Simple coil-powering techniques for generating 10KA/m alternating magnetic field at multiple frequencies using 0.5KW RF power for magnetic nanoparticle hyperthermia

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ABSTRACT

Alternating magnetic field (AMF) configurable at a range of frequencies is a critical need for optimization of magnetic nanoparticle based hyperthermia, and for their application in targeted drug delivery. Currently, most commercial AMF devices including induction heaters operate at one factory-fixed frequency, thereby limiting customized frequency configuration required for triggered drug release at mild hyperthermia (40-42°C) and ablations (>55°C). Most AMF devices run as an inductor-capacitor resonance network that could allow AMF frequencies to be changed by changing the capacitor bank or the coil looped with it. When developing AMF in-house, the most expensive component is usually the RF power amplifier, and arguably the most critical step of building a strong AMF field is impedance-matched coupling of RF power to the coolant-cooled AMF coil. AMF devices running at 10KA/m strength are quite common, but generating AMF at that level of field strength using RF power less than 1KW has remained challenging. We practiced a few techniques for building 10KA/m AMFs at different frequencies, by utilizing a 0.5KW 80-800KHz RF power amplifier. Among the techniques indispensable to the functioning of these AMFs, a simple cost-effective technique was the tapping methods for discretely or continuously adjusting the position of an RF-input-tap on a single-layer or the outer-layer of a multi-layer AMF coil for maximum power coupling into the AMF coil. These in-house techniques when combined facilitated 10KA/m AMF at frequencies of 88.8 KHz and higher as allowed by the inventory of capacitors using 0.5KW RF power, for testing heating of 10-15nm size magnetic particles and on-going evaluation of drug-release by low-level temperature-sensitive liposomes loaded with 15nm magnetic nanoparticles.

Keywords: alternating magnetic field, magnetic nanoparticle, field intensity, coil design, impedance matching.

1. INTRODUCTION

Alternating magnetic field (AMF) has enabled special industrial processes including non-contact heat-processing of conductive materials by way of inductive heating. When AMF is applied to magnetic nano particles (MNP) such as ferrofluids, significant heating of the MNP can be induced. The AMF-mediated heating of MNP has found usefulness for various industrial and medical applications [1, 2]. The mechanisms by which the MNP are heated up when exposed to AMF have been adequately established. The processes contributing to MNPs’ heating under AMF include hysteresis [3], Brownian relaxation [4], and Néel relaxation [5, 6]. Whereas all of these three field-particle interactions are monotonically dependent upon the AMF field intensity (the stronger the field intensity is, the faster the heating becomes), their dependence on the AMF field frequency is diverse. The frequency-dependence of the heating of MNP under AMF can be used to induce highly efficient heating of MNP with the AMF frequency tailored to the MNP, for targeted tumor hyperthermia [7] and localized thermally sensitive payload release [8].
There are theoretical foundations for calculating the AMF frequency at which the highest specific absorption rate can be induced from a mono-dispersed cluster of MNPs [9]. The same theoretical foundations can also predict the optimal size of monodispersed MNPs for the highest heating efficiency at a given AMF frequency. In practice however, the poly-disparsity of MNPs as well as many confounding peripheral parameters can make the frequency-dependence of a specific batch of MNPs complex. With a complex frequency-dependence of the specific absorption rate of MNPs, it becomes imperative to configure the AMF device at a range of frequencies when optimizing the MNP synthesizing and operating conditions for applications including hyperthermia and targeted drug delivery against chronic diseases.

Currently, most commercial AMF devices including induction heaters operate at one factory-fixed frequency (within 10s-100sKHz), thereby limiting customized frequency configuration required for triggered drug release and other applications such as ablations using MNPs. Nearly all AMF devices used for mediating heating of MNPs operate as an inductor-capacitor resonance network that could allow AMF frequencies to be changed by changing the capacitor bank or the coil looped with it. The resonant frequency of an inductor-capacitor network can be determined easily, but to reach the highest field-intensity allowed by the equipment available is an art. When developing AMF in-house, the most expensive component is usually the RF power amplifier, and when an impedance-matching device is unavailable, arguably the most critical step of building a strong AMF field is the impedance-matched coupling of RF power to the coolant-cooled AMF coil. AMF devices running at 10KA/m strength are quite common, but generating AMF at that level of field strength using RF power less than 1KW has remained challenging.

