IEEE
International Magnetics Conference

San Diego, California

May 8-12, 2006

Technical Digests

INTERMAG 2006

http://www.intermagconference.com/intermag2006

CD-11

Magnetic Properties, Self-Temperature Rising Characteristics, and Biocompatibility of NiFe2O4 Nanoparticles for Hyperthermia Applications.

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The interesting of magnetic nanoparticles for biomedical applications such as disease diagnosis using antigen-antibody reaction, drug delivery, hyperthermia, MRI contrast agents, and cell-repairing has been dramatically increased due to their promising physical and biotechnical advantages. In particular, hyperthermia, one of the therapy modalities for cancer treatment, has been considered to be useful for treating localized or deeply-seated tumor cells with temperatures in the range of 41 ~ 45 °C[1]. The main reason is that this modality is expected to effectively reduce the "side effect", which is severely considered in current cancer therapies. The initiative experimental investigations of the application of magnetic materials for hyperthermia were first carried out by Gilchrist et al in 1957 [2]. However, it has been revealed that magnetic mediated hyperthermia has a lot of technical restrictions for the real clinical applications due to the urgently required physical and clinical properties such as high magnetic moment, high magnetic susceptibility including magnetic permeability, heat conduction and deposition rate, specific absorption rate (SAR), and capabilities of controlling particle size, shape, and size distributions.

In this study, magnetic properties and self-heating characteristics, and biocompatibility of NiFe2O4 nanoparticles were investigated in order to confirm the technical and clinical possibilities for hyperthermia applications. The main reason for considering NiFe2O4 nanoparticles as a hyperthermia agent is that these are expected to have urgently required magnetic properties for hyperthermia such as soft magnetism and small magnetic degradation at high frequency [3].

The spinel ferrite, NiFe2O4 magnetic nanoparticles with various sizes were synthesized by using both sol-gel method and "high temperature thermal decomposition method (HTTDM)." Iron(III) acetylacetonate and nickel(II) acetate were used as starting materials and benzyl ether were used as solvents. The particle size, uniformity, and packing density were controlled by heating temperature and reaction time during synthesizing. The self-heating test was carried out under applying magnetic field of 134 Oe and frequency of 100 kHz by using solid state Ni-ferrite nanoparticles. The temperature change by coil was measured at the same time for the comparison with the temperature rising by Ni-ferrite nanoparticles.

The average particle sizes of NiFe2O4 nanoparticles confirmed by TEM were from 6.7 nm to 35 nm. The crystal structure confirmed by XRD was a cubic spinel ferrite structure.

All the Ni-ferrite nanoparticles showed the saturation magnetization between 43.0 and 47.6 emu/g as shown in Fig. 1. In addition, magnetizations of Ni-ferrite were not saturated up to 30 kOe at room temperature. It is plausibly suggested that core magnetization and surface magnetization can be coexisted. In order to confirm the biocompatibility of Ni-ferrites for human body, cytotoxic tests were carried out by using both "Agar overlay test" and "MTT". According to the testing results, NiFe2O4 nanoparticles exhibited no cytotoxicity.

Self-heating temperature rising characteristics of Ni-ferrite nanoparticles is shown in Fig. 2. The temperature was initially risen up to 47.3 °C and then this was stably saturated during applying magnetic field. The stable and nearly saturated temperature rising response of Ni-ferrite is considered as the first observation using nano-size controlled magnetic particles. This characteristic is thought to be promising for real hyperthermia applications. The heat production H0f is 1.07×10^{9} $Am^{-1}s^{-1}$. Maximum temperature and biocompatible heat production value can be regulated by optimizing frequency and applied magnetic field.

In conclusion, it is confirmed that nano-size controlled Ni-ferrites have promising magnetic properties, self-heating temperature rising characteristics and high biocompatibility. These suggested that NiFe2O4 nanoparticles can be considered as one of the bio-potential materials for hyperthermia.

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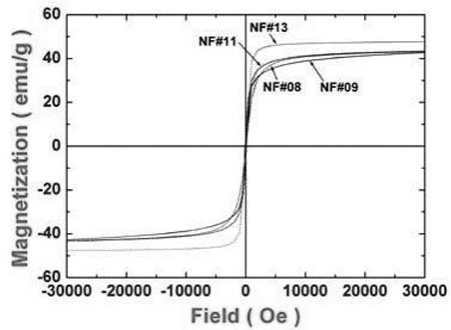

Fig. 1. Hysteresis loops of NiFe2O4 nanoparticles under the external applied magnetic field of 30 kOe by SQUID at room temperature.

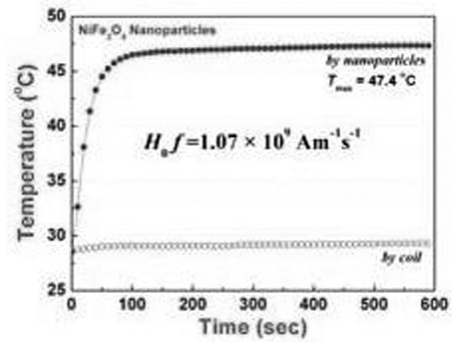

Fig. 2. Temperature rising of NiFe2O4 nanoparticles by self-heating test under 134 Oe at 100 kHz.