Published in final edited form as:

J Vasc Interv Radiol. 2017 November ; 28(11): 1592–1598. doi:10.1016/j.jvir.2017.06.036.

MR Coagulation: A Novel Minimally-Invasive Approach to Aneurysm Repair

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Abstract

Purpose—To demonstrate a proof-of-concept of magnetic resonance coagulation (MRC), in which the MRI scanner-induced RF heating at the end of an intracatheter long wire heats and coagulates a protein solution to effect a vascular repair by embolization.

Materials and Methods—MRC was simulated by finite element modeling of electromagnetic fields and SAR in a phantom. A glass phantom consisting of a spherical cavity joined to the side of a tube was incorporated into a flow system to simulate an aneurysm and flowing blood with velocities of 0–1.7 mL/s. A double lumen catheter containing the wire and fiberoptic temperature sensor in one lumen was passed through the flow system into the aneurysm, and 9 cc protein solution was injected into the aneurysm through the second lumen. The distal end of the wire was laid on the patient table as an antenna to couple RF from the body coil, or connected to a separate tuned pickup coil. A high RF duty cycle Turbo Spin-Echo pulse sequence excited the wire such that RF energy deposited at the tip of the wire coagulated the protein solution embolizing the aneurysm.

Results—The protein coagulation temperature of 60 °C was reached in the aneurysm in ~12 s, yielding a coagulated mass that largely filled the aneurysm. The heating rate was controlled by adjusting pulse sequence parameters.

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Author contributions: O.C.: technical implementation, data collection and analysis, manuscript development and editing; M.Z.: technical implementation, data collection and analysis; E.N: concept development, manuscript development and editing; J.L.A.: concept development, manuscript development and editing.

Conflict of interest: E.N. is an employee of Robin Medical, Inc., which has the rights to develop this technology into commercial use. All other authors have no competing financial interests to declare.

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Conclusion—Magnetic resonance coagulation has potential for embolizing vascular defects by coagulating a protein solution delivered by catheter using MRI scanner-induced RF heating of an intracatheter wire.

Keywords

Interventional radiology; coagulation; vascular repair; aneurysm repair; embolization; MRI heating

Introduction

Intracranial aneurysms occur in an estimated 1–6% of the population(1) with the most common presentation being subarachnoid hemorrhage (SAH).(2) Current treatment methods consist of *i*) microvascular neurosurgical clipping (3), *ii*) endovascular coiling (4), which may be combined with temporary caging for wide-neck aneurysms (5) or *iii*) embolization by a coagulable material, *e.g.*, Onyx (Micro Therapeutics, Irvine, CA, USA) (6) or recently developed polymeric foams (7). Neurosurgical clipping is highly invasive since it entails clipping the aneurysm at its base via an open surgical approach to prevent rupture. Additionally, in clinical trials clipping presents less favorable outcomes compared to coiling (8,9). While minimally invasive, a disadvantage of coiling is the possible reopening of the aneurysm that may be caused by impaction of the coils (8). Finally, embolization by coagulable materials yields improved packing compared to coiling but require the injection of possibly immunogenic foreign materials.

This paper describes a novel minimally-invasive embolization method, magnetic resonance coagulation (MRC), that does not require the permanent implantation of artificial objects (*e.g.*, coils) or foreign materials (*e.g.*, Onyx, polymeric foams) to achieve embolization, and does not necessarily require temporary occlusion of normal blood flow. Instead, a biomaterial that can be coagulated by mild heating is injected into the aneurysm and coagulated using the heat generated by the MRI scanner. The scanner also provides the necessary intraprocedural image guidance, and assesses the efficacy of the repair. The MRI scanner permits fine control and real-time monitoring of the coagulation process and significantly simplifies the embolization procedure.

In this report egg white, a conveniently available protein solution, is used as the biomaterial. In clinical practice, the use of a more human-compatible material such as human serum albumin (HSA), a naturally present blood protein that is nonthrombogenic and non-immunogenic, is envisioned. The MRC concept is illustrated in Fig. 1. The potential of MRC is demonstrated via electromagnetic simulations and phantom experiments that mimic typical conditions encountered in *in vivo* aneurysms.

