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STUDIES ABOUT MAGNETIC HYPERTHERMIA WITH SUPERPARAMAGNETIC NANOPARTICLES

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ABSTRACT: The hyperthermias, as an alternative choice for the cancer therapy, are more and more interesting for many researches. When applying the hyperthermia, the cancerous cells are destroyed by increasing their temperature. The idea of using superparamagnetic nanoparticles in hyperthermia is up-to-date, because it offers the possibility of direct inoculation in the target places of the human body, where they remain locally by applying a magnetic field. If the magnetic field is radio-frequency alternating, the magnetic losses that lead to temperature increase are caused by the Neel relaxation processes. The matrix where they are dispersed and the physical properties of the nanoparticles have a crucial importance in the magnetic hyperthermia applications. In this article, we undertake to realize a analytic study about specific absorption rate behavior that characterize the heating in hyperthermia.
KEYWORDS: magnetic hyperthermia, superparamagnetic nanoparticles, specific absorption rate

❖ INTRODUCTION

Electromagnetic (EM) radiation is a fundamental tool in cancer therapy [1], extensively used for both diagnostics and therapy. Physical interactions between EM waves and living matter can be very different depending on the portion of the electromagnetic spectrum considered. A variety of clinical tools have been established in physical medicine based on direct emission and detection of EM waves such as x-ray radiography, computer tomography scanning (CT scan) and gamma-ray radiotherapy from radioactive isotopes. Many other techniques rely on indirect uses of EM radiation such as positron-emission tomography (PET), magnetic resonance imaging (MRI), and microwave hyperthermia (MWH). In fig. 1 [1] it present a frequency ranges for some of the most used diagnostic/therapy equipments (MFH = Magnetic Fluid Hyperthermia, MRI = Magnetic Resonance Imaging). B. The respective main physical mechanisms at each frequency range. Also shown in (C) is the common nomenclature for the electromagnetic waves at each region: RF = radiofrequency; MW = microwaves; IR = infrared; Vis = visible; UV = ultraviolet and X-Ray.

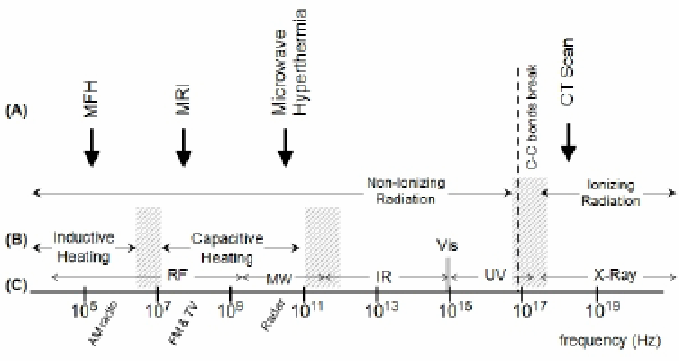

Fig 1.

❖ METHODOLOGY

The hyperthermia in oncology consists of increasing the temperature of the cancerous tumours in order to destroy them [3,4,5], and can be used concurrently with other therapeutic techniques, as chemotherapy or radiotherapy. Lately, the magnetic hyperthermia attracted more and more interest [2, 6, 7, 8, 9, 10 ...], being one of the basic subjects debated at the International Conference of Magnetism that took place, during 26th-31st July 2009, in Karlsruhe, Germany. As a ground rule, the magnetic germs or particles are inoculated directly in the tumour zone. Under the action of the alternative magnetic field, the magnetic particles can generate heat via four different mechanisms [9, 10, 11]:

1) generation of the Foucault currents in conductor materials;
2) losses through hysteresis;
3) losses through Neel magnetic relaxation in superparamagnetic nanoparticle systems;
4) losses through Brown magnetic relaxation Brown in the nanoparticle systems found in slimy suspensions.

The mechanism of producing Foucault currents in conductor materials in a time-variable magnetic field is governed by the electromagnetic induction law. Through this mechanism, a significant heating effect is obtained if the material is under an alternative magnetic field. An example of hyperthermia that uses this method is the inoculation of acicular copper particles in the tumour zone, followed by their excitation in a radiofrequency magnetic field. The significant losses through hysteresis are characteristic to the ferromagnetic materials. But, the usage of this mechanism in hyperthermia is problematical [11] due to the temperature control in a quite limited domain (41-48 ^{o}C). A solution can be the usage of certain materials that have their Curie points around the heating temperature (41-48 ^{o}C), but it's very difficult to find such materials due to their chemistry [11]. A less traumatic solution consists of using an "intelligent" polymer-base ferrogel.

