Gradient Coils for the Focused RF Ablation with Magnetic Fluids

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Introduction: Currently, various types of heat treatment modalities are available like microwave, ultrasound, RF probe and capacitance hyperthermia, magnetic fluid hyperthermia etc., but none of these methods have the ability to accurately deliver high heat energy to deeply seated tumors without damaging the healthy surrounding tissues. In this work, by the effective usage of DC Magnetic Field Gradients a novel RF ablation system was developed which is capable of focusing the heat into very small areas in the order of millimeters. In addition, it was verified that by the utilization of the basic MRI gradient coil technology the developed system can be further improved such that 3D steering of the heating focus can be achieved.

Background: Over the last decade, magnetic particle hyperthermia has been improved by the advent of "magnetic fluid hyperthermia" (MFH) [1], where colloidal dispersions of superparamagnetic iron oxide nanoparticles (magnetic fluids) exhibit an extraordinary specific absorption rate (SAR [W/*g*]) under the AC magnetic field. In a typical MFH treatment, firstly, magnetic fluids are dispersed into target tissue and secondly, by the application of AC magnetic fields, heating of the fluids and correspondingly damaging of the tumors is achieved [1]. But, as a result of the magnetic fluid diffusion from tumor to surrounding tissues or incorrect localization of the fluids in the target tumor area, unwanted heating of the healthy tissues can be seen [2]. To overcome the normal tissue damage drawback of MFH, a focused ablation system should be generated, to heat very small regions without destroying the normal healthy tissue.

Theory: It is well known that under alternating magnetic field, super-paramagnetic nanoparticles are heated as a result of the rotation of the particle itself (Brownian relaxation) [3] and the rotation of the magnetic moment inside the particle (Neel relaxation) [4]. In addition to the alternating field, if a static magnetic field is applied with equal or larger amplitude, the single domain particles and their magnetic moments align with the static field. Thus, Neel and Brownian relaxations are blocked and heating of the particles are diminished. This fact is experimentally shown in previous studies [1] where a static magnetic field perpendicular to AC field is applied to the magnetic fluids and it is observed that, heating is reduced significantly if the amplitude of the static field reaches to the strength of the alternating field. These studies demonstrate us that static magnetic fields can be used to modulate the heating effect of AC magnetic fields on the magnetic domains.

Methods: By depositing appropriate DC magnetic field gradients on the AC magnetic fields one can generate AC field dominant regions and achieve focused heating of the magnetic particles at these regions. Figure 1 shows a system that accomplishes this task. Here two solenoids on the right and left of the figure are fed with equal but opposite DC currents. The static field vectors generated by the solenoids cancel each other at the center of the system and a region with a very small DC magnetic field is formed around the center which can be named as the field free region (FFR). If an alternating magnetic field is applied to the space between the solenoids, alternating field will be dominant in the FFR and only the magnetic particles inside the FFR will be heated. The field free region explained above can be reduced further (i.e., more intense focus can be obtained) by increasing the current magnitudes flowing through the DC solenoids. In addition to that, the position of the focus can also be changed via giving different amplitudes of currents to the DC solenoids. By adding one more solenoid between the lateral DC solenoids of Figure 1, implementation of focused heating applicator can be completed as in Figure 2. The solenoid in the middle (AC Solenoid) generates the alternating magnetic field responsible for the heating of the magnetic particles and other lateral solenoids (DC solenoids) generate a static magnetic field gradient such that a field free region is generated in the middle of them.

Experiments: To validate the focused heating ability of the ablation system several in vitro and in vivo experiments were made. During the experiments three different DC magnetic field conditions were tested by applying static currents(IDC) of 0.5A, 1A and 1.8 A to both DC solenoids. In vitro experiment setup can be seen in Figure 3a. Inside the AC solenoid three spherical plastic cups of diameter 0.4cm were placed which were filled with a magnetic fluid (Liquids Research Ltd.). An AC magnetic field with strength of 4.5kA/m at 80 kHz was applied and corresponding temperature increases of the cups were recorded at different DC magnetic field conditions (Figure 4). In vivo experiments were done on the tails of 200g adult rats. Ferrofluids were injected percutaneously to the tails of the anesthetized rats after that, rat tail was placed along the axis of the solenoids (Fig. 3b). An AC field (7.6kA/m) at 80 kHz was applied and temperature was recorded at different DC field conditions.

