Self-thermoregulating Ferromagnetic FeNi filled Carbon Nanotubes for Magnetic Hyperthermia Cancer Therapy

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Abstract. The mechanism of magnetic hyperthermia is introduced in this article. Superparamagnetic iron oxide nanoparticles have been used in magnetic hyperthermia cancer therapy. But its drawback is uncontrollable excess heat generation to ablate normal cells. Recently a new method using ferromagnetic Fe/Ni alloy have been studied. In this article, I will introduce my research in fabricating multiwall carbon nanotubes filled with Fe/Ni alloy. It is indicated that this nanostructure has the potential to become a guaranteed cancer treatment.

1. Introduction
The application of magnetic nanoparticles in biomedicine has been a hot research field recently. The results prove that carbon nanotubes (CNT) works effectively as a nanocontainer to store the inner active content and isolate it from the outer biological environment [1, 2]. This separation maintains the filling material’s magnetic property and is friendly to outer biological environment, so it attracts lots of interest. According to Pankhurst et al. [3], inner magnetic content can play a key role in magnetic hyperthermia therapy, because its capability to be transferred into tumour zone by gradient magnetic fields and generate heat, which will improve the local temperature and kill cancerous cells, by alternating magnetic fields.

The cancer cell killing phenomenon starts as the targeted tissue’s temperature rises above 42°C. Clinical tests have proved the efficacy [4]. Before this treatment becomes standard, there are still two main tasks need to be solved: First, a successful and safe delivery of the cure to target. Second, inner magnetic material’s capability to keep at the therapeutic temperature is needed [5].

In my work, I replaced the conventional superparamagnetic iron oxide nanoparticles with ferromagnetic FeNi alloy as encapsulated material in CNTs. The goal was acquiring multiwalled carbon nanotubes (MWCNTs) encapsulating iron and nickel compound using chemical vapor deposition (CVD) synthesis. After characterization by SEM, XRD, the sample’s magnetic properties (like Curie temperature) will be measured. The stage results exhibit its potential application prospects in biomedicine.

2. Theory
2.1. Magnetic Hyperthermia
Magnetic hyperthermia, according to Weissker et al., is based on the mechanism that cancer cells will be ablated when raising and keeping the target’s temperature in the range of 42-44°C for a while, at which normal cells will not be damaged [1]. To improve the therapeutic effect, the heat dissipation
must be controlled to stabilize local temperature below 44℃, getting rid of heat excess. Recently an optimized treatment named magnetic fluid hyperthermia (MFH) has been examined successfully [4]. The main procedure of MFH is like this: After being inserted into human body, the magnetic material works in external magnetic fields. There are three steps of the procedure: Gradient fields remove them to the expected area; Static fields locate them at target and alternating fields lead to heat dissipation into surrounding tumors. This procedure makes up the magnetic hyperthermia therapy [2].

Klingeler et al. [6] declared that magnetic fields can be fully applied in biomedicine application because of two advantages: the powerful biocompatibility and unharmful interaction with organisms. There are plenty of possibilities for the magnetic material’s heat generation in magnetic fields. Two main methods among them are ferromagnetic (hysteresis) losses and superparamagnetic (relaxation) losses [7].

2.2. Synthesis of Carbon Nanotubes & Growth Mechanism
Carbon nanotubes’ synthesis has been deeply studied over the years. Among various potential production methods, chemical vapour deposition (CVD) is a simple and perhaps the most reliable method for producing large quantity of products at high quality economically [1].

To fabricate filled CNTs, hydrocarbon compound precursor are needed because they can supply carbon for the CNTs’ formation [2]. We choose the family of metallocenes (Me(C₅H₅)₂ as candidate, where Me is one of the transition metals (Fe, Ni and Co) or their mixture. Metallocene has a dual effect as both the carbon serves as source for CNT formation and metal catalyses the formation process. The metal will also form inner content inside CNTs. We choose metallocenes also because of their appropriate sublimation and decomposition temperature. Through applying metallocenes, the formation of filling content and CNTs will happen simultaneously, so we call this phenomenon an in-situ process [1].

The main setup of CVD includes a horizontal quartz tube and a two-zone furnace. Figure 1 shows the basic setup and process. In the furnace preheater zone, metallocene powder was placed on a quartz boat and sublimated at certain temperature. Then the sublimated metallocene was carried by inert gas flow (like Ar) to the furnace central zone. The decomposition of metallocene and the deposition of grown CNTs happens simultaneously (in-situ process). The products are grown on preset silicon substrate for collection.

![Figure 1. Schematic diagram of the CVD process.](image)

All CNT formation mechanisms are on account of the vapor-liquid-solid (VLS) mechanism [8]. During the growth process metal nanoparticles interact with the CNT sheets [9]. At first, the catalyst metal nanoparticles decompose from the precursor and leads to CNT growth. When metal is used up, the growth slows down and eventually ends. This is the slow growth stage. As metal falls onto the CNT’s tip, the catalytic process restarts. Metal culsters can diffuse into the CNTs’ cavity to form a filling. CNT grows fast until the metal is surrounded by carbon or runs out again. This is the fast growth stage. These two stages transform into another freely in the whole process, and stop when the supply of precursor is drained.