Materials and Methods

Electromagnetic simulation and model description

The feasibility of the proposed technique for directing RF energy from the scanner's body RF coil to the aneurysm was tested by numerical simulation of two device configurations using an electromagnetic finite-element solver (HFSS, Ansys, Inc., Canonsburg, PA, USA).

In one device configuration a standalone wire was used to harvest the RF energy from the scanner. The standalone wire was a polytetrafluoroethylene-insulated 24 American wire gauge (AWG) wire with 0.5 cm exposed at the tip. In the second configuration an RF coil tuned to the scanner's Larmor frequency was used in conjunction with the wire. The aneurysm was modeled as a 15 mm diameter sphere. The sphere's dielectric properties were set to those of blood (10,11).

Phantom, flow and catheter system

A spherical glass aneurysm phantom of 15 mm outside diameter was manufactured (Yankee Glassblower Inc, Concord, MA, USA). A glass phantom was chosen because it is an MR compatible material, easily shaped, and allowed visualization of the coagulum. The smoothness of the glass walls ensured that successful adhesion of the coagulum in vitro would be successful in vivo as well. A peristaltic pump (Cole-Parmer, Vernon Hills, USA) provided a controllable pulsatile saline flow through the phantom. Hemostatic Y-valves permitted the insertion of a DuraFlow 14 Fr double lumen catheter (AngioDynamics, Marlborough, MA, USA) while preventing the introduction of air bubbles into the system. A 26 AWG Teflon insulated silver plated solid copper wire (Alpha Wire, Elizabeth, NJ, USA) was connected to a 30 cm $\times$ 30 cm square RF loop coil tuned to the Larmor frequency. The RF loop coil was placed against the scanner's inner bore. The other end of the wire and a Luxtron fiber optic temperature sensor (LumaSense Technologies, Santa Clara, CA, USA) were inserted into one lumen of the catheter and positioned such that the wire and sensor tips emerged by about 5 mm from the catheter tip. The catheter assembly was guided into the aneurysm. Temperatures were sampled at 1 s intervals.

Chicken egg white, a low-cost protein solution source, was used as the coagulable biomaterial. Ovalbumin, a protein with coagulation properties similar to HSA, is the major protein constituent in egg white.

MRI and magnetic resonance coagulation

Experiments were carried out in a Siemens Avanto 1.5 T (Siemens Healthcare, Erlangen, Germany) scanner using its built-in body RF coil for RF excitation. A high RF duty-cycle turbo-spin-echo (TSE) sequence provided the necessary RF heating. The field-of-view (FOV) was set to 300 mm $\times$ 300 mm with a matrix size of 128 $\times$ 128 and a slice thickness of 5 mm. With the repetition time (TR) set to 300 ms, the total scan duration (heating time) was 2 min. Tuning and detuning the attached RF coil enabled general control over the heating whereas adjusting the TR permitted fine control of the RF duty cycle.

Results

Electromagnetic simulation

Fig. 2 shows the SAR in the aneurysm computed by the simulations on a log scale. Both configurations exhibited increased SAR near the wire tip. However, the maximum SAR for the coil configuration was approximately 40-fold higher than the standalone wire configuration, reaching a maximum of $\sim$ 80 W/kg in contrast to the $\sim$ 2 W/kg attained by the wire configuration.

Saline heating

The heating was initially measured without flow to ensure that the proposed device could provide sufficient heating for coagulation. The coil configuration yielded the greatest heating and allowed simple control of the heating rate by tuning or detuning the resonant circuit comprising the RF coil and was therefore used for all subsequent experiments. The heating sequence was applied for 30 seconds and the temperature rise recorded throughout the experiment with the fiber-optic thermometer. As predicted by a simple heat transfer model of the aneurysm in contact with an infinite heat sink (equivalent to the surrounding tissue remaining at fixed temperature), the temperature rose during heating at a fixed duty cycle to asymptotically approach a maximum temperature, and decayed exponentially toward the baseline temperature when the sequence was turned off (Fig. 4). Using the pulse sequence parameters described above, the temperature increased at a rate of $\sim 2\text{--}3\text{ }^{\circ}\text{C/s}$ reaching the $\sim 60\text{ }^{\circ}\text{C}$ needed to coagulate the protein solution in ~ 12 seconds.

