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Nanoparticle Heating Using Induction in Hyperthermia

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Induction heating is a convenient and flexible method to deliver high-strength magnetic fields to nanoparticles, resulting in a focused and targeted treatment that is gaining considerable interest in the medical research community.

Hyperthermia (or thermotherapy) is a type of cancer treatment that involves heating of tumor cells within the body. Even as far back as 3000 B.C., Egyptian pundits used heat baths to burn subcutaneous tumors. Doctors observed that high heat, such as that resulting from a fever, killed cancer cells and decreased tumors. Hyperthermia treatment of cancer requires directing a carefully controlled dose of heat to the cancerous tumor and surrounding body tissue. Elevating the temperature of tumor cells above the normal body temperature of 37 °C (98.6 °F) results in cell membrane damage, which, in turn, leads to the destruction of the cancer cells. Cancerous tissues continue to be damaged at exposure to the high temperature for an extended length of time.

Nanoparticles are used as the heat generating sources within the cancer cells and the tumors. This high heat must be used wisely—too little heat and the cancer will not be killed. However, if too much heat misses the tumor target, the skin or other healthy tissues can be burned. Induction heating provides the necessary solution for this critical process. It uses a high-frequency alternating magnetic field localized in the area of interest. The nanoparticles placed in the tumors and cancer cells couple to the applied magnetic fields and produce heat. This noncontact form of heat is accurate, repeatable, and safe. Because the applied magnetic field only heats the nanoparticles, the surrounding healthy tissue is not affected. Drug-carrying nanoparticles that release the drug at specific elevated temperatures can also be individually targeted to the tumor or specific parts of the body to obtain tumor cell necrosis.

Nanoparticles

Nanoparticles are objects having a diameter of less than 300 nm (11.8 μin.). These objects are typically made of iron oxides, manganese ferrites, cobalt ferrites, and many other permutations and combinations of various oxides. The underlying characteristic of all these nanoparticles is that their central core is comprised of materials that are magnetic in nature. In addition these nanoparticles have to be biocompatible and are required to be stable in external gravitational and electrostatic fields. Nanoparticles also need to overcome potential magnetic agglomeration because of the nature of their use. To shorten treatment time and minimize discomfort from prolonged heating, the nanoparticles should heat rapidly. To accomplish this, the specific absorption rate (SAR), which is the power of heating a magnetic material per gram of the nanoparticles, should be maximized. The power dissipated by a magnetic material subjected to an alternative magnetic field is expressed in W/g of nanoparticles.

Heating of nanoparticles with induction is believed to be caused by a combination of hysteresis effects, the Néel effect, and Brownian motion. Hysteresis is the continuous reorientation of the magnetic dipoles; the imposed induction magnetic field causes friction that generates heat. The Néel effect is best described as the heating due to supermagnetism. Superparamagnetism is a form of magnetism that appears in small ferromagnetic nanoparticles. In small enough nanoparticles, magnetization can randomly flip direction under the influence of temperature. The typical time between two flips is called the Néel relaxation time. In the absence of an external magnetic field, when the time used to measure the magnetization of the nanoparticles is much longer than the Néel relaxation time, their magnetization appears to be in average zero: they are said to be in the superparamagnetic state. In this state, an external magnetic field is able to magnetize the nanoparticles, similarly to a paramagnet. However, their magnetic susceptibility is much larger than the one of paramagnets. Brownian motion is the random movement of the nanoparticles in a fluid. During in vitro hyperthermia measurements they are generally dispersed in a liquid and form a ferrofluid. When a magnetic field is applied to them, magnetic nanoparticles rotate and progressively align with the magnetic field due to the torque generated by the interaction of the magnetic field with the magnetization. The three factors are believed to combine and produce heat in the nanoparticles.

