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Magnetic study of iron-containing carbon nanotubes: Feasibility for magnetic hyperthermia

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ABSTRACT

We present a detailed magnetic study of iron containing carbon nanotubes (Fe-CNT), which highlights their potential for contactless magnetic heating in hyperthermia cancer treatment. Magnetic field dependent AC inductive heating experiments on Fe-CNT dispersions show a substantial temperature increase of Fe-CNT dispersions in applied AC magnetic fields. DC and AC magnetization studies have been done in order to elucidate the heating mechanism. We observe a different magnetic response of Fe-CNT powder compared to Fe-CNT dispersed in aqueous solution, e.g., ferromagnetic Fe-CNT in powder do not show any hysteresis when being dispersed in liquid. Our data indicate the motion of Fe-CNT in liquid in applied magnetic fields.

1. Introduction

The heating of tissue using magnetic nanoparticles has a great potential as a new treatment approach for cancer thermotherapy. Nowadays, the majority of the research in this field is focused on magnetic iron oxides Fe_3O_4 (magnetite) and $\gamma{-}Fe_2O_3$ (maghemite) which have been proven to be well tolerated by the human body [1–3]. However, metallic iron would offer advantages over its oxides due to higher saturation magnetization, but its application is hindered because of oxidation in biological environment. A possible solution of this problem is the use of iron filled carbon nanotubes (Fe-CNT). Here, the carbon shells efficiently protect encapsulated iron from the biological environment while its magnetic properties are retained [4,5]. Moreover, carbon shells may act as multi-functional containers which can be filled with different materials. Additional material such as a nanothermometer in Fe-CNT would increase the potential of CNT as hyperthermia agents. Attaching functional elements to the outer shell of CNT increase their biocompatibility [4]. Recent studies of cytotoxic effects of Fe-CNT on cells indicated no significant toxicity of Fe-CNT prepared by the same synthesis route [6].

There are several mechanisms for heating of magnetic particles in alternating magnetic fields: ferromagnetic (hysteresis) losses, superparamagnetic (relaxation) losses, eddy currents, etc. Ferromagnetic particles possess hysteretic properties in a time varying magnetic field. The amount of heat is given by the frequency multiplied by the area of the hysteresis loop:

$$P_{FM} = \mu_0 f \oint H\,dM \qquad (1)$$

An alternative mechanism for magnetically induced heating is associated to superparamagnetic or relaxation losses. The term superparamagnetism was introduced by Elmore [7] to describe the magnetic behavior of colloidal systems containing iron oxide particles. When such a colloidal system is removed from a magnetic field, its magnetization relaxes back to zero due to the thermal energy. This relaxation can be connected with either the physical rotation of the particle (Brownian relaxation), or the rotation of the magnetic moment within each particle (Néel relaxation) [8–10]. For small field amplitudes, and assuming minimal interaction between single domain magnetic particles, the response of the magnetization to an AC field can be described in terms of its complex susceptibility

$$\chi = \chi' + i\chi'' \qquad (2)$$

where both χ' and χ'' are frequency dependent. In the case of a superparamagnetic material, the out-of-phase χ'' component results in heat generation, given by

$$P_{SPM} = \mu_0 \pi f \chi'' H^2 \qquad (3)$$

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Eq. (2) implies a positive conversion of magnetic energy into internal energy if M lags H [8].

Note, that in general also eddy currents might cause energy losses in AC magnetic fields. However, magnetic particles used for hyperthermia are too small and AC field frequencies are too low for the generation of any substantial eddy currents. A side effect of eddy currents in a potential medical application is direct heating of human tissue. This effect is not localized precisely at a certain target position but causes non-specific inductive heating. Therefore, it is important to minimize the eddy currents on human tissue which implies limitations of the magnetic field strength and the frequency which can be safely applied in hyperthermia treatment [8,10].

In the present work we study the magnetic properties of iron containing CNT and their heating potential in an alternating magnetic field. The main goal of this study is to show the feasibility of this material for magnetic hyperthermia and to discuss the possible heating mechanisms.

2. Experimental

Iron containing multiwalled carbon nanotubes (Fe-MWCNT) have been synthesized by the aerosol-assisted CVD technique [11,12], which is based on a liquid starting material consisting of a metal–organic catalyst compound (ferrocene) solved in a hydrocarbon (cyclohexane or acetonitrile). The obtained material is a composite of diamagnetic multi-walled CNT and Fe-particles which are applied as catalyst during the synthesis. There is always one Fe particle for each MWCNT and the diameters of the MWCNT are determined by the size of the catalyst particles. After the synthesis, our MWCNT have outer diameters between 10 and 40 nm while the inner diameters as well as the size of the Fe-particles range between 5 and 20 nm. Most of the Fe-particles look like drops with a smaller and a larger side. The length of the CNT amounts around 20 μm.

