Effect of High Ac Magnetic Field On Magnetic Nanoparticles for Magnetic Hyperthermia and Radiation/Chemotherapy Applications

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ABSTRACT

This study presents a setup that generates, within minutes, controlled and constant heating temperatures of 47C and 53C, well in excess of required temperatures for mild hyperthermia (42C). The heating nano-elements used are magnetic particles with Curie temperatures of 47C and 53C. The particles are heated via an applied external AC B field. The particles could potentially be injected deep into a tumor (i.e. used as temperature controlled thermo-seeds) , preheating the tumor, procedure making the radiation and/or chemotherapy treatment much more effective.

Numerous past studies have shown high synergies between magnetic hyperthermia and chemo/radiation therapy.

Keywords: magnetic nanoparticle, high AC magnetic field, magnetic hyperthermia, radiation/chemotherapy applications.

1 INTRODUCTION

There are numerous studies in the field that explain and model the behavior and heating properties of magnetic nanoparticles (NPs) when exposed to an alternating magnetic field [1,2]. Particularly for applications such as magnetic hyperthermia and chemotherapy, where high synergies have been noted [3,4,5], NPs magnetic heating is of great interest and importance. The NPs are used as magnetically controlled nano-thermoseeds.

These and other studies have shown significant NPs temperature increase at frequencies well above 50kHz to 10MHz [6-8]. For the range under 50kHz the work of Hergt et all, and Andrae et all, are particularly noted [9-11].

This study investigates the NP heating due to an AC magnetic field for magnetic hyperthermia applications at frequencies well below 50kHz. Two different chemical composite materials are investigated.

2 ANALYSIS OF MAGNETIC HYPERTHERMIA

Magnetic hyperthermia is an invasive method of providing heat at the site of the tumor by applying an external magnetic field to the magnetic particles at the tumor site. Ideally, the NPs could be injected directly into a tumor and when exposed to an AC magnetic field the NPs heat up, heat that conducts into the immediate surrounding tissue and tumor cells.

The use of NPs with Curie temperature in the range between mild hyperthermia and ablatation is desired in order to provide control and a safeguard against overheating the normal cells in the tissue.

Numerous past studies had found that the viability of tumor cells is reduced and their sensitivity to chemotherapy and/or radiation greatly increase when the malignant cells are heated to temperatures above 42C [12-14].

The studies by Ito et all [15] suggested that when the tumor's temperature is maintained above 42C for at least 30minutes, the tumor/cancer is destroyed. Raising the temperature of the tumor is an extremely efficient way to selectively destroy cancer cells.

However, numerous other studies suggest for increased effectiveness the use of magnetic thermo-seeds (magnetic hyperthermia) be used in conjunction with radiation and/or chemotherapy as an adjunct therapy [16-20].

The objective of this research is to investigate the behavior and heating mechanism of two different NP materials in AC B fields of under 50 kHz. The NPs could be used as magnetically controlled nano-thermoseeds. By analyzing the heating mechanism and studying the magnetic behavior of different materials, a more practical and efficient device for magnetic hyperthermia may be developed, thus providing optimal effectiveness for the treatment of tumor/cancer.

In this study, the goal is to produce and measure mild to high hyperthermia (47C) and thermo-ablatation (53C) heating in a testing time of maximum 30 minutes, also suggested by other similar studies [21-23].

3 MATERIALS AND METHODS

Figure 1 and 2 depict the experimental setup. An adjustable AC magnetic field of 0-600 Gauss is generated by two large ferrite core, high permeability, electromagnets driven by two 1kW power signal generator at frequencies from zero to 50 kHz.

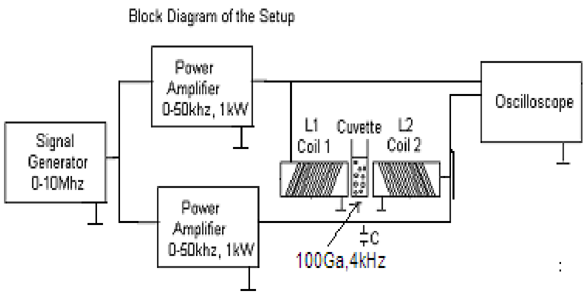

Figure 1. Block diagram of the setup

In this study, a sine wave, 50% duty cycle, 4kHz, 100Ga AC B field is used for all experiments.

The magnetic NPs are suspended in water and are contained in a 4ml, 1cm^2 cross section, plastic cuvette. The cuvette is placed between the two electromagnet cores as shown in Figure 1. A 2mm foam insulation on each side of the cuvette and the electromagnets provides additional heat insulation during experimentation. Both electromagnet coils are air cooled using four fans (two fans/coil).

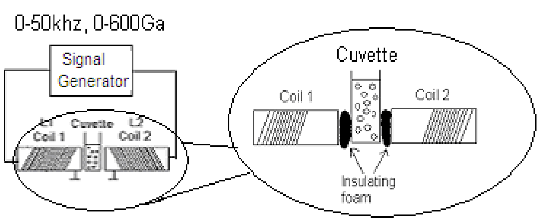

Figure 2. Simplified experimental setup

The NPs used are mixtures of Cu-Ni-Gd with Tc of 53C (sample1) and Cu-Ni mixtures with 47C (sample2) respectively. The size distribution of nearly spherical NPs is 30nm -120nm (fig 3), locally synthesized by a physical method, by melting and ball-milling method. [24] The NPs are then mixed with water in different weight ratios.