In this work we report some laboratory instrumentation techniques useful to building 10KA/m AMFs at different frequencies using a 0.5KW 80-800KHz RF power amplifier [10]. Among the techniques indispensable to the functioning of these AMFs, a simple cost-effective technique was an adaptable rotational tapping method for continuously adjusting the position of an RF-input-tap on a single-layer or the outer-layer of a multi-layer AMF coil for maximum power coupling into the AMF coil. These in-house techniques when combined facilitated 10KA/m AMF at frequencies of 208KHz and higher as allowed by the inventory of capacitors using 0.5KW RF power, for testing drug-release by low-level temperature-sensitive liposomes loaded with 15nm magnetic nanoparticles.

2. A BRIEF SURVEY OF RF POWER PER AMF FIELD STRENGTH

The AMF devices used for heating MNPs are demonstrated at many different frequencies and a large range of peak field intensities. AMF field parameters found from a few previous studies are listed in the following Table 1. For the purpose of referencing how much RF power has been used in generating an AMF field intensity of 10KA/m (1KA/m=12.57 Oe) for testing of in vitro sample or rodent tissues. From these reports, it can be appreciated that producing AMF of 10KA/m strength, at a frequency of 100sKHz, within a working volume of ~2cm in diameter using less than 1KW of RF power is challenging.

Table 1 AMF field parameters reported by some previous studies

<table>
<thead>
<tr>
<th>AMF field intensity (KA/m)</th>
<th>AMF frequency</th>
<th>Dimension of AMF applicator</th>
<th>RF peak Power (KW)</th>
<th>RF power (KW) per 10KA/m AMF strength</th>
<th>reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>103.5</td>
<td>153KHz</td>
<td>1cm wide region</td>
<td>25KW</td>
<td>2.4</td>
<td>[11]</td>
</tr>
<tr>
<td>23.87</td>
<td>765KHz</td>
<td>23mm diameter 3-turn</td>
<td>4.5KW</td>
<td>1.9</td>
<td>[12]</td>
</tr>
<tr>
<td>100</td>
<td>135-440KHz</td>
<td>7.5 turn 3 cm length &amp; 2.54 cm inner diameter</td>
<td>2.4KW</td>
<td>9.9</td>
<td>[14]</td>
</tr>
<tr>
<td>8</td>
<td>230KHz</td>
<td>2.4KW</td>
<td>3.3</td>
<td>[15]</td>
<td></td>
</tr>
<tr>
<td>7.6</td>
<td>150KHz</td>
<td>2KW</td>
<td>3.8</td>
<td>[16]</td>
<td></td>
</tr>
</tbody>
</table>
3. SOME DESIGN CONSIDERATIONS FOR IN-HOUSE DEVELOPMENT OF AMF OPERATING AS AN INDUCTOR-CAPACITOR RESONANCE NETWORK

Most devices used for AMF applications, commercial or in-house alike, operate as an inductor-capacitor network where the coil generating the AMF is used as an inductive component in the network that resonates with a capacitor for operating the AMF at one frequency only or a capacitor bank for selecting the AMF operating frequency. The basic modules needed for constructing an AMF device using inductor-capacitor resonance network for applications in hyperthermia and thermal-release of drug is schematically illustrated in Figure 1. The modules include:

- The AMF coil and the coil-support. The AMF coil, the inductive component of the resonance circuit, generally comprises of a single-layer solenoid with several turns that passes a current of 10s of Amperes in order to generate a field at the order of 10KA/m (125.60e) at the center region of the coil. The size and shape of the AMF coil-support determines the types of in vitro samples or in vivo tissues that can be placed in the AMF. The large current running through the AMF coil generating significant amount of heat due to resistance also requires the coil to be continuously cooled by a coolant. As a result, hollow, bendable and highly conductive tubing such as copper tubing with a round or rectangular cross-section is used toward an AMF device.