Results: As shown in Figure 4, the temperature rise of the central cup doesn't change while the temperature rise of the lateral cups decreases as the amplitude of the DC solenoid current increases. This shows us that focusing is achieved successfuly by increasing the DC solenoid currents. Also it can be seen that, by giving different amounts of currents to the DC solenoids the position of the focus can be changed (rightmost plot in Fig.4). In in-vivo experiments AC field exposure lasts nearly 25 minutes and temperatures above 46ºC were obtained for all three experiments. Significant slimming and molting was observed on three of the rat tails. As shown in Fig5, size of the molting region decreases as the applied static magnetic field strength increases, again this verifies macroscopically that an ablation with higher intensity is achieved as the currents of the DC solenoids increased. Also for the microscopic verification, rat tails were examined histologically and results will be available soon.

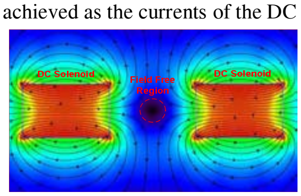

Figure 1. Opposed solenoids produce a field free region(FFR) in the middle of the solenoids.

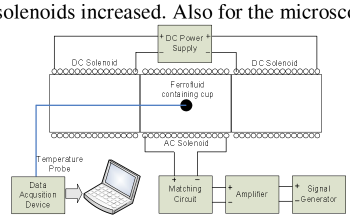

Figure 2. General experimental setup used in the experiments.

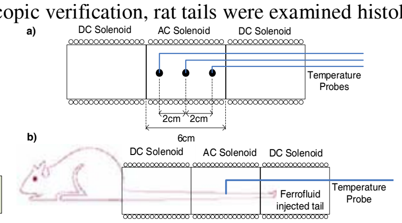

Figure 3. a) In vitro experiment setup, b) in vivo experiment setup.

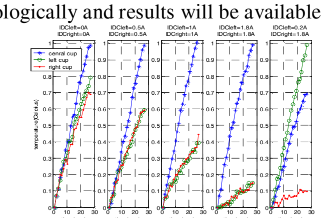

Figure 4. Temperature vs. time graphs of the in vitro experiments.

Discussion: The presented system with solenoids creates a magnetic field gradient very similar to Helmholtz coils (Z-gradient coils). This system has the ability to change the position of the focus in one dimension (along the z axis). We made several simulations with Comsol Multiphysics software and saw that by using basic gradient coil configurations of MRI scanners, two and three dimensional movement of the heating focus can also be obtained. Figure 6 shows a system with saddle (Y gradient) and Helmholtz (Z gradient) coils, which is capable of 2D steering of the focus in the y-z plane. Also 3D movement of the focus can be easily done by adding X gradient saddle coils into the system of Figure 6. In addition to that, Helmholtz pair of the gradient coil system can be used to supply the AC field that is responsible for the heating of the magnetic fluids. This analysis shows us that basic gradient coil design (with 1 Helmholtz and 2 saddle coil pairs) can be used to build a focused RF applicator, where gradient coils are used for the generation and shifting of the heating focus and Helmhotz pair is also used as the RF field source.

Figure 5. Tails, 24 hours after the ablation a) For IDC=0.5A FFR≈22mm b)For IDC=1A FFR≈15mm c)For IDC= 1.8A.FFR≈7mm

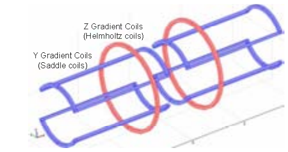

Figure 6. Y and Z Gradient coils capable of 2D steering of the heating

Conclusion: In this work a novel focused ablation system, capable of heating deeply seated tumors without damaging any surrounding tissue is presented and verified through experiments. The developed system can be implemented much more effectively by using the basic gradient coil systems of MRI, which will additionally provide the shifting of the heating focus in 3D. A further study can be the testing of other possible gradient coil configurations to find the optimal coil system that produces the highest intensity focus with the easiest focus shifting ability.

References: [1] 1993 *Int. J. Hyperthermia* 9 51–68, [2] J. Mater. Chem., 2004, 14, 2161-2175, [3] Phys. Rev. 130, 1677-86, [4] Neel L 1949 Ann. Geophys. 5, 99-136.

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