2.3. Thermoregulation
Curie temperature (\(T_C\)) is the temperature where a material’s permanent magnetism transforms into induced magnetism [1]. Permanent magnetism is caused by the spontaneous magnetic moments alignment and induced magnetism is caused by the external-magnetic field-driven disordered magnetic moments. As the temperature goes up, thermal motion breaks the dipoles’ ferromagnetic status. When the temperature exceeds Curie temperature, a phase transition occurs in the material and it can no longer maintain the permanent magnetization, where the macro phenomena is that its magnetized state breaks, although it still behaves paramagnetically to external magnetic fields. Self-thermoregulation can be achieved based on this principle, and it indicates that Curie temperature is a threshold for controllable heat generation.

![Figure 2](image-url)

**Figure 2.** Theoretical and experimental Fe-Ni phase graph with T-composition curves. Inset red vertical line shows composition ratio (27% Ni in FeNi phase) for \(T_C\) of 100°C [10].

Based on the work from Miller et al. [10], the \(T_C\) of the composite can be tuned by changing its proportion. Figure 2 is the Fe-Ni dual phase diagram, it clarifies the compositional dependence of \(T_C\). The composition is a mixture of different phase of iron (\(\alpha\)-Fe and \(\gamma\)-Fe) and FeNi alloy phase. After annealing and quenching process, the iron-contained phases will transform into solely fcc \(\gamma\)-Fe phase. The ratio of Fe:Ni decides \(T_C\), with the result of 120°C for 27% Ni composition (Fe\(_{73}\)Ni\(_{27}\)). Miller et al. proved that the experimental result is very close to the theoretical value at 100°C. A lower percentage of Ni in FeNi will lead to a lower \(T_C\), and this character can be exploited in magnetic hyperthermia therapy to achieve controlled heat dissipation.

3. **Experimental**

3.1. 1\(^{st}\) Synthesis (Fe) and 2\(^{nd}\) Synthesis (Fe, Ni)

In the CVD process, powder of 60 mg ferrocene (or 40 mg ferrocene/20 mg nickelocene mixture) was placed on a silica boat. The precursor was sublimated in the preheater zone at 185°C. The the metallocene vapor was transferred by the Ar flow into the CVD central zone with the temperature set at 970°C. In the central zone, two silicon substrates were placed at 5 cm distance one after another. Sublimation process took 2 mins and decomposition process lasted for no less than 10 mins. Then the central reactor was cooled to room temperature at natural rate. At last the substrates (with filled CNTs deposition) were removed out. Then we collect sample by scratching the substrates.

3.2. Characterization
For characterization, we employed scanning electron microscopy (SEM) with a FEI Inspect F microscope. X-ray diffraction (XRD) analysis was performed in Xpert-Pro diffractometers (with Cu Kα source). Rietveld refinement method was applied to refine and measure the relative abundances of different phases. The principle of refinement is based on the least squares method which will minimize the sum of squared deviations of regression values from the measured values.

4. Results and Discussions
SEM images of the substrate-grown CNTs showed the diameter and growth morphology in Figure 3. These CNTs oriented randomly in unfixed direction, especially not straight on the tip. But they were lined up orderly from base.

![SEM images](image)

Figure 3. (A) and (B) are SEM images of CNTs from 1st synthesis. (C) and (D) are SEM images from 2nd synthesis sample. (A) and (C) reveals the morphology of CNTs from the 2nd substrate placed in the furnace at a temperature near 904°C, (B) and (D) are from the first substrate at 775°C.

Figure 4 displays XRD and Rietveld refinement of the two samples (Fe and FeNi filling). For the first sample, the relative abundance of the phases was approximately 11.6% Fe₃C, 16.6% α-Fe and 71.9% C. Nearly no Fe₃O₄ and γ-Fe were found. For the second sample grown at 904°C, the relative abundance of the phases was 12.6% α-Fe, 4.0% γ-Fe and 81.7% C. There is no existence of Fe₃C and Fe₃O₄. The result indicates Fe₃C is an transitional product in MWCNTs’ formation. At a higher operating temperature above 900°C, the compound will decompose into carbon and iron separately. Also at higher temperature, it is verified that a portion of α-Fe will transform into γ-Fe.

For the second synthesis, XRD and Rietveld analysis indicate the presence of FeNi alloy. For the first sample, the relative abundance of the phases was 6.8% FeNi, 18.7% α-Fe, 2.9% Ni and 69.7% C. The amount of γ-Fe is almost zero. For the second sample, the relative abundance was 15.5% α-Fe, 5.8% γ-Fe and 77.1% C. The amount of Ni is negligible (both Ni and FeNi alloy). The result indicates
that with the temperature increase, the metastable phase of FeNi will transform into stabilized iron phases, so it seems FeNi phase will not exist at higher temperature (above 900°C).

Figure 4. XRD diffractogram (black line) and Rietveld refinement (red line) of the (A, B) Fe-filled MWCNTs and (C, D) FeNi filled MWCNTs extracted from the CVD central zone at the decomposition temperature at 775°C (A, C) and 904°C (B, D).

5. Conclusions
The CVD synthesis, employing metalloocene as precursors, was convenient to acquire CNTs encapsulated with ferromagnetic material. The percentage of FeNi can be tuned by changing the ratio of ferrocene and nickelocene. To achieve the proper-tuned $T_C$ at ideal value, we have examined at different decomposition temperature. The optimal temperature in experiments to get ferromagnetic material filled CNTs is 775°C. Based on plenty of literature review, above 700°C the relatively stable $\gamma$-FeNi alloy will form in the filling content. From XRD analysis of the first sample in second synthesis, we can find that the ratio of Ni in FeNi is approximately 20%. This result means the sample has a $T_C$ lower than 100°C ($T_C$ of Fe$_{73}$Ni$_{27}$ sample). We have got preliminary samples for investigation, further research on more precise tuning $T_C$ is needed.

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