- The capacitor bank consists of heavy-duty (large current and large peak voltage) capacitors. For these capacitors, electrical conduction with the AMF-coil inductor enables resonance and thermal conduction with coolant is needed for dissipating the heat deposited in the capacitor due to internal loss.

- An energy-feeding device to compensate the loss within the inductor-capacitor network when it resonates at 100s KHz range, and the method/device to couple the energy into the coil to maintain the resonance. An RF power amplifier operating at sub-MHz band or a pulse amplifier is needed.

- The structure rendering mechanical integrity as well as enhanced electrical grounding for equipment safety and operator safety, similar to what is needed for the RF module in an MRI scanner.

- A cooling device to circulate coolant through the AMF coil and remove the heat generated by other components including the capacitor.

- A field-pickup device for measuring the strength of the AMF field.

- A magnetically compatible temperature sensor for real-time monitoring of the temperature of the sample.

![Figure 1. Schematic diagram of an inductor-capacitor network for producing AMF for thermal mediation of magnetic particles for hypothermic and drug delivery applications.](http://spiedigitallibrary.org/s/termsofuse.aspx)
4. PRACTICAL IN-HOUSE TECHNIQUES FOR AMF DEVELOPMENT

In this work, we present some practical techniques for in-house modular development of an AMF device based on inductor-capacitor network and RF power coupling using auto-transformer. The individual critical techniques/procedures for modular assembly of the AMF device are outlined in below.

4.1 Structural integrity, grounding, and cooling.
A long and large aluminum plate of ½” thickness was used as the structural chassis as well as the grounding connection of the AMF coil-capacitor network. The heavy-duty capacitors are bolted together by a connection plate at the bottom and another connection plate at the top (Figure 2). The connection plate at the bottom was bolted to the chassis. Two smaller aluminum structures with a half-circular groove were used to press each of the two ends of the copper tubing against the capacitor connection plate, to provide both electrical connection and thermal conduction. Selection of the capacitor combination can be done easily by removing a bolt of the top connection plate and placing a high-voltage insulating sheet between the capacitor to be disconnected and the connection plate. The entire capacitors banks are insulated by large transparent structures built with plastic sheets.

Coolant circulated by a closed loop chilling system is preferred. When closed loop coolant is not available, tap water could be an effective alternative. In our AMF system, the tap water as the coolant was circulated into the copper tubing terminal at the chassis ground, by plastic tubing. The coolant returning to the sink from the copper tubing terminal at the non-ground end of the capacitor was directed to drain to the sink, away from any metal components of the sink. The plastic tubing running the returning coolant was also winded into a long coil to reduce hazard caused by the high voltage when the coolant exiting the inductor-capacitor network.

![Figure 2. Structural components for integrating grounding, electrical connection, and cooling needs.](image)

4.2 RF power coupling into the AMF coil without commercial impedance-matching device
For in-house development of the AMF device and when an impedance matching device is unavailable, the most challenging issue is arguably the method of transferring the maximum power from the RF power amplifier to the AMF coil. A transformer can allow matching any impedance between the primary coil to be powered by the RF amplifier and the secondary coil that produces the AMF. This configuration is however difficult to produce in AMF regime, by using hollow bendable tubing. Additionally, the need to cool the primary tubing when high AMF field is needed also complicates the in-house design.
A much more in-house-friendly configuration of the AMF coil that facilitates cooling of the coil and RF coupling to the coil is to set tapping terminals on to the coil so the coupling of RF power into the AMF coil can be adjusted by way of auto-transformer. The placement of the tapping terminal, however, can be confounded by the adjacency of the neighboring turns of the coil. This is because it is difficult to place several tapping terminals to a coil when the coil materials are also to be insulated by (self-adhesive) insulating film. The use of tubing materials with insulating coating will ease the coil development; however, it will not completely eliminate the technical difficulty of adding terminals needed for RF coupling. Shown in Figure 3 is an AMF coil of 40mm-diameter core that had seven tapping terminals built into the coil for adjusting the RF coupling into the coil.