In case of mono-domain particles, where there are no domain walls, when the particles are immersed into a solid matrix or when dispersed particle systems are in high frequency magnetic fields, the inversion of the particle magnetization is realised through the rotation of the particle, and these rotation processes cause losses due to the Neel relaxation processes. In case the magnetic particles are in a liquid matrix, if the frequency of the excitation magnetic field is not too high, the particles tend to rotate until they reach a minimum energy position. These rotation processes lead to losses due to the Brown relaxation.

The measure that characterize the efficiency of the transformation of these losses, via those four mechanisms described above, it is known in the literature as the *specific absorption rate* (SAR), and it is defined as the absorbed power per the mass unit of the tumour material, at a given strength of the excitation magnetic field. The SAR amplitude is given by

$$SAR = A.f, \tag{1}$$

where *A* is the specific area of the hysteresis loop (i.e. specific losses) at the frequency and magnetic field at which the experiment is conducted.

Recent experimental researches [12] showed that, at a given amplitude of the excitation field, at the same frequency, the specific absorption rate is higher in case of using superparamagnetic nanoparticles in radiofrequency fields. These observations, and the fact that the magnetic nanoparticles can be more easily inoculated in the tumour, explain the interest for using them in the magnetic hyperthermia.

To calculate *A* and interpret hyperthermia experiments, two models -valid in different regimes- can be used. First, when the applied magnetic field is small compared to the saturation field of the NPs, the linear response theory can be used. In this case [12],[13],[14], the hysteresis loop is an ellipse of area [12]:

$$A = \frac{\pi\mu_0 H_{max}^2}{\rho} \cdot \chi"(f), \tag{2}$$

$$\chi" = \frac{\mu_0 M_s^2 V}{3k_B T} \cdot \left(\frac{f\tau_N}{1 + (f\tau_N)^2} \right) \tag{3}$$

*M*s is the saturation magnetization, ρ the density of the material (for magnetite 8300 kg/m^3).

$$\tau_N = \tau_0 \exp\left(\frac{KV}{k_B T} \right) \tag{4}$$

is the Néel relaxation time, and τ0 the interwell relaxation time. The linear theory is suitable to interpret hyperthermia experiments on superparamagnetic NPs, since the rather weak magnetic field used (generally up to 30 mT) is far from the saturation field of the NPs.

If we consider Brown relatation time:

$$\tau_B = \frac{3\eta V_H}{k_B T}, \tag{5}$$

where η is the liquid matrix dinamic viscosity coefficient, V_H is hydrodynamic magnetic nanoparticles volume, in eq. 1 and 2 τ_N becomes total relataxion time $\tau = \tau_N + \tau_B$.

❖ DISCUSSION

The most studied superparamagnetic nanoparticles for hyperthermia are those of magnetite, due to their very low toxicity. To be possible to be used in hyperthermia, the magnetic nanoparticles are coated with a carbon layer, to make them biocompatible, and immersed in dextran [15] or polymers (for example, polyvinyl alcohol [16]), to make them biodegradable. For a better penetration of the nanoparticles in the cancerous cells, they are coated with a bioactive compound, as antibodies or proteins [15].

Jennifer L. Phillips, in the paper "A Topical Review of Magnetic Fluid Hyperthermia", available online on the Internet network, describes the possibility of using magnetic fluids in hyperthermia. The superparamagnetic nanoparticles are dispersed in water or hydrocarbon with neutral ph and physiological salinity. The resulted ferrofluid is directly injected in the tumour and a radiofrequency magnetic field is applied.

If the problem of the magnetic nanoparticle inoculation in the tumour zone is rather solved, there are no complex studies to clearly present the relation between the physical properties of the nanoparticle systems and their thermal efficiency in the hyperthermia therapy, or the modality to control the thermal efficiency by controlling the physical proprieties in a way that implies low costs and small technological efforts.

The heating capacity of a magnetic material or electromagnetic device is quantified through the specific absorption power rate (SAR), defined as the amount of energy converted into heat per time and mass. In terms of the usual experiments and parameters for magnetic colloids, the loss power per gram of Fe3O4 is obtained from the heating curves within the initial T temperature rising interval through the definition [1] where c_s is the sample heat capacity, defined as a mass-weighted mean value for a given concentration of magnetic material, calculated as

$$SAR = c_s \frac{\Delta T}{\Delta t} \cdot \frac{1}{m_{mag}} \tag{6}$$

$$c_s = \frac{m_{mag} c_{mag} + m_l c_l}{m_{mag} + m_l} \tag{7}$$

with c_{mag}, m_{mag} and c_l, m_l being the specific heat capacities and masses of magnetic material and liquid carrier, respectively.

