy liver tissue [11]. Inducing local heating can be accomplished using iron-based magnetic nanoparticles, which are extremely biocompatible [17, 18]. This technique is minimally invasive and can deliver an adequate heat dose to the targeted region while avoiding injury to the healthy tissue located in the surrounding area. In this technique, heat is generated by applying an alternating magnetic field to the nanoparticles within the target tissue [19]. The choice of nanoparticles depends on the ranges/levels of temperature, heat production efficiency, treatment duration, toxicity, solubility in biofuels fluids, damage to the healthy tissue, and efficiency in destroying the cancerous tissue. The favorable nanoparticles should have high coefficients of extinction and adsorption in the range of biological windows (680–1400 nm) in the target tissue [20–22]. Moreover, the delivery of heat to the target tissue would also be affected by various factors such as size, geometry, environment, and structure of nanoparticles [23, 24].

The mass oscillation of electronic charge density in metals causes localized surface plasmon resonance (LSPR), an electromagnetic state [25]. When plasmons are subjected to certain electromagnetic disturbances, the charge density may not be zero in some areas, resulting in the generation of a restoring force that induces an oscillating charge distribution [26, 27]. Resonance occurs when the electromagnetic disturbance and plasma oscillation have the same frequency. Four factors affecting the oscillation frequency are electron mass, electron density, charge distribution size, and shape [23]. The surface plasmon resonance (SPR) or LSPR and the extinction coefficient can be adjusted within the desired window by modifying the nanostructure composition. Gold is biologically compatible as it is a noble metal that is thermally and chemically stable [23, 28, 29]. Despite these good properties of gold for heat treatment, pure gold would result in a poor extinction rate. Silver nanoparticles are the other nanoparticle category that has been widely used in medical trials regarding their antibiotic potential. However, when they are used alone, the Ag+ produced through oxidation could hinder the heat production process [30, 31]. It is of note that silver alone is not biocompatible. Therefore, bimetallic nanoparticles have favorable optical properties (better heat generation properties) than single metal nanoparticles [32]. In recent years, the use of two-dimensional (very thin) materials, especially graphene and Transition Metal Dichalcogenides (TMDC), for heat treatment has received much attention [33]. Of the four commonly used TMDCs (namely MoS2, WS2, MoSe2, WSe2), only MoS2 is biodegradable, and it is eliminated from the body within approximately one month [34, 35].

Wang et al used graphene oxide to treat cancer and compared the results with those of MoS2. Based on the obtained results, MoS2 nanomaterials exhibited about 7.8 times more energy absorption, as graphene oxide led to a much higher extinction coefficient than graphene. Moreover, MoS2 can be heated rapidly under NIR laser radiation. As a result, high-efficiency MoS2 nanomaterials have gained popularity owing to their effective response to NIR light radiation in cancer treatment [22, 34, 36]. Recently, magnetic nanoparticles have been
considered an essential agent in hyperthermia. Employing these magnetic nanoparticle carriers would increase the penetration/absorption of the drug in the cancer cell membrane. Hence, they can prevent systematic administration and side effects, and increase the therapeutic effects of anti-cancer drugs [37–46]. When magnetic nanoparticles are exposed to the AC field, the processes of hysteresis, Neel, and Brownian relaxation occur, which may trigger the heating process. Neel relaxation occurs due to the rotation of magnetic moments inside the nanoparticle while the particle is stationary. Brown relaxation results from the general rotation of particles. These mechanisms lead to the production of volumetric heat induced by the electromagnetic field [41]. Iron oxide has been extensively studied because of its fascinating properties such as easy synthesizing process, low cost, biocompatibility, depth of penetration, and, most importantly, superparamagnetism compared to other materials [42, 43]. Although iron oxide nanoparticles are biocompatible, they are usually coated with biocompatible polymers to prevent oxidation for hyperthermia treatment [44, 45]. In addition, we coat iron oxides that are not detected by the immune system and are excreted as an external agent. As a result, the half-life of these substances increases, and there is no need to use high doses [46]. In hyperthermia, iron oxide nanoparticles cause cell apoptosis, necrosis, and cell growth inhibition. Moreover, this superparamagnetic nanoparticle is the most commercial type of nanoparticle for treating hyperthermia because of its biocompatibility, magnetic ability, and functionalization. $\text{Fe}_3\text{O}_4$, as a combination of divalent and trivalent iron oxides, is the most common form of iron oxide [47].

In this paper, relying on effective medium theory, bio-heat and magnetic equations were employed to investigate the extinction coefficients and SPR as a function of core radius, the number of layers, environment effect, and the percentage of alloy compounds for the $\text{Fe}_3\text{O}_4$ – $\text{Au}$ – $\text{Ag} @\text{MoS}_2$ structure.

2. Materials and methods

Compared to their bulk materials, MNPs have demonstrated superior properties such as larger surface-to-volume ratios, excellent reactivity, and unique magnetic responses [48, 49]. This is despite their sizes being comparable to biomolecules [50]. For the production of MNPs, it is preferable to use materials that have high saturation magnetizations, such as pure metals (Fe, Co, Ni, etc.), alloys (FeCo, alnico, permalloy, etc.), and oxides (Fe$_3$O$_4$, γ-Fe$_2$O$_3$, CoFe$_2$O$_4$, etc.). Pure metals can produce higher saturation magnetizations; however, this does not make them appropriate for use in clinical settings due to their high toxicity and oxidative properties [47]. Magnetic nanoparticles have been considered for cancer treatment because they can be used as sources of spot heat in the presence of radiofrequency RF magnetic fields. Because there is a limited range of amplitude and magnetic field frequency for biologically induced heating, this treatment method is restricted. To be biologically feasible, the combination of H field strength and frequency $f$ should be in the range $H \times f \leq 4.85 \times 10^8\text{Hz} - \text{A m}^{-1}$ [51].

