MR guided intramyocardial injection of contrast medium: tracing delivery to infarct borders

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Introduction

Recently, molecular interventions, targeted directly at the myocardium in order to initialize angiogenesis or to increase the amount of contractile myocytes in patients with ischemic heart disease, have been introduced. In contrast to systemic administration, local delivery allows for accomplishing a high concentration while minimizing systemic side-effects. In order to provide a minimally invasive technique, intramyocardial injection has been attempted with catheter-based approaches. In the majority of such studies, fluoroscopy was employed. The drawback of this approach is the inability to directly delineate the myocardium. In contrast, MRI provides for the delineation of myocardium and ischemically injured regions.

Accordingly, the purpose of this study was to assess the feasibility of percutaneous MR-guided intramyocardial injection of Gd-DTPA-BMA in normal and infarcted hearts. In normal hearts, T1 values and the size of the enhanced region were measured for different contrast agent concentrations. Based on these measurements, the more qualified concentration was applied to animals with myocardial infarction (MI), in order to evaluate the feasibility of targeting injections at the border of the infarct and to visualize the distribution of injected contrast medium with regard to the infarct.

Methods

Two groups of 6 pigs (45 kg) were included into the study. Experiments were performed using a 1.5 T closed bore system (ACS NT, Philips, Best, The Netherlands). For real-time image-guidance, a radial steady-state free-precession sequence with TR 2.5 ms, TE 1.2 ms, 45° flip angle, 80 radials, 8 mm slice thickness, matrix 128x128, FOV 320x320 mm², and a frame rate of 15/sec, was applied. A 3 mm long stainless steal needle, mounted on a 5 F catheter, was repeatedly guided from a carotid artery sheath into the left ventricle and inserted into the myocardium for injections at different locations. 2 ml of Gd-DTPA-BMA (Omniscan, Amersham Bucheler, Braunschweig, Germany) was injected at concentrations of 0.05 and 0.1 mmol/ml. Local changes of T1 values and the size of the enhanced region were measured 3, 15, and 30 min after injection, using the Look-Locker sequence.

In the second group, reperfused myocardial infarction was induced by occluding the left anterior coronary artery for 45 minutes, with a balloon catheter. In order to delineate the infarcted myocardium, SHU555A (Schering, Berlin, Germany)—a small particle of iron oxide (SPIO)—was injected intravenously, at a dose of 1.4 ml. T1 values of ischemically injured and remote myocardium were measured with the Look-Locker technique. As soon as sufficient contrast between both regions was achieved, a 0.1 mmol/ml Gd-DTPA-BMA solution, mixed with blue dye for tissue staining, was injected intramyocardially at two regions on the border of the infarct. After the interventions were finished, the hearts were excised and stained with 2,3,5-triphenyltetrazolium chloride (TTC), to delineate the infarct.

Results

In all animals, the catheter was clearly visible and could be directed into the left ventricle and inserted into the myocardium (Fig 1). Injections of Gd-DTPA-BMA and distribution within the myocardium at the injection site caused a local increase of signal intensity on real-time images (Fig 1). We did not observe side effects of intramyocardial injection of the contrast medium, such as changes in the heart rate or arrhythmia. The Lock-Locker sequence showed a decrease of the T1 value from 750 ms to 458 ms, after injection of 0.05 mmol/ml Gd-DTPA-BMA and 242 ms after injection of 0.1 mmol/ml Gd-DTPA-BMA. The injection sites remained visible as regions of higher signal intensity, compared to remote myocardium, over the course of the observation period. However, T1 values at the injection sites, as well as the size of the hyperenhanced regions, slowly increased, most probably due to the diffusion of the contrast medium solution within the tissue.

In all 6 animals with MI, injection of SHU 555A caused a significant decrease of the T1 value of the infarct (778 ± 63 ms before, and 641 ± 67 ms 2 h after injection of SHU 555A). The contrast between the infarct and remote myocardium was sufficient for delineating the infarct on real-time images (T1 remote myocardium 2 h after injection: 702 ± 19 ms). In all 7 animals, the catheter could be directed into the border region of the infarct. Two injections were performed at different locations. Injection sites, infarct region, and remote myocardium, could clearly be differentiated over the course of the observation period.

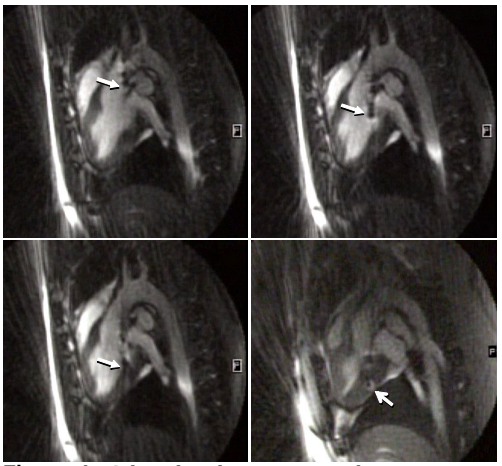

Figure 1: Selected real-time images, long axis view. The catheter is advanced into the left ventricle (top row) and then inserted into the myocardium (bottom, left, arrow). During injection of Gd-DTPA-BMA solution, there is a growing area of high signal intensity within the myocardium surrounding the needle tip (bottom, right, arrow).

Discussion

The technique described here may be used for the minimally invasive delivery of substances, such as gene-constructs, to the myocardium. If a high molecular contrast medium is intravenously injected, the infarct can stably be delineated over the course of the intervention. By using extracellular contrast medium as tracer, intramyocardial injection sites remain visible for a sufficient long period of time, so that repeated injections into the same region with consecutive local overdosing during an intervention with multiple injections can be avoided.