Development of an Intravascular Heating Source Using an MR Imaging Guidewire

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Purpose: To develop a novel endovascular heating source using a magnetic resonance (MR) imaging guidewire (MRIG) to deliver controlled microwave energy into the target vessel for thermal enhancement of vascular gene transfection.

Materials and Methods: A 0.032-inch MRIG was connected to a 2.45-GHz microwave generator. We 1) calculated the microwave power loss along the MRIG, 2) simulated the power distribution around the MRIG, 3) measured the temperature increase vs. input power with the MRIG, and 4) evaluated the thermal effect on the balloon-compressed/microwave-heated aorta of six living rabbits. In addition, during balloon inflation, we also simultaneously generated high-resolution MR images of the aortic wall.

Results: The power loss was calculated to be 3.9 dB along the MRIG. The simulation-predicted power distribution pattern was cylindrically symmetric, analogous to the geometry of vessels. Under balloon compression, the vessel wall could be locally heated at 41°C with no thermal damage apparent on histology.

Conclusion: This study demonstrates the possibility of using the MRIG as a multifunctional device, not only as a receiver antenna to generate intravascular high-resolution MR images of atherosclerotic plaques and as a conventional guidewire to guide endovascular interventions during MR imaging, but also as a potential intravascular heating source to produce local heat for thermal enhancement of vascular gene transfection.

based vascular gene transfection. To this end, we 1) calculated microwave power loss along the MRIG to determine the adequate microwave power input, 2) simulated microwave power distribution around the active imaging/heating region of the MRIG (centered at the conjunction of the inner and outer conductors of the MRIG) to determine the pattern of power distribution at the target, 3) measured the temperature increase vs. microwave input power with the MRIG to establish a microwave heating protocol, and 4) measured the thermal effect on the balloon-compressed/microwave-heated target vessel wall correlated with histology to ensure the safety of the MRIG as an intravascular heating source in vivo.

MATERIALS AND METHODS

Devices

We used a clinical size, 0.032-inch diameter MRIG that has been successfully used to generate intravascular high-resolution MR images of the atherosclerotic vessel wall and for guidance of vascular interventions during MR imaging (7,8). The MRIG was a loopless antenna that consisted of an 8-cm long conducting wire that was an extended inner conductor from a 25-inch long coaxial cable. The inner conductor of the MRIG consisted of a gold-plated nitinol wire with a radius of 0.1 mm. The dielectric was polytetrafluoroethylene $\varepsilon_r = 2$ and had a radius of 0.33 mm. The outer conductor consisted of nitinol ($\varepsilon = 1 \times 10^8$ S/m) with a radius of 0.42 mm. The MRIG was connected either to an external 2.45-GHz microwave generator (Opthos Instruments, Rockville, MD) for heating, or connected to a MR scanner for imaging.

Evaluation of Microwave Power Loss along the MRIG

Before using the MRIG to deliver microwave energy into a target vessel, the first concern was power losses along the MRIG because the diameter of MRIG is small and its electrical resistance is relatively high. We calculated microwave power loss along the MRIG by modeling a lossy transmission line with distribution parameters. The formula for the attenuation factor is given in Ulaby (10).

Evaluation of Microwave Power Distribution around the MRIG

The power distribution was calculated from the root-mean-square (RMS) electric field (E) distribution (11). The electric field distribution was calculated by assuming a discretized balanced cosine current on the MRIG and integrating the electric field from each current element, as described by Simon et al (12). The localized power distribution of the MRIG was calculated for tissue electrical conductivity ($\sigma = 2.5$ S/m), and tissue dielectric constant ($\varepsilon_r = 55$), which are representative values for human tissue at 2.45 GHz (13).

In order to characterize the distribution of the heating power along the MRIG, we defined a half-power heating length as the length over which half of the entire emission power is deposited.

Evaluation of Temperature Increase Vs. Input Microwave Power With the MRIG

To investigate the feasibility of using a MRIG to deliver microwave power to the vessel and establish a heating protocol for the enhancement of vascular gene transfection, we tested the temperature increase vs. input microwave power in vivo. We used one New Zealand white rabbit, approximately 5 kg in weight, with an aorta approximately 6 mm in diameter. All animals were treated according to the “Principles of Laboratory Animal Care” of the National Society for Medical Research and the “Guide for the Care and Use of Laboratory Animals” (NIH Publication No. 80-23, revised 1985). The Animal Care and Use Committee at our institution approved the experimental protocol.

