Development of an Intravascular MR-imaging/RF-Heating/Temperature-Monitoring System for Thermal Enhancement of Vascular Gene Therapy

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Introduction:

Previous studies have confirmed the possibility of using an intravascular MR imaging-guidewire (MRIG) as a heating source to enhance vascular gene transfection/expression [1,2]. In clinical practice, we need a method to monitor and control the contribution and level of local heating at the target vessels. This motivated us to develop a novel intravascular system that can perform MR imaging, radiofrequncy (RF) heating, and MR temperature monitoring simultaneously in an MR scanner.

Materials and Methods:

Figure 1 presents the design of the intravascular MR-imaging/RF-heating system. The MRIG was placed within the guidewire channel of a gene delivery balloon catheter and connected to the common port of a custom-made filter box or duplexer. The filter box was implemented with (i) a low pass filter (cut-off frequency, f_{co}, 90MHz) that was connected to a 1.5 T MR scanner (GE Medical Systems, Milwaukee, WI) for MR imaging/thermal mapping of the target vessels; and (ii) a high pass filter (cut-off frequency, f_{co}, 150MHz) that was connected to an external RF generator for simultaneously delivering external RF heat to the target vessels via the MRIG. The optimum RF heating frequency was determined by mathematical simulation of RF power loss along the MRIG and RF power distribution deposited in the target tissue at different frequencies. The MR thermal mapping was obtained by using a proton resonance frequency (PRF) method. To test the functionality of the MR/RF system in vitro, we placed the MRIG in the center of a gel-made phantom and connected it to an external 180-MHz RF generator through the filter box. A 3-inch surface coil and MRIG were used for imaging/mapping. The temperature was increased by inputting 6-watt RF power for six minutes and cooled down by turning off the generator. MR thermal mapping was obtained with consecutive images and was found to be comparable to the simulation results of the power distribution.

To validate, in vivo, the feasibility of the intravascular MR/RF system for simultaneous heating and thermal mapping, four New Zealand white rabbits with aortas approximately 5 mm in diameter were used. Through a laparotomy, we positioned both a 5F balloon catheter with the 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. The sensitive portion of the fiber-optic sensor was attached side-by-side onto the balloon. Thus, inflation of the balloon with 37^{0}C saline propelled the fiber-optic sensor against the arterial wall. Then, we 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 intravascular MR-imaging/RF-heating system was set using the procedure described above for the in vitro study. MR thermal maps were obtained using multiphase fast GRE with fat suppression, 50-ms TR, 30 flip angle, 25-cm FOV, 128x128 matrix, 5-mm slice thickness, 32-kHz bandwidth, and 2 NEX, in which 9 ms of TE with a high SNR was pre-selected by varying TE from 5 ms to 20 ms. Subsequently, the temperature curve was created by placing a 3x1 mask (0.6mmx0.2mm) along the fiber-optic sensor on the series of MR thermal mapping images, and the thermal mapping curve was compared with the curve from actual temperature measurements recorded by the thermometer with the fiber-optic sensor.

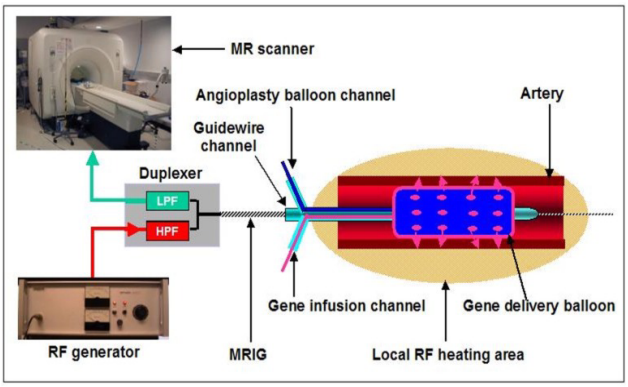


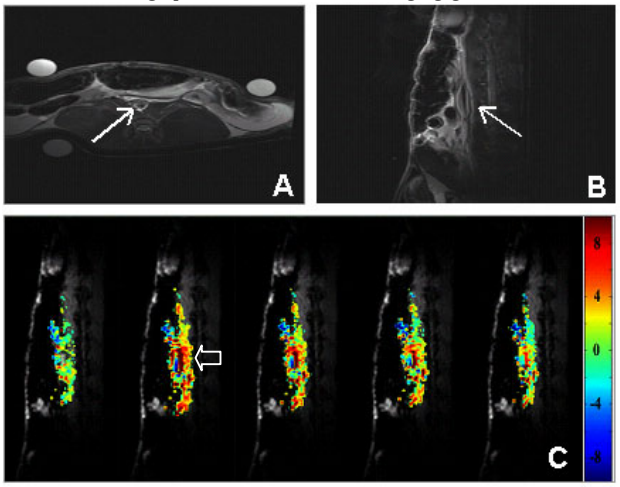
Fig. 1. Design of the intravascular MR-imaging/RF-heating system for thermal enhancement of vascular gene transfer. LPF=low pass filter, HPF= high pass filter. MRIG=MR imaging-guidewire.

Results:

The in vitro study showed that the MR/RF system could simultaneously produce RF heating and MR imaging/MR thermal mapping using the same MRIG. Figure 2 shows the results from the in vivo studies. The target aortic wall was heated up to 44^{o}C from a baseline temperature of 37^{o}C by operating the RF generator at 4 to 5 watts for about 4 minutes, and thermal mapping was obtained and registered to the anatomical MR image of the aorta. The temperature curve was obtained at the fiber-optic sensor location from the series of MR thermal maps using a 3x1 mask, thus matching the sensing area of the independent temperature sensor. Figure 2D shows that the estimated temporal curve is comparable to the actual temperature curve measured using the Fiso thermometer with a standard deviation error of 1.2^{0}C.

Conclusion:

We demonstrate an MR-imaging/RF-heating system that provides two simultaneous functions: (a) creating local RF heat at the target vessel wall to enhance vascular gene transfer; and (b) generating MR thermometry to simultaneously monitor RF heating at the target vessels in vivo. This technique presents a potential tool for intravascular MR/RF-based vascular gene therapy.



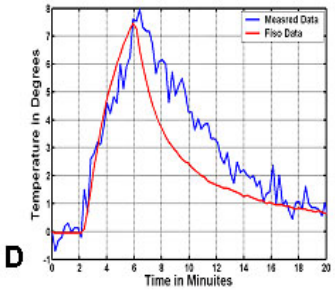


Fig. 2: Axial (A) and sagittal (B) MR localization images. The arrows in (A) and (B) indicate the location of the fiber-optic sensor and the balloon. (C) A series of MR thermal mapping were overlapped on sagittal MR images, showing that the peak heating (the dark red color, arrow) at the target aorta is achieved with image frame 2. (D) The temporal temperature curve obtained from MR thermal mapping (blue), which is comparable to the actual temperature recorded with sensor (red curve).

References :

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2. Du X, et al. Radiology 2004 (Accepted)

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