In this section, we examine the optical, magnetic and, thermal properties of the $\text{Fe}_3\text{O}_4$, $\text{Au}$ – $\text{Ag} @\text{MoS}_2$ structure figure 1. First, we relied on the dedicated equations to model the effect of the number of layers on the optical properties of the nanoparticle, then we examined the different percentages of the alloy components and calculated the extinction efficiency and SPR. In the third section, regarding the magnetic nanoparticles, we examined the governing equations of magnetism; and finally, we investigated the bio-heat equations and temperature distribution. This study relied on the effective medium theory, which is based on the weighted average theory, Bruggeman’s theory, and Maxwell Garnet’s theory [52–55].

2.1. Effective medium theory for MoS$_2$ coated with Au-Ag

In this section, we employed the governing equations for the number of layers using effective medium theory. Maxwell-Garnet’s theory is based on the Clausius-Mossotti relation, which considers the correlation between polarization $\varepsilon_0$ and the dielectric phenomenon [56]. In this regard, it is supposed that several layers of different nanoshells are stacked on top of each other [56]. As shown in figure 1, there is an Au-Ag spherical nanoshell with an inner radius of $t_{\text{core}}$ and a thickness of $t_{\text{sh}}$ surrounded by MoS$_2$, with a thickness of $t_{\text{ms}}$ while the core of this nanoparticle is of $\text{Fe}_3\text{O}_4$ (15, 20 and 25 nm). The refractive index of the tumor for liver is 1.349 [57]. $\varepsilon_{\text{core}}(\omega)$, $\varepsilon_{\text{sh}}(\omega)$ and $i = 1, 2, \ldots$ denote the dielectric function of the core and the shell, respectively. The dielectric performance of the target external environment is frequency-dependent, which is equal to $\varepsilon_0(\omega)$ [58]. According to Maxwell–Garnet’s theory, the dielectric effect between the core and the first shell is formulated as follows [58]:

$$
\varepsilon_{\text{eff}, 1} = \frac{\varepsilon_{\text{core}}(1 + 2\varphi) + \varepsilon_{\text{sh}}(2 - 2\varphi)}{\varepsilon_{\text{sh}}(2 + \varphi) + \varepsilon_{\text{core}}(1 - \varphi)}
$$

(1)
Where the volume fraction of the new layer is obtained from:

\[ \varphi_i = \left( \frac{r_i-1}{r_i} \right)^3 \]  

(2)

and for other layers, equation (3) could be derived from equations (2) and (3)

\[ \varepsilon_{\text{eff},2} = \frac{\varepsilon_{\text{eff},1}(1 + 2\varphi_1) + \varepsilon_{\text{shell}}(2 - 2\varphi_1)}{\varepsilon_{\text{shell}}(2 + \varphi_1) + \varepsilon_{\text{eff},1}(1 - \varphi_1)} \]  

(3)

The radius of the new layers is calculated as follows:

\[ r_i = r_{i-1} + t_d \]  

(4)

Here, \( t_d, r_{i-1} \) indicate the radius of the layer and the thickness of the lower shell, respectively.

Then, for calculating the efficiency of extinction, scattering, and absorption, equation (5) was used [58]:

\[
E_{\text{extinction}} = 4\pi Im \left[ a + \frac{x^2}{12} + \frac{x^4}{30} (\varepsilon_{\text{eff},n} - 1) \right] \\
E_{\text{scattering}} = \frac{8}{3} \left[ a^2 + \frac{x^4}{900} |\varepsilon_{\text{eff},n} - 1|^2 \right] \\
E_{\text{absorption}} = E_{\text{ext}} - E_{\text{aca}}
\]  

(5)

Wherein \( x = kr_n, k = \left( \frac{2\lambda}{\Lambda} \right) \) corresponds to the wavenumber of the incoming light (a and b). The coefficients related to dielectric calculations are obtained through the following equations [58]:

\[
a = \frac{\varepsilon_{\text{eff},n} - \varepsilon_x}{\varepsilon_{\text{eff},n} + 2\varepsilon_x} \\
b = \frac{\varepsilon_{\text{eff},n} - \varepsilon_x}{\varepsilon_{\text{eff},n} + 3\varepsilon_x}
\]  

(6)

(7)

Here, \( \varepsilon_x \) is the dielectric function for the external medium.

2.2. Effective medium theory for MoS₂ coated Au-Ag for different volume fraction

Relying on the weighted average theory, the effective dielectric functions can be calculated for silver- and gold-based alloy nanoparticles using equation (8) [59].

\[ \varepsilon_{\text{alloy}} = d\varepsilon_S + (1-d)\varepsilon_G \]  

(8)

d shows the volume fraction of gold that occupies the environment. \( \varepsilon_{\text{alloy}}, \varepsilon_S = 3.7, \varepsilon_G = 9.8 \) indicate the dielectric coefficients of alloy, silver, and gold, respectively [60].
In Bruggeman’s theory, several different materials can be used to create a heterogeneous environment. In this case, materials have the same contribution and the effective dielectric performance in equation (9) [56]:

\[
\frac{\varepsilon_{\text{core}} - \varepsilon_{\text{eff},\text{a}}}{\varepsilon_{\text{core}} + 2\varepsilon_{\text{eff},\text{a}}} + d\frac{\varepsilon_{\text{shell}} - \varepsilon_{\text{eff},\text{a}}}{\varepsilon_{\text{shell}} + 2\varepsilon_{\text{eff},\text{a}}} = 0
\]  \tag{9}

Wherein, the dielectric function of the shell and the core are \(\varepsilon_{\text{s}}\) and \(\varepsilon_{\text{s}}\), respectively. \(d\) and \(d' = (1 - d)\) are the occupied fraction of the nucleus, and \(\varepsilon_{\text{eff}}\) denotes the effective dielectric coefficient.