Through a laparotomy, we positioned both a 5-F balloon catheter with a balloon portion 6 mm in diameter and 2 cm in length (Boston Scientific, Boston, MA), and a 0.6-mm fiber-optic temperature sensor (FISO Technologies, Ste-Foy, Quebec, Canada) into the lower abdominal aorta at a level 2 cm below the renal arteries (Fig. 1). The sensor portion of the fiber-optic probe was attached side-by-side onto the balloon. Thus, inflation of the balloon with $37^\circ$C saline propelled the fiber-optic probe against the arterial wall. We then placed the MRIG into the balloon catheter so that the active imaging/heating region of the MRIG was positioned in the center of the balloon. The MRIG was connected to an
external 2.45-GHz microwave generator, and the fiber-optic sensor was connected to a digital thermometer (FISO Technologies, Canada). Subsequently, we operated the microwave generator, at different power levels from 2 to 24 watts (W), to deliver thermal energy to the MRIG. The steady-state temperature increases after several seconds were recorded using a digital thermometer. We repeated the heating experiments in triplicate. The results were then converted to a curve of temperature increases vs. input microwave powers.

**Evaluation of the Thermal Effect on a Target Vessel Wall With the MRIG**

In our experimental setting, the target vessel wall was locally heated during mechanical compression by the inflated balloon. The mechanical compression would facilitate the microwave heating-induced thermal damage on the balloon-stressed target vessel wall. We evaluated, in vivo, the potential thermal damage from microwave heating/balloon compression by examining the histological differences before and after microwave heating at the target in living animals. In addition, during the in vivo experiments we also tested the possibility of simultaneously generating high-resolution MR images of the target vessels using the same heat-delivery MRIG with the inflated balloon in the same target vessel.

We used six New Zealand white rabbits, approximately 5 kg in weight. With the same surgical method mentioned above, we positioned the 0.032-inch MRIG, along with the 5-F balloon and the 0.6-mm fiber-optic temperature sensor, into the aorta. Then, while inflating the balloon with saline, we heated the targeted aorta with the MRIG for 20 minutes by operating the microwave generator at 20–25 W, which resulted in a temperature increase to 41°C at the target aortic wall.

MR imaging was performed in a 1.5-Tesla MR scanner (GE Medical System, Milwaukee, WI). We acquired high-resolution axial and sagittal images with two pulse sequences: 1) T1-weighted imaging with a spin-echo (SE) sequence of 500/11 msec TR/TE, 4- and 8-cm field of view (FOV), and 256 × 256 matrix; and 2) T2-weighted imaging with a fast SE (FSE) sequence of 2000/100 msec TR/TE, 15.6-kHz bandwidth, 4- and 8-cm FOV, and 256 × 256 matrix. During MR imaging, the MRIG was connected to the MR imaging preamplifier and operated in the receive-only mode.

Immediately after the heating, we harvested the heat-targeted aorta and non-heated aorta (as a control) for histological examination. The specimens were embedded in paraffin, cut into 5-μm slices on a cross-sectional view, and stained with Masson Trichrome stain.

**RESULTS**

The calculated microwave power loss along the MRIG was 6.21 dB/m. Because the MRIG was 25 inches (0.63 m) in length, the power loss along the MRIG was 3.9 dB.
The pattern of simulated power distribution was cylindrically symmetric, analogous to the geometry of vessels, and was localized to the target vessel area (Fig. 2). The calculated half-power heating length was 1.7 cm at the microwave frequency, which is close to the 2-cm length of the 5-F catheter balloon. The measurements of temperature increase vs. input microwave power are shown in Figure 3. Although some microwave energy was lost through the MRIG during microwave energy transfer, we could achieve the desired temperature of 41°C at the target vessel wall in vivo.

During MR imaging, we were able to monitor the inflation/deflation of the balloon. On T1- and T2-weighted MR images, we could visualize the balloon-inflated target aortic wall at a resolution of 157 μm (Fig. 4).

Clinically, all rabbits survived during the experiments. Histopathologically, in both gross and microscopic examinations, there were no findings of thermal damage, such as vacuolization, coagulation, or carbonization (Fig. 5). We did not find any evidence of possible mechanical injury to the vessel wall due to the insertion of the MRIG.