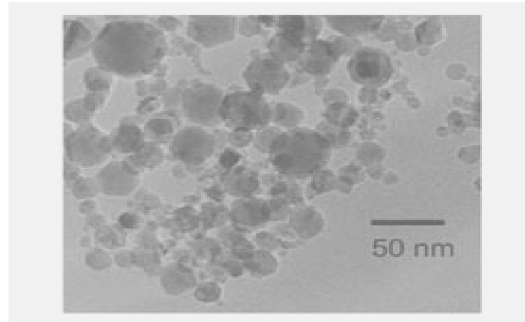

Figure 3. TEM image of the particles used

Biocompatibility and toxicity are serious concerns for *in vivo* hyperthermia when using magnetic NPs, thus only biocompatible, in acceptable quantities, NPs (5mg/kg-patient, 0.35g/70kg avg. patient) suggested by other studies [12,25] are used in this study. Also, to simulate as much as possible a real clinical situation a realistic 30min period is assumed for an actual magnetic hyperthermia treatment. All experiments last for 40min (10min rise time and a 30min actual heating treatment).

The temperatures on the ferrite cores, around the cuvette as well as inside the cuvette are constantly measured for the duration of 40 min/experiment.

4 RESULTS AND DISSCUSIONS

Figure 4 and 5 show the magnetic heating results for different water and NPs mixtures. Within less than 10min, temperature increase from 7C to almost 30C (sample1, fig 4), and 4C to 23C (sample2, fig 5) were measured in the plastic cuvette.

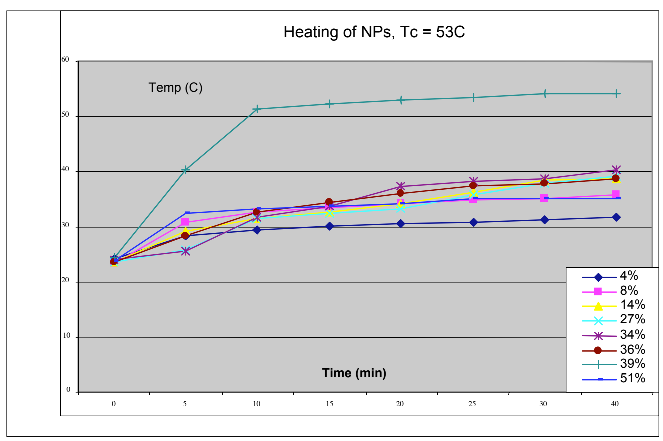

Figure 4. Temperature increase for Sample1 (Tc = 53C)

Figure 4 shows the highest temperature increase (30C) achieved with a 39% mixture of NPs and water by weight (39% NPs to 61% water; 0.35g NPs). The smallest temperature increase (7C) is obtained by a 4% NPs to 96% water.

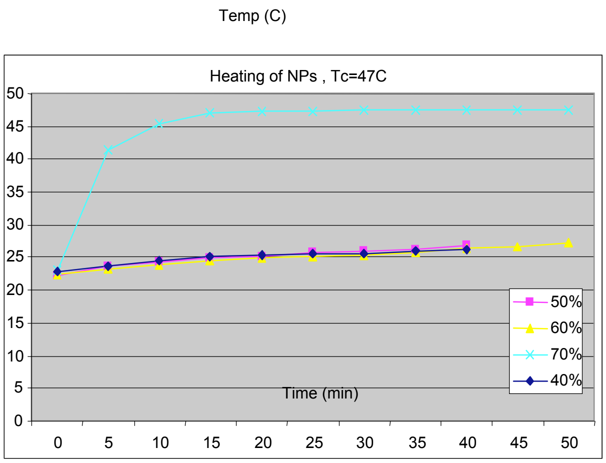

Figure 5. Temperature increase for Sample2 (Tc=47C)

Similarly, Figure 5 shows the highest temperature increase (23C) achieved with a 70% mixture of NPs and water by weight (70% NPs to 30% water; 0.35g NPs). The smallest temperature increase (4C) is obtained by all other mixtures.

These results show the potential of the experimental setup and the type of NPs used for mild hyperthermia applications where only 42C heating is needed. However, for improved effectiveness against tumor cells, magnetic hyperthermia should be used in conjunction with radiation and/or chemotherapy. Magnetic hyperthermia should be seen not as a stand alone treatment but rather as an adjunct treatment to radiation and chemotherapy.

This preliminary study of magnetic hyperthermia also shows that the increase in temperature of the NPs mixtures may be achieved within the time duration of a normal radiation/chemotherapy session (30min).

Also this preliminary result confirms that at Curie temperature (Tc) the NPs reach magnetization saturation and become paramagnetic, i.e. they can not heat up any further. This temperature remains constant even if the amplitude of the applied field further increases.

Controlled magnetic hyperthermia can be achieved by synthesizing NPs of desired Curie temperature. The desired range of Curie temperatures could be obtained by varying the weight percentage of nickel and copper based on the phase diagram.

ACKNOWLEDGEMENT

This study is supported by Florida State University Research Foundation.

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