![Figure 3](image-url)  
**Figure 3:** An AMF coil of 40mm in core diameter that had multiple tapping terminals built into the coil for tuning the RF coupling into the coil.

Shown in Figure 4 is an AMF coil of 17mm useful core diameter that had a rotatable tapping terminal for continuously adjusting the position of an RF-input-tap on a single-layer or the outer-layer of a multi-layer AMF coil for adjusting the RF power into the AMF coil.

![Figure 4](image-url)  
**Figure 4:** (Top) an AMF coil of 17mm in useful core diameter that had a continuous rotatable tapping terminal built into the coil for adjusting the RF coupling into the coil. (Bottom) The AMF coil and the capacitor banks, as well as the close-up view of the rotatable tapping terminal.
5. AMF GENERATION AND HEATING OF MNPS

5.1. AMF system
Two AMF inductor-capacitor networks units are built. One AMF solenoid coil is shown in Figure 3, and the other solenoid coil is shown at the bottom panel of Figure 4. The RF signal from a function generator was connected to a class-B power amplifier (ULTRA 06-800, T&C Power Technologies, Rochester, NY) capable of delivering 550W to a 50Ohm load for RF frequency between 100KHz—800KHz (the full-width at half maximum bandwidth). The chassis of the RF power amplifier was also physically grounded to the earth potential. The amplified RF signal was fed to the solenoid between the earth potential and selected taps of coil above the earth potential, using either the seven discretely placed terminals on the 40mm core AMF coil, or the rotatable terminal on the 17mm-diameter AMF coil. The forward and reverse RF powers were monitored an oscilloscope through an in-line power read-out interface built-in with the RF power amplifier. The magnetic field strength at the center of the AMF applicator was measured using a single-turn read-out coil of an area A that was connected to a Tektronix 2445B oscilloscope. The magnetic field intensity $H_0$ [unit: KA/m, 1KA/m -12.56 Oe] was estimated by $H_0 \approx B_0/\mu_0 = \varepsilon_0/(\mu_0 2\pi f_0 \cdot A)$ where $B_0$ is the magnetic flux density [unit Tesla], $\mu_0 = 4\pi \times 10^{-7}$ Vsa$^{-1}$m$^{-1}$ is the permeability of free space, $\varepsilon_0$ is the amplitude of the inducted voltage signal measured from the read-out coil, $f_0$ is the AMF frequency, and $A$ is the area of the read-out coil. The temperatures of the samples placed in AMF were measured using fluoro-optic temperature sensors connected to a Reflex quad-channel signal conditioner (Neoptix, Quebec, QC, Canada) or a TMI quad-channel temperature signal conditioner (Quebec, QC, Canada).

The 40mm core-diameter AMF coil as shown in Figure 3 has been iterated many rounds. The following table lists the field frequency and intensity achieved in one of the iterations. The 17-mm core AMF coil generated frequencies at 208KHz and above, depending upon the capacitor combinations, all at a field intensity above 126Oe at the RF forward power of 0.5KW.