In order to have a non-magnetic control material, Fe-MWCNT were annealed at the temperature 2500 °C and under argon atmosphere. Detailed magnetic studies of the purified MWCNT show a clear diamagnetic behavior [13]. Other control materials are MWCNT filled with non-magnetic CuI particles (CuI-MWCNT) and carbon wrapped Cu nanowires. CuI-MWCNT have been produced by post-synthesis filling method. This technique includes the synthesis of empty MWCNT, opening of their ends and filling with CuI [14]. Carbon coated Cu nanowires have been produced by thermal decomposition of copper(II)-acetylacetonate in a closed, evacuated quartz ampule as described in Ref. [15].

Magnetic properties have been studied using a commercial Quantum Design MPMS (magnetic property measurement system) SQUID (superconducting quantum interference device) magnetometer. The samples have been investigated as dry powders. The field dependence of the static (DC) magnetization $M(H)$ was measured at room temperature in magnetic fields up to 1 T. Temperature dependence of the magnetization $M(T)$ was measured in a magnetic field of 10 Oe for zero-field-cooled (ZFC) and field-cooled (FC) cases. In the case of ZFC magnetization measurements, the sample was firstly heated from room temperature up to 400 K, then cooled down to 5 K in zero magnetic field. Then, after applying the magnetic field ($H = 10$ Oe), the magnetization measurements were performed upon warming. For FC magnetization measurements, the sample was cooled in the same magnetic field ($H = 10$ Oe) down to 5 K and the magnetization was measured in the warming cycle up to 400 K under applied magnetic field.

To study the inductive heating effect and the magnetic behavior of Fe-MWCNT in liquid media, Fe-MWCNT were dispersed in aqueous solution. In order to obtain a stable suspension Fe-MWCNT were mixed 1:1 weight ratio with human albumin and dispersed in phosphate buffered saline (PBS) using ultrasonication. The concentration of the obtained dispersion was 5 mg/ml. The magnetic properties of Fe-MWCNT in dispersion were studied in DC and AC magnetization measurements. The field dependence of the DC magnetization $M(H)$ was studied in magnetic fields up to 1 T using a SQUID magnetometer. First, the liquid samples were studied at room temperature ($T = 300$ K) and then frozen at $T = 260$ K, at which temperature the magnetization measurements were performed. AC susceptibility measurements were performed on both Fe-MWCNT powder and Fe-MWCNT dispersion at room temperature ($T = 300$ K) in a commercial Quantum Design PPMS (physical property measurement system), using the ACMS (AC measurement system) option, for frequencies f of 33–9333 Hz and a magnetic field strength of 10 Oe.

The heating effect of MWCNT in alternating magnetic fields was studied using an experimental setup which consists of a high-frequency generator with an impedance matching network and a water-cooled magnetic coil system. The coil contains five turns; the height of the coil is 40 mm and the diameter of the inside bore is 30 mm. For such a coil geometry the setup provides alternating magnetic fields with the frequency $f = 139$ kHz and the magnetic field strength of 0–120 kA/m. For temperature isolation of the samples during the measurements we used an evacuated glass dewar vessel placed in the coil. The temperature change per time unit was determined using a fiber-optic temperature controller (Luxtron One), which is suitable for measurements in high-frequency magnetic fields.

3. Magnetic properties

The magnetic field and the temperature (FC and ZFC) dependence of the magnetization of Fe-MWCNT powder is presented in Fig. 1. At room temperature, the material shows a coercivity (H_C) of 200 Oe and a saturation magnetization (M_S) of 8.2 emu/$g_{Fe-MWCNT}$. By comparing M_S with the saturation magnetization of bulk iron $M_{bulk} = 217$ emu/g, the mass ratio of iron in Fe-MWCNT can be estimated to 0.038 g_{Fe}/g_{CNT}. Note that the energy dispersive X-ray spectroscopy (EDX) shows an iron concentration in Fe-MWCNT of around 3 ± 1 wt%. This result agrees to our magnetization analysis which however yields the content of magnetic material with a much higher precision than EDX. The temperature dependence of the FC and ZFC magnetization up to 400 K reveals a pronounced ferromagnetic behavior of the Fe-MWCNT in the measurement temperature range and, therefore, at all temperatures used in medical hyperthermia.

In Fig. 2, the magnetic field dependence of the magnetization of Fe-MWCNT in dispersion is presented. Fe-MWCNT in liquid dispersion show no visible hysteresis and behave like a superparamagnetic system. However, after freezing the same dispersion shows a magnetic behavior similar to the powder. We hence conclude that the observed superparamagnetic behavior of Fe-MWCNT in liquid is associated with the motion of Fe-MWCNT under exposure to the magnetic field.

Fig. 3 presents the AC susceptibility of Fe-MWCNT powder and Fe-MWCNT dispersion at room temperature. In the case of Fe-MWCNT dispersion the AC susceptibility related to the mass of iron is higher than for Fe-MWCNT powder.

4. Heating in AC magnetic fields

Our inductive heating studies shown in Fig. 4 reveal a substantial heating effect of the Fe-MWCNT suspension in AC