Effect of flow on heating rate

Thermal bioregulation mechanisms including blood flow help dissipate heat in tissues which can affect the maximum temperature achievable in vivo. The effect of different flow rates on the achievable temperature rise was therefore studied. The heating experiment was repeated multiple times for flows in the range $0\text{--}1.7\text{ mL/s}$ and the temperature rise in the aneurysm measured. This range of flows is representative of different clinical paradigms in aneurysm repair with a flow of 0 mL/s being equivalent to a balloon-assisted embolization (12), whereas 0.5 mL/s is the flow rate past cerebral aneurysms in small vessels (13) with unobstructed blood flow. The heating rate (initial slope of the temperature vs. time curve) for each experiment was calculated by fitting the temperature T as a function of time t to the equation $T = A - B \exp(-t/C)$ using the Levenberg-Marquardt algorithm (14) with A , B and C adjustable parameters.

The relationship between the heating rates and the corresponding flow rates was determined by a linear least-squares fitting of the data. Although increased flow resulted in smaller heating rates (due to increased heat transport out of the aneurysm by flowing saline), heating was nevertheless sufficient for coagulation even at the largest flow rate tested as shown in Fig. 5.

Coagulation

The heating pulse sequence was activated with the flow rate set to 0.5 mL/s to simulate an unobstructed embolization procedure. The temperature was allowed to rise unperturbed for $\sim 15\text{ s}$ to exceed the $60\text{ }^{\circ}\text{C}$ needed for coagulation. When the temperature reached $\sim 80\text{ }^{\circ}\text{C}$, 6 cm^3 of egg white was injected into the catheter. Since the egg white was initially at room temperature, its injection caused a temporary drop in temperature, so the temperature was allowed to recover back above $60\text{ }^{\circ}\text{C}$ prior to injecting the remaining 3 cm^3 of egg white (left panel of Fig. 6). In total, 9 cm^3 of egg white was injected into the catheter to ensure that the resulting coagulum would fill up a significant portion of the aneurysm in order to facilitate visualization. This quantity of injected protein solution also dictated the $\sim 2\text{ min}$ total heating time to ensure full coagulation. The resulting coagulum, shown in the right

panel of Fig. 6, was densely packed around the heating wire with no coagulum present in the adjoining tubes indicating good adhesion to the aneurysm walls.

Real-time monitoring of the coagulation

The egg white magnetic relaxation and tissue properties change progressively as a result of the coagulation and thus provide a means of tracking the state of the coagulation. Because magnetization transfer (MT) imaging (15) provides the greatest contrast between coagulated and uncoagulated albumin proteins it was used to monitor the progression of the coagulation. The pre- and post-coagulation MT images (Fig. 7) illustrate the feasibility of intraprocedural monitoring of the coagulation process.

Discussion

In this study, MR-mediated RF ablation (16), a recently introduced method, that harnesses the energy generated by the scanner for use in RF ablation was adopted for heating a coagulable material (a protein solution) to embolize a vascular defect. The method does not require an external RF power generator or electrical connections to any external system, avoiding the need for a grounding pad to complete the electrical path and eliminating the possibility of accidental skin burns (17,18,19) due to poor contact of the grounding pad.(20) The RF energy generated by the MR scanner is focused using a passive conductive device (*e.g.*, a wire) to obtain localized heating. Unlike this study, previous studies (21,22) of RF induced heating relied on custom RF coils and necessitated the use of ionizing imaging modalities for treatment monitoring.

Minimally-invasive vascular embolization methods reduce recovery times and yield better clinical outcomes compared to surgical clipping (8,9). Nevertheless, given their use of foreign agents or materials, current embolization methods are susceptible to an immune response as well as inflammation, which can, in some cases, be severe (23,24). In contrast, HSA is a non-thrombogenic and non-immunogenic protein naturally found in human blood plasma. These properties, along with a low temperature of coagulation (50–60 °C) render it attractive for in vivo use.