Induction Heating

A basic induction heating setup is shown in Fig 1. The induction heating setup consists of a high-frequency power supply that takes the input from the alternating current (ac) line mains. This power supply unit converts regular line frequency (50 or 60 Hz) to a high-frequency

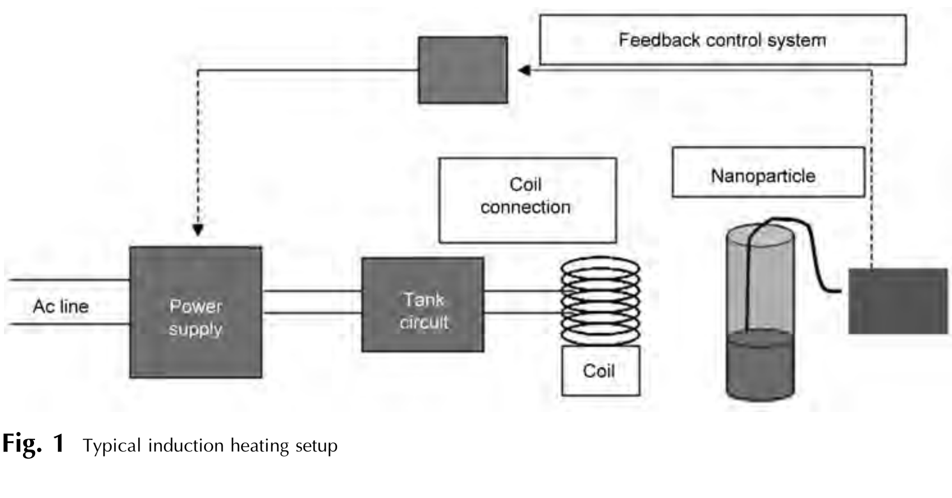

Fig. 1 Typical induction heating setup

signal, typically operating between 10 and 400 kHz. This high-oscillating signal is then fed to a tank circuit that feeds the water-cooled induction heating coil. The high-frequency signal generates a high-frequency magnetic field inside the induction heating coil. The sample consisting of the nanoparticle mixture is placed inside this induction heating coil. It interacts with the high-frequency magnetic field and produces heat. An optional fiber-optic thermocouple can be used to measure the temperature of the nanoparticle mixture. The thermocouple is immune to the radio frequency interference and can be used during the heat cycle. Its output can then be fed to a controller that can regulate the rate of increase of temperature as well as maintain a particular sample at temperature for a specific amount of time.

Magnetic Field Strengths. Typical induction heating coils are made of hollow copper tube with water as a cooling medium flowing through the inside. The most common type of coil is a simple solenoid or a helical coil (Fig. 2). The copper coil is described by the size of the copper tube, the inside diameter ($d = 2a$, where a is the radius) bore produced by the wound copper tube, the number of turns (N) of the copper tube, and the length (L) of the entire stack of the copper tubes. The current (I) flows through the copper to create the magnetic field.

The magnetic field generated by the solenoid coil, H, along its axis of height L and radius a, with N turns of current I is given by (Ref 1):

$$H = \frac{K_0}{2}\left(\frac{-z+\frac{L}{2}}{\left[\left(z-\frac{L}{2}\right)^2+a^2\right]^{\frac{1}{2}}} + \frac{z+\frac{L}{2}}{\left[\left(z+\frac{L}{2}\right)^2+a^2\right]^{\frac{1}{2}}}\right)$$

where $K_0 = \frac{NI}{L}\ \frac{NI}{L}$.

The midplane of the solenoid is $z = 0$; ends of the coil are $z = \pm L/2$. At the ends of the solenoid, therefore, the magnetic field strength is:

$$H = \frac{K_0}{4}\left(\frac{L}{[L^2+a^2]^{\frac{1}{2}}}\right)$$

Figure 3 shows the magnetic field along the axis for a finite length solenoid coil. As might be expected, the magnetic field intensity is the largest in the center of the coil, $z = 0$, and drops off as one traverses to the ends of the coil.

Experimental Setup. An induction heating coil setup operating at 300 kHz is presented here. The coil consists of seven turns and is made from 6.35 mm (0.25 in.) copper tube. It has an inductance measure of 1.1 uH. Using a power supply that is capable of operating between 150 to 400 kHz, this induction heating coil operates at 303 kHz with a 0.25 ufd value capacitance. When operating at 4.4 kW there are 375 amps flowing through the copper. The magnetic field at the center of the coil is therefore given by:

$$H = \frac{K_0}{2}\left(\frac{-z+\frac{L}{2}}{\left[\left(z-\frac{L}{2}\right)^2+a^2\right]^{\frac{1}{2}}} + \frac{z+\frac{L}{2}}{\left[\left(z+\frac{L}{2}\right)^2+a^2\right]^{\frac{1}{2}}}\right)$$

where $N = 7$, $I = 375$ amps, and $a = 12.7$ mm (0.5 in.). Hence, $H = 52.4$ kA/m.