<table>
<thead>
<tr>
<th>Freq(KHz)</th>
<th>88.8</th>
<th>108.0</th>
<th>140.6</th>
<th>149.5</th>
<th>156.6</th>
<th>209.5</th>
<th>320.13</th>
<th>419.0</th>
<th>520.0</th>
<th>846.0</th>
<th>1105.0</th>
</tr>
</thead>
<tbody>
<tr>
<td>Field (Oe)</td>
<td>220</td>
<td>220</td>
<td>220</td>
<td>220</td>
<td>220</td>
<td>52</td>
<td>112</td>
<td>77</td>
<td>52</td>
<td>52</td>
<td>52</td>
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</tbody>
</table>

Figure 5(a) displays the initial temperature rise per second, measured from a magnetic nanoparticle sample of 10nm average diameter but unspecified volume concentration at frequencies specified in Table 1 and normalized at AMF field intensity of 100Oe. The theoretical estimation was based on 100Oe AMF field intensity, 1.3% volume fraction of magnetite with a mono-dispersion of 10nm size, and 2nm hydrodynamic thickness. Figure 5 (b) displays the temperature rise over 5 minutes measured from an aqueous sample of 1mg/mL magnetic nanoparticle (10nm) concentration versus that from a control solution, under AMF of 1.105MHz and 52 Oe.

Figure 5. Measurement of temperature rise of MNPs under AMF. (a) The initial rate of temperature rise (deg/sec) at 100Oe AMF field strength for different AMF frequencies. The simulation is based on mono-dispersion of 10nm magnetite, and 1.3% volume fraction of MNPs in the aqueous solution. (b) SPION aqueous solution at 1mg/mL concentration versus the same amount of control solution.
Figure 6(a) displays the initial temperature rise per second, measured from a magnetic nanoparticle sample of 10nm average diameter but unspecified volume concentration at varies frequencies, using the 40-mm core AMF coil at one of the iterations of the coil development. The AMF field strength was controlled at the same 203Oe for the frequencies including 88.8, 108.0, 149.5, and 156.6 KHz, for the results shown in Figure 6 (a). The AMF field strength was controlled at the same 50Oe for the frequencies including 209.5, 550.0, 846.0 KHz, and 1.105MHz, for the results shown in Figure 6 (b).

Figure 6. (a) Measurement of temperature rise of MNPs under AMF at the same field strength of 203Oe, at frequencies of 88.8-156.6KHz. (b) Measurement of temperature rise of MNPs under AMF at the same field strength of 50Oe, at frequencies of 209.5KHz to 1.105MHz.

Figure 7 presents the heating rates of several samples available in our laboratories when exposed to an AMF of 1.1MHz frequency and field strength of approximately 150 Oe. The samples include in-house synthesized iron oxide solution with unspecified iron oxide concentration, 0.9% saline, a commercial sample of 15nm iron-oxide particles dissolved in PBS with an unspecified iron oxide concentration, and low-level-temperature-sensitive liposome with encapsulation of iron oxide, at an unspecified concentration. An interesting observation from Figure 7 is the heating of saline.

Figure 7. The heating rates of four samples when exposed to an AMF of 1.1MHz at field strength of approximately 150Oe.
6. CONCLUSIONS

Alternating magnetic field (AMF) configurable at a range of frequencies is a critical need for optimization of magnetic nanoparticle based hyperthermia, for their application in targeted drug delivery. When developing AMF in-house, the most expensive component is usually the RF power amplifier, and arguably the most critical step of building a strong AMF field is impedance-matched coupling of RF power to the coolant-cooled AMF coil. AMF devices running at 10KA/m strength are quite common, but generating AMF at that level of field strength using RF power less than 1KW has remained challenging. We practiced a few techniques for building 10KA/m AMFs at different frequencies, by utilizing a 0.5KW 80-800 KHz RF power amplifier. Among the techniques indispensable to the functioning of these AMFs, a simple cost-effective technique was the tapping method for discretely or continuously adjusting the position of an RF-input-tap on a single-layer or the outer-layer of a multi-layer AMF coil for maximum power coupling into the AMF coil. These in-house techniques when combined facilitated 10KA/m AMF at frequencies of 88.8 KHz and higher as allowed by the inventory of capacitors using 0.5KW RF power, for on-going evaluation of drug-release by low-level temperature-sensitive liposomes loaded with 15nm magnetic nanoparticles.

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