In this paper the hypothesis that MR RF heating can be used to successfully occlude an aneurysm by coagulation of an injected protein solution was tested using egg white as an inexpensive substitute for HSA. The findings (Figs. 6 and 7) support this hypothesis.

Temperatures approaching 100 °C were achieved in seconds despite a flow of cooler, room temperature, saline. Since protein solutions begin to coagulate at temperatures on the order of 60 °C, the temperatures achieved in these experiments are more than sufficient to coagulate the protein on contact, as demonstrated in Fig. 6.

The equilibrium temperature reached depended on the sequence parameters (pulse amplitude, duty-cycle, flip angle) as well as the saline flow rate. However, following coagulation, increasing the flow rate had minimal impact on the temperature within the aneurysm, indicating the effectiveness of the coagulum at halting the flow inside the aneurysm.

Alternative embolization methods occasionally rely on balloon-assisted techniques to facilitate coagulation by restricting blood flow past or into the aneurysm, albeit at the cost of undesirable arterial blood flow reduction (25). Because inadequate blood perfusion can cause irreversible tissue damage in minutes (26) procedure durations must strictly limited to avoid the damage caused by cerebral hypoperfusion. Additionally, in some cases (12) the tortuosity of brain vessels may prohibit the use of balloons altogether. In contrast, the proposed method allows coagulation in narrow neck aneurysms under normal flow and could therefore mitigate the risk of cerebral hypoperfusion and the consequent neurological damage.

Coagulable materials offer improved packing of the aneurysm and do not depend on the development of occlusive thrombus, and may therefore reduce the rate of recanalization (27,28). Unlike Onyx or more recent polyurethane based foams that solidify with heating (7), the proposed method offers the same packing benefits but without the use of potentially immunogenic materials and, importantly, the treatment can be monitored with MRI, a non-ionizing imaging modality. Real-time MR guidance is a rapidly developing field and has been shown to yield improved localization over fluoroscopy (29). In MRC, catheter guidance is facilitated by the visual artifact induced by the increased local B_1 field caused by the heating wire.

A key concern in aneurysm repair is the increased risk of thromboembolic complications following treatment. As shown in Fig. 6, the albumin coagulated under typical aneurysmal flow conditions adhered to the smooth glass aneurysm walls long after the experiment was terminated and did not flow downstream, reducing the risk of stroke in a clinical setting. It is likely that coagulated albumin will adhere at least as well to aneurysm walls. Nevertheless, an intraluminal filter or balloon can be used to ensure retention of the introduced albumin inside the aneurysm thereby mitigating any embolization risk.

This study has a number of limitations. The glass aneurysm phantom is an idealization of the shape of an actual small-neck aneurysm. Glass lacks the surface, mechanical, chemical and electrical properties of real aneurysms. Adherence of the coagulum to the aneurysmal wall in vivo is likely to be better than to glass. However, the compliance and continual movement of arterial and aneurysmal walls in vivo could lead to loss of adherence. The electrical behavior of the wire is likely to be different when immersed in an environment with electrical conductivity to the surrounding tissue, rather than in the electrically insulating phantom. The phantom is a large scale model of the geometry that might be encountered in a real aneurysm. The vessel diameter and the catheter size required in an actual MRC procedure will be much smaller which may require the use of alternative temperature monitoring methods (30,31).

The heating curves often display instability as the asymptotic temperature is reached. This is likely due to unstable flow (e.g., convection and turbulence) at the wire tip, boiling or bubble formation, thermal or electrochemical corrosion of the wire tip surface, cycles of buildup and breakthrough of an insulating layer, and similar effects. These can lead to a foamy or flocculent coagulum which is porous, less coherent and prone to disintegration. Bubble formation and heating of adjacent tissues are critical safety concerns. Based on the

simulation results of Fig. 3 and other RF heating studies conducted on ex vivo liver tissue (16) the heating of adjacent tissues is likely to be minimal. Nevertheless, additional research will be needed to conclusively address these issues.