2.3. Magnetic equations

When an alternating magnetic field is used, the magnetic nanoparticles injected into the tumor generate heat in the radial direction. The partial differential equations of heat generation/ transmission within the interface material between the tumor and the surrounding tissue are [51, 61]:

\[
P = \pi \mu_0 S H^2 f \frac{2\pi f r}{1 + (2\pi f r)^2}
\]

\[
S = \frac{\mu_0 A^2 v_n}{k_B T}
\]  \tag{11}

Here \(\mu_0, S, H, f, \tau, A, v_n\) are, the permeability of free space, initial susceptibility, amplitude, frequency, effective relaxation time, nanoparticle saturation magnetization, and nanoparticle volume, respectively [61].

In MHT, superparamagnetic nanoparticles in a ferrofluid are put into the tumor, and a noninvasive RF field is used to kill the cancer cells. AC magnetic fields make the magnetization vector relax and give off heat repeatedly. Eddy currents, hysteresis, resonance, and relaxation losses are the heat generation mechanisms for magnetic nanoparticles exposed to an AC magnetic field [51].

The equations of heat generated by magnetic nanoparticles using Neel relaxation and Brownian relaxation are as follows [13, 62]:

\[
\tau_{\text{Brownian}} = \frac{3\eta V_H}{k_B T} \quad \text{and} \quad \tau_{\text{Neel}} = \tau_0 \exp \left(\frac{K V_n}{k_B T}\right)
\]  \tag{12}

\[
V_H = \frac{\pi}{6} (r + 2\delta)^3
\]  \tag{13}

\[
V_n = \frac{\pi}{6} r^3
\]  \tag{14}

Here \(V_H, V_n, \tau_0, \eta, \, \delta, \, r, \, \text{and} \, K\) are the hydrodynamic volume of the nanoparticle, nanoparticle volume, attempt period, viscosity, ligand layer thickness, the radius of nanoparticle, and nanoparticle anisotropy constant, respectively.

And the effective relaxation time is calculated by:

\[
\frac{1}{\tau} = \frac{1}{\tau_{\text{Brownian}}} + \frac{1}{\tau_{\text{Neel}}}
\]  \tag{15}

Table 1 lists the values required to calculate heat generation in tumor and healthy tissue. These losses are reduced as the temperature of the ferromagnetic material gets closer to the Curie temperature, \(T_{\text{C}}\). Heating can be self-regulating if the composition of a material is tuned so that the temperature coefficient is brought close to the maximum temperature desired [51]. This strategy keeps the tissues from becoming overheated. Eddy currents, hysteresis, resonance, and relaxation losses contribute to the dissipation of applied magnetic energy by magnetic nanoparticles during MHT. When the Curie temperature is low, the magnetic properties are highly temperature-dependent [51]. Saturation magnetism is the first temperature-dependent magnetic property. The saturation magnet is calculated using Bloch’s classical law [63] as follows:

\[
M_s(T) = M_{s0} \left[1 - \left(\frac{T}{T_{\text{C}}}\right)^\alpha\right]
\]  \tag{16}

Here \(M_{s0}\) and \(\alpha\) are saturation magnetization at 0 K and Bloch’s exponent, respectively, and the value of \(\alpha\) equals \(\frac{2}{5}\).

Temperature also affects metabolic heat production and heat sources from circulation. The following formula can be used to calculate metabolic heat production as a function of tissue temperature [63]:

\[
Q_{\text{Metabolism}} = Q_{M0} [1 + 0.1(T - 310.15)]
\]  \tag{17}

Here \(Q_{M0}\) is basal metabolic rate.
And blood circulation heat source is calculated by [42]:

\[ Q_{\text{Blood}} = W_{\text{Blood}} C_{\text{Blood}} (310.15 - T) \]  

(18)

Here \( Q_{\text{Blood}} \), \( W_{\text{Blood}} \) and \( C_{\text{Blood}} \) are heat sources due to blood circulation, blood perfusion rate and, blood specific heat, respectively.

Magnetic anisotropy is another important property in MNPs since it influences magnetization, remanence, reversibility, and relaxation. As a result, this parameter can also affect the temperature production process [72]. The temperature dependence of magnetic anisotropy is determined using the classical Akulov’s theory as follows [62]:

\[ K = \left( \frac{M_s(T)}{M_{s0}} \right)^n K_{\text{eff}} \]  

(19)

For uniaxial and cubic magnets, \( n \) equals 3 and 10, respectively. On the other hand, the anisotropy of magnetization at 0 K is represented by the \( K_{\text{eff}} \).

2.4. Bioheat

As cancer cells die, the proteins and biological structures decay, and the blood pressure in the tumors may drop, while at the same time, the healthy tissue would not change dramatically. Penne’s bio-heat equation is thus used to model the process of heat dissipation within a tumor. Nanoparticles are considered a source of point heat. In 1948, Penne developed the equation for heat transfer in biological tissues, which includes a term for heat transfer due to blood perfusion [73, 74]. This model is commonly used for tissues with small blood vessels.
\[
\begin{align*}
\left(\rho c_p\right)_f \frac{\partial T_{r(x,t)}}{\partial t} &= k \left[ \frac{\partial^2 T_{r(x,t)}}{\partial x^2} + \frac{\partial^2 T_{r(x,t)}}{\partial y^2} + \frac{\partial^2 T_{r(x,t)}}{\partial z^2} \right] \\
&+ p_{\text{blood}} C_{\text{blood}} W_{\text{blood}}(T_a - T_{r(x,t)}) + Q_{\text{Metabolism}(x,t)} + Q_{\text{gen}(x,t)}
\end{align*}
\]

