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Thermosensitive Ni-based magnetic particles for self-controlled hyperthermia applications

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ABSTRACT

A number of ferromagnetic alloys in the bulk-form “thermoseeds” have been investigated for localized self-controlled hyperthermia treatment of cancer by substituting V, Mo, Cu, and Ga for Ni. The samples were prepared by arc-melting technique and annealed at 1223 K (950 °C) for 12 h in sealed quartz tubes. The structural, magnetic, and magnetocaloric properties of the samples were studied, using room temperature X-ray diffraction and a Superconducting Quantum Interference Device (SQUID) magnetometer. The magnetocaloric parameters (magnetic entropy changes, refrigeration capacity (RC), and hysteretic effects) have been calculated. It has been shown that recrystallization, i.e., annealing time and temperature, is crucial for controlling the heating characteristics of the seeds. A linear decrease in Curie temperature (T_C) from 380 K (107 °C) to 200 K (−73 °C) was observed with increasing substitution of Ni by V, Mo, Cu, and Ga, while the magnetization value remained nearly constant for all substitutions. The optimal composition of these Ni-based alloys has been determined in order to allow self-controlling hyperthermia, implying a Curie temperature near the therapeutic level, 315–318 K (41–45 °C). The results showed that an extraordinary self-regulating heating effect has been achieved in Ni-based magnetic materials, which may create new vistas for hyperthermia cancer treatment.

1. Introduction

Hyperthermia is a rapidly developing treatment method for cancer in which the target tissue is heated above the normal body temperature [1–5]. Hyperthermia has been used for many years to treat a wide variety of tumors in patients and also used in conjunction with other forms of cancer therapy, such as radiation therapy and chemotherapy [6,7]. This method is used to increase the temperature of a tumor to 315–318 K (41–45 °C) because temperatures higher than 314 K reduce the viability of a tumor cell [8–10]. The healthy cells can withstand such conditions, while the cancer cells cannot. When tumor cells are heated, the blood vessels are unable to dilate, resulting in the poor dissipation of heat as the tumor is a tightly packed group of cells having poor blood circulation. The poor dissipation of heat in tumor accumulates harmful metabolic byproducts and low pH, resulting the self-destruction of the abnormal growth [11].

Conventional hyperthermia treatment is fulfilled by heating the patient's body in a water bath (general hyperthermia) and by applying radio and microwave radiation (local hyperthermia). There are many side effects of these convention hyperthermia methods due to an uneven spread of heat inside the tumor and tissue. This inspired the development of a new method in which “local” heating was achieved due to remagnetization losses in magnetic materials referred to as magnetic hyperthermia [12,13]. This magnetic hyperthermia allows a more uniform dissemination of heat and therefore the side effects are not as severe as in conventional hyperthermia methods. In magnetic hyperthermia the temperature of body is heated up to a certain temperature using magnetic thermoseeds or magnetic nanoparticles subjected to alternating magnetic fields. The most common method of heating in magnetic particles is to take advantage of the hysteresis in ferromagnetic particles to release heat. Other methods of heating take advantage of relaxation losses in supermagnetic particles [14,15]. The specific absorption rate (SAR) is a parameter quantifies the transformation of the energy of the alternating electromagnetic field into heat, which is calculated as:

$$\mathrm{SAR} = f \cdot X$$

where f is the frequency of the electromagnetic field and X is the hysteresis area, i.e., specific energy observed in one cycle of remagnetization:

$$X = \int H\, dB$$

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where B is the magnetic induction. Therefore, highly hysteretic magnetic particles are desirable.

Another mechanism of heating which is different from the local magnetic hyperthermia effect is the magnetocaloric effect (MCE) [16–19]. At present main research for the for the magnetocaloric materials is directed for the magnetic refrigeration. However we try to use another perspective applications of these materials in the field of medicine. The MCE occurs as the result of the alignment of magnetic moments with an external applied magnetic field. The alignment reduces the magnetic randomness, or the magnetic component of the total entropy. This reduction of magnetic entropy must be compensated by the increase of another form of entropy and, in the case of magnetocaloric (MC) materials, is channeled into phonons, or *heat*. Because the mechanism of heating in this case is different from that of the conventional magnetic hyperthermia, it is named as "magnetocaloric hyperthermia" [20]. There are three quantities that are usually reported for MCE: the magnetic entropy change (ΔS_M), the refrigeration capacity (RC), and the adiabatic temperature change (ΔT). For a thermodynamic Carnot cycle the energy observed in one cycle in a magnetocaloric material is calculated as [20,21]:

$$\Delta Q = \Delta T \cdot \Delta S_M$$

Thus, the magnetocaloric contribution to heating in this type of hyperthermia is significant for a materials with large MCE parameters.

Magnetic losses in magnetically ordered ferro- and ferri-magnetic materials have a number of advantages as they diminish at the Curie temperature (T_C). As a result, magnetic hyperthermia treatments could be free from external temperature control when T_C is tuned to the therapeutic temperature range. In order to prevent the overheating of normal cells, the development of magnetic materials which are not affected by alternating magnetic field above 318 K (45 °C) has become essential. Nowadays, much of the research is focused on candidate materials composed of noble metals, rare-earth metals, their respective alloys, and intermetallic compounds. Ni-Cr [22], Fe_3O_4 [23], Cu-Ni [24], La-Ag and La-Na [25], and $Gd_5(Si_{1-x}Ge_x)_4$ and $(Gd_{1-x}Er_x)_5Si_4$[26] have been investigated as thermoseeds and nanoparticles for use in the localized self-controlled hyperthermia treatment for cancer. Recently, Gautam et al., explain the possibility of using the self-regulating Ni based seed encapsulated in titanium capsule for the treatments of solid Tumors [27]. We believed that these materials are applicable for medical propose as large numbers of research is going on for the Ni-based alloys for the hyperthermia treatment of cancer.