Subsequent investigations must include varying the protein concentration of the solution. A higher concentration will require less energy to coagulate because less solvent (water) need be heated to the coagulation temperature, and the resulting coagulum will have a higher Young's modulus (because the coagulum will be less diluted with water). However, a higher concentration results in a more viscous solution, making injection through a long narrow lumen difficult. Studies using HSA, and studies in animal models of aneurysm will need to be conducted.

It is tempting to envision using an interventional guidewire for the conductive wire in MR coagulation. The wire used in this proof-of-concept study was a standard solid copper wire which exhibits good RF electrical conductivity and is completely nonmagnetic. Stainless steel and Nitinol alloys commonly used in guidewires have much lower electrical conductivity compared to silver or copper, and tend to have high magnetic susceptibility which introduces image artifacts. Copper and its alloys have high electrical conductivity and magnetic susceptibilities close to that of water and tissue and may have the requisite mechanical properties necessary for guidewires. A study of the suitability of different interventional guidewires for MRC is beyond the scope of this paper and will be examined in future work.

In conclusion this study has demonstrated the potential of magnetic resonance coagulation for embolizing a vascular defect in a phantom by coagulating a protein solution delivered by catheter using MRI scanner-induced RF heating of an intracatheter wire.

Acknowledgments

We thank R. Gilberto González for help with concept development. Clip art from Servier Medical Art image bank (www.servier.com) was used in Figure 1.

Grant support: This research was supported by the Center for the Integration of Medicine and Innovative Technology (CIMIT) grant 13-1180/grant W81XWH-09-2-001 from U.S. Army Medical Research and Materiel Command (USAMRMC) and NIH grants RR023009 and P41RR14075.

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Fig. 1. Magnetic resonance coagulation (MRC) concept. (a) MRI scanner magnet assembly. (b) Body RF coil. (c) Patient table. (d) Long wire RF pickup antenna magnetically coupled to body coil; RF pickup may be optionally enhanced with tuned RF pickup loop (e) connected to free end of wire. (f) Protein solution and (g) saline for flushing sharing one lumen of catheter (h) inserted percutaneously into femoral aorta. (i) Fiber optic temperature sensor sharing second lumen of catheter with wire. (j) Cerebral aneurysm.

Fig. 2.

Axial, coronal and sagittal maps of the local SAR on a log scale for the simulated standalone wire (a) and coil (b) configurations of the proposed device. Although both configurations showed increases in the SAR, the SAR for the coil configuration was ~40 fold greater.

Fig. 3. Local SAR as a function of position for the coil configuration of the device. Note that despite the large SAR attained in proximity to the wire, the heating is highly localized and therefore unlikely to adversely impact neighboring tissues.

Fig. 4.

Temperature measured while the heating pulse sequence was activated (a). The temperature rose exponentially until the pulse sequence was turned off (b) and then decayed exponentially as well. The high temperatures achieved were significantly above the ~60 °C needed for protein coagulation.

Fig. 5.

Heating rate as a function of the saline flow rate. Increased flow rate caused a faster heat exchange between the inflowing room temperature saline and the saline in the aneurysm resulting in a lower rate of temperature increase within the aneurysm.

Fig. 6.

Temperature profile for a coagulation experiment under flow (left). The room temperature egg white injected when the temperature reached $\sim 75^{\circ}\text{C}$ (a) caused a temporary drop in the measured temperature (b). A second egg white bolus was injected after allowing the temperature to recover back to its previous value (c). The heating pulse sequence was turned off after 80 seconds and the sample allowed to cool (d). The resulting coagulum in the aneurysm (right panel) demonstrates that despite the significant flow and smoothness of the glass walls the coagulated albumin nevertheless adhered to the aneurysm.

Fig. 7. Magnetization transfer (MT) images acquired before (a) and after (b) a coagulation. The hyperintense regions (white arrow) in the difference image (c) indicate the location and morphology of the coagulum. MT MRI enables intraprocedural monitoring of the coagulation progress.