**DISCUSSION**

The present study demonstrates the potential of using the MRIG as a multifunctional device for vascular gene therapy, not only as a receiver antenna to generate intravascular high-resolution MR imaging of the target vessel wall and as a conventional guidewire to guide endovascular interventions (7,8), but also as an intravascular local heating source to deliver controlled therapeutic heat into target vessels. The advantages of using the MRIG as an intravascular local heating source include: 1) the thin MRIG can be easily positioned, via any endovascular interventional device, into a target vessel to generate local and axisymmetric heating at the target; 2) the MRIG produces a power distribution that is cylindrically symmetric and analogous to the geometry of vessels and localized to the target vessel area; and 3) the MRIG can be used as a multifunctional device to simultaneously generate imaging and heating at the target vessels, and thermal power input through the MRIG can be easily controlled at the external mi-
crowave generator. In addition, it should be greatly beneficial to combine MR thermal mapping techniques with our current design, to monitor and control the location, distribution, and extent of the delivered therapeutic heat at the target vessels during MR imaging.

In our experimental setup, the resistance of the MRIG was relatively high because the outer conductor of the 0.032-inch MRIG is made of nitinol ($\sigma = 10^6$ S/m). There is about 60% input power lost along the MRIG, and 40% input power is used to heat the target. When inputting 24 W of power, the heat strength at the active imaging/heating region of the MRIG is 5.65 W/cm, and the average power lost along the remaining region of the MRIG is 0.23 W/cm, which is much less than that at the active imaging/heating region, and, therefore, there is no significant temperature increase along the MRIG. To decrease the resistance of the MRIG, we may coat the inner surface of the outer conductor (tube) with copper ($\sigma = 5.8 \times 10^7$ S/m) or silver ($\sigma = 6.2 \times 10^7$ S/m), and, thereby, its power loss will be decreased from 6.21 dB/m to 2.65 dB/m. Thus, along the 25-inch long MRIG we used, the total power loss would decrease to 1.7 dB. The same coating method should enable the construction of a 0.014-inch MRIG to fit the local heating requirement in the coronary artery.

The results of the present study showed that the localized microwave power distribution radiated from the active imaging/heating region of the MRIG is cylindrically symmetric, analogous to the geometry of vessels, and covers the heated area of the target. This simulated power distribution indicates that 2.45 GHz microwave power is an ideal heating source, which can be delivered by the MRIG to locally heat the target vessel rather than a large volume of the body. Theoretically, the higher the microwave frequency, the more concentrated the microwave power distribution and the smaller the half-power heating length. However, the surface electrical resistance of the MRIG is proportional to the square root of the working frequency. The higher the frequency, the higher the power loss along the MRIG will be. Thus, it is necessary to balance the benefits of local heating and the electrical resistance of the MRIG for the power transmission. In principle, we could use low-frequency microwave power if it satisfies the demands of intravascular local heating. In our study, operating the microwave generator at 2.45 GHz ($\sigma = 2.5$ S/m, $\varepsilon_r = 55$) resulted in the 1.7-cm half-power heating length deposited in the surrounding media, which is close to the 2-cm length of the 5-F catheter balloon. If we heat the target vessel using a one-GHz generator ($\sigma = 1.5$ S/m, $\varepsilon_r = 60$) (13), we should achieve a half-power heating length of 2.8 cm. For our purposes of intravascular local heating with a 2-cm long balloon, the 2.45-GHz microwave generator is an adequate choice with an acceptable power loss.

This study shows that it is possible to simultaneously generate high-resolution MR imaging of a target vessel wall during the inflation of a gene delivery balloon for vascular gene transfer, which should enable simultaneous monitoring and guiding of catheter-based vascular gene delivery and distribution (9). Our histologic results have proven that in the current experimental setting, it is safe to create local heating in target vessels using the 0.032-inch MRIG to deliver 2.45 GHz microwave thermal energy. Although our in vivo studies show no abnormal manifestations in either clinical or histologic validations, we need to establish a therapeutic heating/thermal safety guideline to ensure that the MR imaging/microwave heating system can be used safely and efficiently for MR imaging-based vascular gene therapy.

In addition, we need to design a “switch” or duplexer between the two components of MR imaging and microwave heating, to enable simultaneous generation of high-resolution MR imaging, MR thermal mapping, and local heating of the gene-targeted vessel wall during the same MR examination.

In conclusion, the present study demonstrates the possibility of using the MRIG as a multifunctional device, not only as a receiver antenna to generate intravascular high-resolution MR imaging of atherosclerotic plaques of the vessel wall and as a conventional guidewire to guide endovascular interventions during MR imaging, but also as an intravascular heating source to produce local heat for thermal enhancement of vascular gene transfection. This study has established the groundwork to further refine a MR imaging/microwave heating system for the enhancement of vascular gene therapy, and for the management of cardiovascular atherosclerotic diseases using intravascular MR imaging-based vascular gene therapy.

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REFERENCES