The study we performed on spherical magnetite nanoparticles with specific heat capacities c_{mag} = 0.67 J/gK, mass m_{mag} = 1g and diameter 9 nm in water with mass 5 mg and specific heat capacity c_l = 4.18 J/gK and dinamic viscosity coefficient $\eta=0.633\cdot10^{-3}$ Ns/m^2. The physical properties of the magnetite nanoparticles is: saturation magnetization M_s = $4.7\cdot10^5$ A/m and effective anisotropy constant K=1900 J/m^3. Initially we consider the system temperature 37.5 degrees Celsius. We believe that the maximum intensity alternating magnetic field applied is between 100 mT 1mT's frequency range between 10kHz and 100 kHz.In first phase we study how depend SAR of frequency and maxim magnetic intensity of magnetic field applied.Rezult is present in fig.2,3.

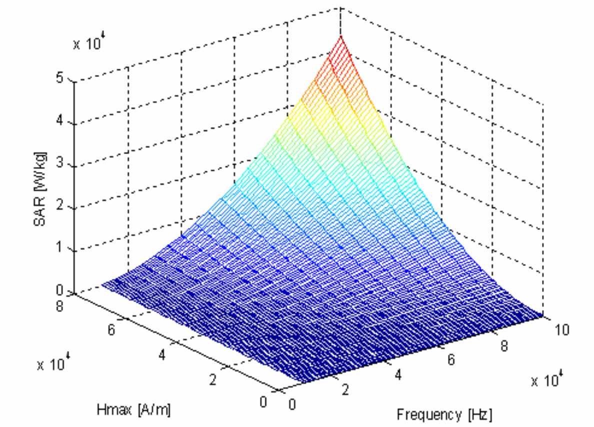

Fig.2

From Fig. 2.3 Note that SAR increases with increasing frequency and amplitude of applied magnetic field.

In Figure 3 is seen as keeping the value constant amplitude magnetic field intensity, it can get a SAR increase if applied field frequency increases.

Then we study how depend the temperature growth of of frequency and maxim magnetic intensity of magnetic field applied. Result is present in fig.4,5.

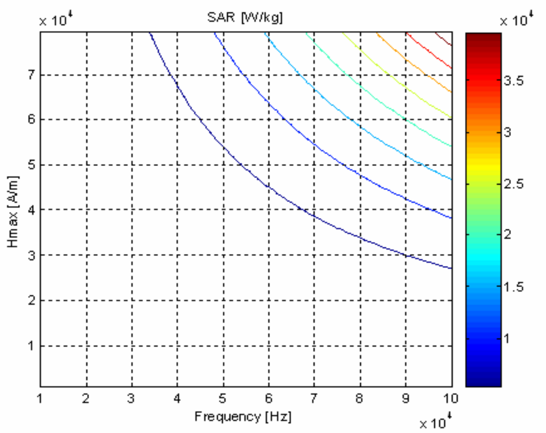

Fig. 3

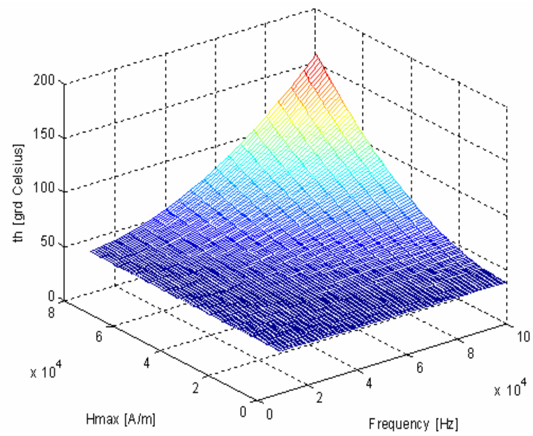

Fig. 4

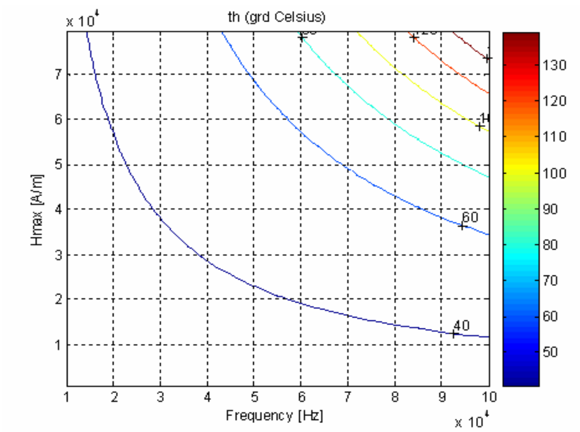

Fig. 5

From Fig. 4.5 Note that the tumor tissue temperature increases with increasing frequency and amplitude of applied magnetic field.

In Figure 5 is observed as a nursery for the temperature meant units when working in weak magnetic fields should work at high frequencies.

❖ CONCLUSION

In this article, we realise a analytical study that implies the analysis how certain physical properties that maxim intensity of magnetic field applied and frequency of magnetic field, influence the temperature in the tumour zone and, in the same time, to obtain a theoretical tool for controlling the temperature in the magnetic hyperthermia by controlling this physical properties.

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