The general form of the bio-heat equations in cartesian coordinates are presented in equation (20) [75]:

Here, the subscript \( t \) refers to tissue. The boundary conditions due to continuous temperature and heat flux at the tumor boundary are:

\[
\begin{align*}
T_r(R, t) &= T_a(R, t) \\
\sigma_r \frac{\partial T_r(R, t)}{\partial r} &= \sigma_a \frac{\partial T_a(r, t)}{\partial r} \\
T_f(0, t) &= \text{finite} \\
T_f(r, 0) &= T_a(r, 0) = T_0
\end{align*}
\]

Wherein, \( \nabla^2 \) is the Laplace operator, \( t \) is time, \( K \) is thermal conductivity, and \( C \) is the specific heat. \( Q_{\text{Metabolism}} \) and \( Q_t \) indicate the generators of metabolic heat and the internal heat generated by external sources, respectively. The first part \( (k \nabla^2 T) \) is the heat transfer in the tumor due to the temperature gradient, and the second part of equation (20) is the heat transfer is heat due to blood flow. The third and last parts are related to intra-tissue heat, which results from tissue metabolism and external heat source. The term \( \rho c_T \frac{dT}{dt} \) refers to the changes of temperature flux [73]. \( T_f \) and \( T_a \) denote the temperature of the tumor and the surrounding tissues, respectively [62, 73].

2.5. Arrhenius equation

At all stages of treatment, it is vital to spare healthy tissues from unnecessary thermal therapy. In this regard, we will calculate the temperature distribution in the surrounding tissues. These equations have to include the temperature distribution in these two areas. The degree of damage to the tumor tissue should be modeled/estimated as a function of the laser irradiation time \( t \) and the distance from the center of the tumor \( r \).

Here \( f_{\text{initial}} \) shows blood flow before starting treatment [76]:

\[
f_{\text{blood}} = (1 - e^{-\Omega(r,t)}) f_{\text{initial}}
\]

\( \Omega(r, t) \) is thermal damage to the tumor tissue according to the Arrhenius equation [76].

\[
\Omega(r, t) = \int_{t=0}^{t=t} A_f \exp\left(-\frac{E_a}{RT(r, \tau)}\right) \, dt
\]

Here, \( A_f, E_a \) and \( R \) are Arrhenius constant, activation energy, and the global gas constant, respectively.

3. Results

3.1. Effect of number of layers and radius of nanoparticle on the extinction peak and SPR

The intensity of the extinction peaks decreases when the number of layers increases. The shells and core radius are obtained using equation: \( r_{i-1} = r_i - t_i \), which depends first on the last shell radius and then on the radius of the underlying layers and their thickness. On the other hand, the plasmonic peak will have the effect of redshift wavelength. If \( N = 0 \) (no layer), the peak of extinction will be at its maximum value, representing the peak of surface plasmon intensification. The cause of this phenomenon is the excitation of free electrons on the alloy surface. As the number of MoS2 layers increases, the SPR peak will move towards the redshift wavelengths; hence, the intensity of the extinction peak will decrease. This is because as the number of layers increases, fewer electrons participate in the surface plasmon resonance reaction, resulting in fewer oscillating electrons and ultimately, reducing the extinction coefficient. As the number of shell layers increases, the effect of the phase delay will increase as well, but the hybridization power will decrease so that the peaks will move to the redshift wavelength. In this light, as the number of MoS2 layers increases, the temperature will increase significantly. Moreover, by changing the nanoparticle radius, the number of participating electrons will change, which in turn causes the displacement of the extinction, plasmonic peaks, and the creation of the dominant phase delay effect.

3.2. Effect of gold and silver alloy thickness on plasmonic peaks for hyperthermia application

The relationship between polarization and dielectric performance was investigated using the Clausius-Mossotti relationship. A spherical nanotube with an inner radius of \( r_i \) and a thickness of \( t_0 \) was surrounded by a MoS2 shell with a thickness of \( t_M \), and was modeled as depicted in figure 1. Figure 3 shows that as the thickness of the alloy shell decreases, the power of composition will decrease, while the effect of the phase delay will prevail and lead to the shift of the peak towards the redshift. In addition, as the thickness of our shell decreases, the free
electrons participating in the SPR oscillations decrease, which reduces the height of our annihilation peak. This observation is due to the decrease in plasmon hybridization power and an increase in the optical phase delay effect. Figure 3 illustrates the different thicknesses of gold and silver alloy nanoshells. Although the intensity of the SPR peak is stronger for the nanospheres with the larger thickness of alloy, it resides in the blue shift wavelength range and outside the biological window range. As a result, by adjusting the thickness of the alloy nanoshell, the desired peak can be easily placed in the biological windows.

3.3. Effect of gold and silver alloy percentage on plasmonic peaks for hyperthermia application

The effect of alloy percentage on plasmonic peaks can be investigated using equation (8). Since it is possible to change the percentage of gold and silver during the experimental stages, it is necessary to check. According to figure 4(a), as the percentage of gold increases, the extinction cross-section decreases, and the peak of the surface plasmon moves toward the red transition. In contrast, as the percentage of silver increases, this trend will be reversed. On the other hand, it should be noted that with an increase in the percentage of silver, the biocompatibility and stability of nanoparticles decrease. Silver alone can produce Ag + ions with a greater ionic radius than iron, and it can form a three-layer structure, reducing the extinction efficiency. Figure 4(b) shows the effect of gold and silver alloy composition on SPR and extinction coefficient.