The magnetic field along the axis of the coil is also calculated using this equation and is shown in Fig. 3.

An interesting phenomenon is experienced when currents this high at these frequencies are forced to flow through the small copper tube. The high current flowing through the copper tube causes the water inside the tube to heat as it spirals inside the helical coil. By the time the water runs through the coil, temperatures of 49 to 65 °C (120 to 150 °F) have been recorded. Typical flow through the coil was measured at 0.125 gpm. Figure 4 shows the thermal gradients set up on the surface of the coil.

It is also observed that this heat produced by the resistance heating of the copper of the coil radiates to the sample and distorts the absolute heating attained in the sample. A simple but innovative solution counteracts this heating effect. A 1.5875 mm (0.0625 in.) diameter nonconducting tube made of synthetic fluorine-containing resin is wound in the shape of a solenoid and is placed between the sample and the induction heating coil. Care is taken that this solenoid does not physically touch the sample or the copper of the coil to prevent any conductive heat transfer. Air is then blown through the solenoid to dissipate any heat coming from the induction coil to the sample. This isolates the sample from any external heat input and only true heat produced in the nanoparticles is measured using the fiber-optic thermometer. The various components of this system are the polyurethane coil and a ceramic paper insulation (Fig. 5).

REFERENCE

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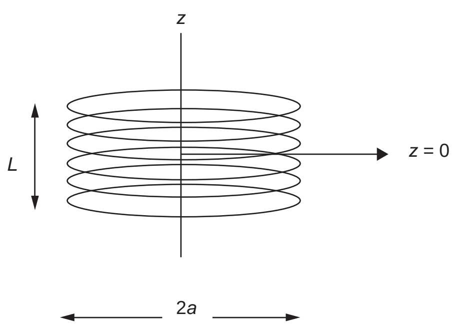

Fig. 2 Typical induction coil

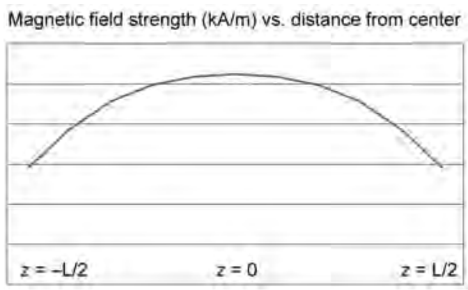

Fig. 3 Magnetic field along the axis of a solenoid coil

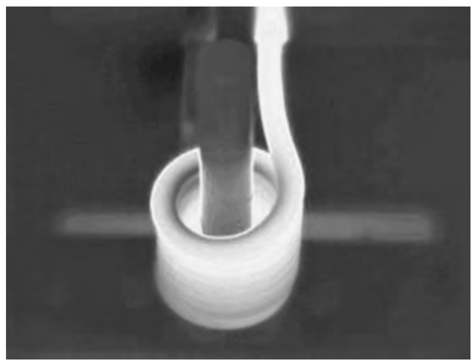

Fig. 4 Thermal gradient through an induction heating coil

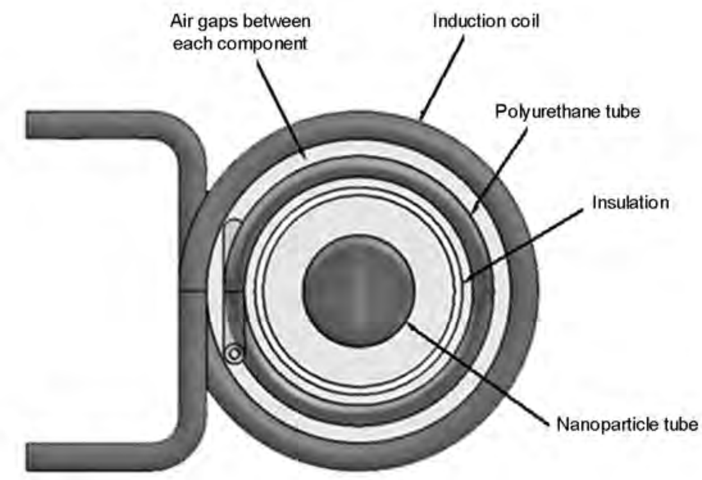

Fig. 5 Insulation setup for experiments