The objective of this study was to synthesis the Ni-based alloys with different compositions in which large, self-regulated heating powers occur at the precisely correct temperature to be used as a safe and effective form of hyperthermia treatment of cancer cells. These magnetic materials not only heat rapidly but the heating effect also stops abruptly after the temperature exceeds that needed to destroy tumor tissue, keeping it too low to affect normal healthy tissue. This may lead to a unique self-regulated heating effect with a large loss power which is unmatched by other conventional ferromagnetic materials.

In the present work, detailed studies of the crystal structural and magnetic properties have been performed for $Ni_{1-x}Z_x$ (Z=V, Mo, Cu, and Ga) binary alloys as a thermoseeds for hyperthermia applications. We present experimental result that reveal a linear change in magnetic ordering temperatures over a wide range with the change in doping concentrations. The main aim of this paper was to explore magnetic materials that have properties suitable for use in self-controlled magnetic hyperthermia, i.e., Curie temperature equal to 318 K (45 °C).

2. Experimental techniques

Three grams samples of $Ni_{1-x}Z_x$ (Z=V, Mo, Cu, and Ga) binary alloys were fabricated by conventional arc-melting in an argon atmosphere using high purity (4N) elements. The ingots were re-melted four times to ensure homogeneity. The alloys with $< 0.2\%$ weight loss were considered for the study. The samples were annealed at 1223 K (950 °C) for 12 h in high vacuum ($\approx 10^{-4}$ Torr) and cooled at a rate of 4 °C per minute to room temperature. The phase purity and crystal structures were determined by powder X-ray diffraction (XRD) using Cu Ka radiation. The magnetic and magnetocaloric properties were measured using a Quantum Design superconducting quantum interference device magnetometer (Quantum Design, Inc.) in a temperature range of 10–400 K and in magnetic fields up to 5 T. The magnetic entropy changes (ΔS_M) values were calculated from isothermal magnetization curves using the Maxwell relation [28]. The refrigeration capacity (RC) has been calculated by integrating ΔS_M (T, H) curve over the full width at half maximum using relation (2) [29].

$$\Delta S_M(T, H) = \int_0^H \left(\frac{\partial M(T, H)}{\partial T}\right)_H dH \tag{1}$$

$$\mathrm{RC} = \int_{T_1}^{T_2} \Delta S_M(T) dT \tag{2}$$

3. Results and discussion

The room temperature XRD patterns of $Ni_{1-x}Z_x$ (Z=V, Mo, Cu, and Ga) are shown in Fig. 1. All compounds possess a cubic phase which is similar to the XRD patterns of pure Ni without extra or split peaks. The small peak at low angle corresponds to beta line of Cu Ka radiation. Thus, single phase composition was achieved over the full range of Z concentrations.

The magnetization versus temperature data measured in a field H=100 Oe for annealed $Ni_{1-x}Z_x$ (Z=V, Mo, Cu, and Ga) alloys are shown in Fig. 2. Similar types of M(T) curves have been detected for all concentrations. The data show that there is a clear indication of the magnetic transformation (Curie transition) at different temperatures depending on x. The annealed sample shows a sharp Curie transition, whereas the un-annealed sample does not show a clear transition (see Fig. 1 in Supplementary information). This is because annealing eliminates residual stresses and lattice defects, allowing for the recrystallization and refining of the magnetic properties [30]. This indicates that the heat treatment has a strong influence on the magnetic properties of these Ni-based alloys. Also from Fig. 2, one can see that a systematic decrease in the Curie temperature with increasing V, Mo, Cu, and Ga concentrations while the magnetization

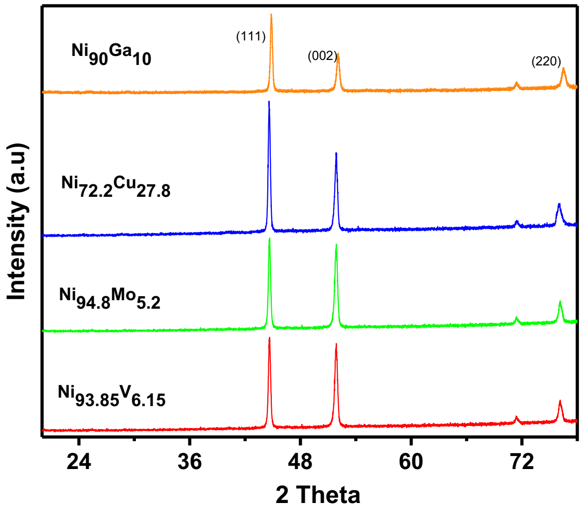

Fig. 1. Room temperature XRD patterns of selected $Ni_{1-x}Z_x$ (Z=V, Mo, Cu, and Ga) binary alloys.