3.4. Effect of nanoparticle thickness and radius

Figure 5 illustrates the effect of internal radius and shell thickness on SPR locations figure 5(a) and the extinction efficiency for a specific wavelength related to the laser. According to figure 5, as the nanoparticle thickness increases, the plasmon peak will move towards the blue shift wavelengths. This is because as the MoS₂ shell thickness increases, the hybridization power decreases, and the phase delay effect prevails. Moreover, as the radius of the nanoparticles increases, the number of conductive electrons available to participate in the group oscillation reaction increases, leading to the production of plasmonic peaks in the redshift range.

3.5. Effect of magnetic field on tissue

The temperature distribution inside the liver tissue is calculated by Penne’s biothermal equation. This equation is used to predict heat loss within the tumor during heat generation through laser radiation and using mechanisms such as conductivity, convection, radiation, and metabolism. The bioheat transfer equation of Penne’s in spherical coordinates for a tumor of radius R can be represented as equation (20). In this regard, using equation (20) and boundary conditions presented in equations (21)–(24), we conclude that the temperature at the r = R boundary will be high due to tissue homeostasis. The thermal penetration of magnetic hyperthermia into the tumor is primarily modeled through the partial differential equation (PDE) by a heat source in spherical coordinates. The heat source depends on the power density, which in turn depends on the type and amount of nanoparticles used for the patient. Although the specific heat and density of the target tissue can be measured experimentally, it is more challenging to determine the heat conductivity. In this model, we observe that the produced heat inside the tumor would be transmitted to the surrounding healthy tissues. Since low toxicity to healthy tissues is a priority within treatment, the temperature of the surrounding healthy tissue will increase to an acceptable level in a short period of time. Figure 6(a) shows a temperature increase for 15 s in the tumor tissue. Over time, the temperature will increase up to 45 °C. By moving away from the tumor, the temperature will reach its normal state. Since in the MHT technique, we can control the temperature in the required range, the temperature does not exceed the range limit. According to figure 6(a), it can see that at intervals beyond of 2.5 cm, the temperature is in its normal state and will not harm the patient and the healthy tissues.

In figure 6(b), the induced temperature is investigated as a function of radius. As can be seen in this figure, the tumor temperature rises rapidly within 15 s up to 42.5 °C. Meanwhile, a temperature increase is also observed in the liver tissue up to 40 °C, while for the surrounding tissues, the amount of temperature increase can be ignored. In 30 s, the temperature of the tumor tissue would reach the maximum desired temperature, while the temperature of the liver tissue would stay around 39 °C–40 °C. Since the temperature of the target tissue does not exceed the desired range in the self-controlling magnetic hyperthermia, the maximum tolerable temperature for the liver tissue is about 40 °C.

4. Discussion

The physical properties of Fe₃O₄ – Au₀.25Ag₀.75@MoS₂ nanoparticles for different Au-Ag and MoS₂ shell thicknesses, different alloy compositions, and different refractive indices were theoretically investigated using effective medium theory with Penne’s and Magnetic biothermal equations. In the LITT technique, a cavity must be created inside a part of the tissue, and the photothermal technique cannot be used for deep tissues such as the brain and liver. Moreover, the temperature should not exceed 45 °C; therefore, the MHT method was
The motivation to concentrate on this compound is that pure gold nanoparticles have low thermal stability, and non-coated gold nanoparticles would have some limitations such as functionalization [23, 28]. Silver, also, is not stable despite its high dispersion efficiency [24, 30, 31]. Therefore, the composition of nanoparticles of noble metals has better optical properties and higher stability than the monometallic state, especially because coated nanoparticles induce less toxicity [23]. One of the benefits of using Fe$_3$O$_4$ over other magnetic materials is that iron oxide can penetrate deep tissues. On the other hand, MoS$_2$ coating is more biocompatible than other two-dimensional materials such as graphene, and has a higher refractive index and subsequently higher heat generation efficiency. According to figure 2, it can be observed that the dimensions, number of layers, and the surrounding environment have a significant effect on the extinction coefficient and
SPR peak. It should be noted that the nanoparticles used in the treatment of tumors residing in the liver must have proper optical coefficients and size. Since high extinction coefficients will cause damage to healthy tissues, the nanoparticles must have optimal dimensions to be able to move through thin arterial vessels. According to figure 2 and the structure of the liver, it can be seen that the best dimensions and number of layers were 25 nm, and 2 layers of MoS$_2$ coating as shown in figure 7, we have shown which is the most suitable optical response compound by examining other structures. The peaks move toward the first biological window in this structure and are located within the first biological window. Since liver tissue is soft, it is best to place our light response in the first biological window to minimize tissue damage. According to figure 7, the reason for selecting nanoparticles with a radius of 25 nm and 2 layers was to locate the peaks in the biological window range and the appropriate extinction coefficients in the tumor tissue.

Since the laser used in the heating method is a diode laser with a range wavelength of 808 nm, increasing the number of MoS$_2$ layers would result in the production of peaks at higher wavelengths and better spectral overlap with the laser wavelength. This would ultimately lead to efficient heat production and an increase in temperature. In figure 8, we investigated the coefficients of extinction, absorption, and scattering in tumor tissue with nanoparticles with a radius of 25 nm with 2 layers of MoS$_2$. It was observed that the scattering in this condition was minimal while the maximum amount of absorption and extinction occurred. Moreover, the extinction rate in liver tissue with this structure had the lowest value compared to the other compounds.

According to figure 5, we found that by using a suitable structure, we can make nanoparticles with high absorption efficiency in biological windows while exhibiting less side effects, which will eventually lead to the application of low-power lasers with less unwanted damage to the healthy tissues. The investigation of the alloy coating thickness on the tumor tissue revealed that the best thickness for the alloy is 3 nm since it leads to a
favorable extinction coefficient and the peak in the redshift wavelength range for the tumor tissue. Figure 8 shows that the maximum value for extinction and absorption coefficients occurred with a refractive index of 1.34. On the other hand, the scattering coefficient can be ignored.

Since using only silver nanoparticles can be very toxic and pure gold nanoparticles would result in a low extinction rate and stability, different compounds for the nanoparticle should be examined. The graph presented in figure 4(b) shows that Ag_{0.75}Au_{0.25} compound would have relatively more significant plasmonic peaks in the biological windows.

According to figure 5(a), the spectral regions located in the biological window have a suitable radius and thickness for being used in hyperthermia, because their peaks would occur in the range of biological windows. In figures 5(b), (a) constant wavelength of 808 nm was set to determine the maximum extinction efficiency. In this
case, more transparent areas indicate more efficient size and thickness, and subsequently higher extinction efficiency.

Finally in figure 6, through applying a magnetic field, the amount of possible damage to the tumor and healthy tissue was examined, which reached the desired temperature quickly, but according to the MHT technique, the temperature will not exceed the desired level. The results suggest that the strength of the magnetic field and the duration of treatment can be so severe that healthy tissue would also be damaged.

5. Conclusion

The results of this study showed that the most efficient structure is Fe₃O₄ / Au-Ag(3nm)/MoS₂. Fe₃O₄ magnetic nanoparticles were used to treat liver cancer using a magnetic field, wherein gold and silver alloy coatings were used to prevent oxidation, since gold alone does not perform well at biological windows, and silver alone is toxic. The combination of Au₀.₃₅Ag₀.₆₅ has the highest coefficient of destruction and SPR in biological windows. MoS₂ was used as the final coating because it increased the body's stability and biological compatibility. The 2-layer coating of MoS₂ would have the best extinction coefficient and SPR coefficient compared to other numbers of layers.
Data availability statement

All data that support the findings of this study are included within the article (and any supplementary files).

Declaration section

XXX.

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Availability of data and material

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Author contributions

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Tina Seyedjamali, Mohammadreza Kazem Farahzadi and Hossein Arabi. The first draft of the manuscript was written by Tina Seyedjamali and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Ethics approval

In this work, no person or tissue was used in the laboratory, and the coefficients for liver tissue were used according to the data in the articles.

Not applicable.

Consent to participate

Not applicable.

Consent for publication

Not applicable.

ORCID iDs

Tina Seyedjamali https://orcid.org/0000-0001-7320-9110

References

[1] Le Brun A and Zhu* L 2018 Magnetic nanoparticle hyperthermia in cancer treatment: history, mechanism, imaging-assisted protocol design, and challenges Theory and Applications of Heat Transfer in Humans 2 631–67
[2] Jianqing W and Ping Z 2022 Surgery, chemotherapy and radiotherapy may promote cancer growth speeds and shorten patient lives Journal: Global Journal of Cancer Therapy 1 046–9
[3] Baskar R, Dai J, Wenlong N, Yeo R and Yeoh K-W 2014 Biological response of cancer cells to radiation treatment Frontiers in Molecular Biosciences 1 24
[4] Sharma S, Shrivastava N, Ross F and Thanh N T K 2019 Nanoparticles-based magnetic and photo induced hyperthermia for cancer treatment Nano Today 29 100795

[5] Wu J, Ma X and Wang Y 2013 Hyperthermia cancer therapy by magnetic nanoparticles BENG

[6] Richardson H H, Carlson M T, Tandler P J, Hernandez P and Govorov A O 2009 Experimental and theoretical studies of light-to-heat conversion and collective heating effects in metal nanoparticle solutions Nano Lett. 9 139–46

[7] Betteaib A, Wzal P K and Averrill-Bates D A 2013 Hyperthermia: cancer treatment and beyond Cancer treatment- Conventional and Innovative Approaches 43564 257–83

[8] Deb P K, Al-Ijadi B, Akkireddi R R, Al-Aboudi A and Tekade R K 2019 Biomaterials and nanoparticles for hyperthermia therapy Biomaterials and Bionanotechnology (Amsterdam: Elsevier) 375–413

[9] Cruz M M et al 2017 Nanoparticles for magnetic hyperthermia Nanostructures for Cancer Therapy (Amsterdam: Elsevier) 485–511

[10] Skandalakis G P et al 2020 Hyperthermia treatment advances for brain tumors Int. J. Hyperth. 31 3–19

[11] Zou H et al 2020 Application of photodynamic therapy for liver cancer Gastrointest. Oncology 11 431

[12] Johannsen M et al 2005 Clinical hyperthermia of prostate cancer using magnetic nanoparticles: presentation of a new interstitial technique Int. J. Hyperth. 21 637–47

[13] Suleman M and Riaz S 2020 In silico study of hyperthermia treatment of liver cancer using core–shell CoFe2O4@MnFe2O4 magnetic nanoparticles J. Magn. Magn. Mater. 498 166143

[14] Ng E Y K and Kumar S D 2017 Physical mechanism and modeling of heat generation and transfer in magnetic fluid hyperthermia through Néelian and Brownian relaxation: a review Biomed. Eng. Online 16 1–22

[15] Papadopoulos C et al 2020 Magnetic fluid hyperthermia simulations in evaluation of SAR calculation methods Physica Med. 71 39–52

[16] Ostapenko V V et al 2005 Immune-related effects of local hyperthermia in patients with primary liver cancer Hepatogastroenterology 52 1502

[17] Pan J, Xu Y, Wu Q, Hu P and Shi J 2021 Mild magnetic hyperthermia-activated innate immunity for liver cancer therapy JACS 143 8116–28

[18] Kandasamy G, Sudame A, Luthra T, Saini K and Maity D 2018 Functionalized hydrophilic superparamagnetic iron oxide nanoparticles for magnetic fluid hyperthermia application in cancer liver cancer treatment ACS omega 3 3991–4005

[19] preprint Banura N, Mimura A, Nishimoto K and Murase K 2016 Heat transfer simulation for optimization and treatment planning of magnetic hyperthermia using magnetic particle imaging arXiv preprint arXiv:1605.08139

[20] Weissleder R 2001 A clearer vision for in vivo imaging Nat. Biotechnol. 19 316–7

[21] Smith A M, Mancini M C and Nie S 2009 Second window for in vivo imaging Nat. Nanotechnol. 4 710–1

[22] Wang X, Chang J and Wu C 2019 MoS2-based biomaterials for cancer therapy Biomaterials in Translational Medicine (Amsterdam: Elsevier) 141–61

[23] Ma Y-W, Zang L-H, Wu Z-W, Yi M-F, Zhang J and Jian G-S 2015 The study of tunable local surface plasmon resonances on Au–Ag and Ag–Ag core–shell alloy nanostructure particles with DDA method Plasmonics 10 1791–800

[24] Bansal A, Selkon J S and Verma S 2014 Scattering efficiency and LSPR tunability of bimetallic Ag, Au, and Cu nanoparticles Plasmonics 9 143–50

[25] Ma Y-W, Wu Z-W, Zang J-H, Zhang J, Jian G-S and Pan S 2013 Theoretical study of the local surface plasmon resonance properties of silver nanosphere clusters Plasmonics 8 1351–60

[26] Novotny L and Hecht B 2012 Principles of Nano-Optics. (England: Cambridge University Press) (https://doi.org/10.1017/CBO9780511979493)

[27] Shufford K L, Ratner M A and Schatz G C 2005 Multipolar excitation in triangular nanoprisms J. Chem. Phys. 123 114713

[28] Abadeer N S and Murphy C J 2016 Recent progress in cancer thermal therapy using gold nanoparticles The Journal of Physical Chemistry C 120 4691–716

[29] Amendola V, Pilot R, Frasconi M, Marago O M and Lati M A 2017 Surface plasmon resonance in gold nanoparticles: a review J. Phys. Condens. Matter 29 203002

[30] Simkó M, Fries R, Greifler S, Simkö M, Gázsi A, Fiedeler U and Nentwich M 2010 How Nanoparticles Enter the Human Body and Their Effects There (http://bw.oeaw.ac.at/nanotrust-dossier)

[31] Singh P and Upadhyay C 2018 Role of silver nanoshells on structural and magnetic behavior of Fe3O4 nanoparticles J. Magn. Magn. Mater. 458 39–47

[32] Carrillo-Torres R et al 2016 Hollow Au–Ag bimetallic nanoparticles with high photothermal stability RSC Adv. 6 41304–12

[33] Li Y et al 2016 Measurement of the optical dielectric function of monolayer transition-metal dichalcogenides: MoS2, MoSe2, WS2, and WSe2 Physical Review B 90 205422

[34] Wang J and Yang M 2019 Two-dimensional nanomaterials in cancer theranostics Theranostic Bionanomaterials (Amsterdam: Elsevier) 263–88

[35] Ansari N and Ghorbani F 2018 Light absorption optimization in two-dimensional transition metal dichalcogenide van der Waals heterostructures Nano Lett. 20 1179–85

[36] Weismann M and Panou N C 2016 Theoretical and computational analysis of second- and third-harmonic generation in periodically patterned graphene and transition–metal dichalcogenide monolayers Physical Review B 94 035435

[37] Li et al 2016 Current investigations into magnetic nanoparticles for biomedical applications J. Biomater. Res. A 104 1285–96

[38] Biehl P, Von der Lühe M, Dutz S and Schacher F H 2018 Synthesis, characterization, and applications of magnetic nanoparticles featuring polywurtzite coatings Polymers 10 91

[39] Bu L et al 2019 Cancer stem cell-platelet hybrid membrane-coated magnetic nanoparticles for enhanced photothermal therapy of head and neck squamous cell carcinoma Adv. Funct. Mater. 29 1807733

[40] Zaviska V et al 2019 Effect of magnetic nanoparticles coating on cell proliferation and uptake J. Magn. Magn. Mater. 472 666–73

[41] Dieckhoff J, Eberbeck D, Schilling M and Ludwig F 2016 Magnetic-field dependence of Brownian and Néel relaxation times J. Appl. Phys. 119 04M503

[42] Wang X, Gu H and Yang Z 2005 The heating effect of magnetic fluids in an alternating magnetic field J. Magn. Magn. Mater. 293 334–40

[43] Hergt R et al 2004 Maghemite nanoparticles with very high AC-losses for application in RF–magnetic hyperthermia J. Magn. Magn. Mater. 270 345–57

[44] Thomas R, Park I-K and Jeong Y Y 2013 Magnetic iron oxide nanoparticles for multimodal imaging and therapy of cancer Int. J. Mol. Sci. 14 15910–30

[45] Mandal M et al 2005 Magnetically targeted magnetic nanoparticles with tunable gold or silver shell J. Colloid Interface Sci. 286 187–94

[46] McNamara K and Tofail S A 2015 Nanoysystems: the use of nanoalloys, metallic, bimetallic, and magnetic nanoparticles in biomedical applications Phys. Chem. Chem. Phys. 17 27981–95
[47] Wu K, Xu D, Liu J, Saha R and Wang J-P 2019 Magnetic nanoparticles in nanomedicine: a review of recent advances Nanotechnology 30 502003
[48] Haja L and Guttmann A 2016 The use of magnetic nanoparticles in cancer theranostics: toward handheld diagnostic devices Biotechnol. Adv. 34 354–61
[49] Haun J B, Yoon T J, Lee H and Weissleder R 2010 Magnetic nanoparticle biosensors Wiley Interdiscip. Rev. Nanomed. Nanobiotechnol. 2 291–304
[50] Srivastava P, Sharma P K, Muheem A and Warsi M H 2017 Magnetic nanoparticles: a review on stratagems of fabrication and its biomedical applications Recent patents on drug delivery & formulation 11 101–13
[51] Ondcek C et al 2009 Theory of magnetic fluid heating with an alternating magnetic field with temperature dependent materials properties for self-regulated heating J. Appl. Phys. 105 07B524
[52] Bohren C F and Huffman D R 2008 Absorption and Scattering of Light by Small Particles (United States: Wiley) (https://doi.org/10.1002/9783527618156)
[53] Bruggeman V D 1935 Berechnung verschiedener physikalischer konstanten von HETEROGENEN substanzen. I. dielektrizitätskonstanten und leitfähigkeiten der mischkörper aus isotothenen substanzen Ann. Phys. 416 636–64
[54] Maxwell J 1906 Garnetti, ‘Colours in metal glasses, in metallic films, and in metallic solutions. II Philos. Trans. R. Soc. London, Ser. A 205 237–88
[55] Kuzma A et al 2012 Influence of surface oxidation on plasmon resonance in monolayer of gold and silver nanoparticles J. Appl. Phys. 112 103531
[56] preprint Gutierrez Y et al 2017 Evaluation of effective medium theories for spherical nano-shells arXiv preprint arXiv:1705.02248
[57] Giannios P et al 2016 Visible to near-infrared refractive properties of freshly-excised human-liver tissues: marking hepatic malignancies Sci. Rep. 6 1–10
[58] Diaz-HR R, Esquivel-Sirvent R and Noguez C 2016 Plasmaemic response of nested nanoparticles with arbitrary geometry The Journal of Physical Chemistry C 120 2349–54
[59] Ma H, Liu X, Gao C and Yin Y 2020 The calculated dielectric function and optical properties of bimetallic alloy nanoparticles The Journal of Physical Chemistry C 124 2721–7
[60] Pinchuk A, Kreibig U and Hilger A 2004 Optical properties of metallic nanoparticles: influence of interface effects and interband transitions Surf. Sci. 557 269–80
[61] Singh G, Kumar N and Avti P K Effects of spatial distribution patterns of magnetic nanoparticles on temperature distribution in magnetic hyperthermia 2018 EMF-Med 1st World Conf. on Biomedical Applications of Electromagnetic Fields (EMF-Med), 2018: IEEE 1–2
[62] Ebrahimi M 2016 On the temperature control in self-controlling hyperthermia therapy J. Magn. Magn. Mater. 416 134–40
[63] Heisenberg W 1985 Zur theorie des ferromagnetismus Original Scientific Papers Wissenschaftliche Originalarbeiten: Springer 49 580–97
[64] O’Neill D, Peng T and Payne S 2009 A two-equation coupled system model for determination of liver tissue temperature during radio frequency ablation 2009 Annual Int. Conf. of the IEEE Engineering in Medicine and Biology Society, IEEE 3893–6
[65] Dimitri M et al 2019 A new microwave applicator for laparoscopic and robotic liver resection Int. J. Hyperth. 36 75–86
[66] Wolf D 1990 Chapter 94 evaluation of the size shape, and consistency of the liver Clinical methods: the History Physical, and Examination 107
[67] Hu P et al 2017 High saturation magnetization Fe3O4 nanoparticles prepared by one-step reduction method in autoclave J. Alloys Comp. 728 88–92
[68] Haemmerich D, Dos Santos J, Schutt D J, Webster J G and Mahvi D M 2006 In vitro measurements of temperature-dependent specific heat of liver tissues Med. Eng. Phys. 28 194–7
[69] Popa A et al 2022 The non-invasive ultrasound-based assessment of liver viscosity in a healthy cohort Diagnostics 12 1451
[70] Zhao J et al 2017 Evaluating the significance of viscoelasticity in diagnosing early-stage liver fibrosis with transient elastography PLoS One 12 e0170073
[71] Maenosono S and Saia S 2006 Theoretical assessment of FePt nanoparticles as heating elements for magnetic hyperthermia IEEE Trans. Magn. 42 1638–42
[72] Nayek C, Mannk K, Imam A, Alqaqsrawi A and Obaidat I 2018 Size-dependent magnetic anisotropy of PEG coated Fe3O4 nanoparticles; comparing two magnetization methods JOP Conf. Series: Materials Science and Engineering, JOP Publishing 305 (England) 012012
[73] Raoof S, Khalil S, Khan A, Lee J, Kim H S and Kim M-H 2020 A review on numerical modeling for magnetic nanoparticle hyperthermia: progress and challenges J. Therm. Biol 91 102644
[74] Arkin H, Xu L and Holmes K 1994 Recent developments in modeling heat transfer in blood perfused tissues IEEE Trans. Biomed. Eng. 41 97–107
[75] Gutierez G and Giordano M 2008 Study of the bioheat equation using Monte Carlo simulations for local magnetic hyperthermia ASME International Mechanical Engineering Congress and Exposition 48715 1279–85
[76] Skinner M G, Iizuka M N, Kohlos M C and Sheras M D 1998 A theoretical comparison of energy sources-microwave, ultrasound and laser-for interstitial thermal therapy Phys. Med. Biol. 43 3535