Development of a catheter for MRI-guided intramyocardial injection

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Introduction

Application of substances targeted at the myocardium in order to initialize angioneogenesis, or to increase the amount of contractile myocytes or contractility of resident myocytes, is already being performed for patients suffering from ischemic heart disease. The substances are directly injected into the myocardium to reach high local concentrations and minimize systemic side-effects. Up to now these injections were performed during bypass-surgery. However, a catheter-based approach could make this new therapy available for a broader range of patients and would allow repeated interventions. MRI guidance is preferable over other imaging guiding techniques, since MRI provides differentiation between ischemically injured and remote myocardium and delineation of the catheter at the same time. However, for percutaneous intramyocardial injection a dedicated catheter is needed, which enables guidance into the left ventricle and provides for bending of the catheter tip inside the heart, in order to precisely reach the target areas. At the same time, perforation of the myocardium, with the potential sequel of pericardial tamponade must be avoided. With this in mind, the aim of this study was to develop a dedicated catheter for MRI-guided intramyocardial injection, and explore the potential for MR-guided intramyocardial injection in vitro and in vivo.

Methods

A coaxial catheter consisting of an inner needle catheter and an outer guiding catheter was developed and build. The inner needle catheter carries a short needle, consisting of non-ferromagnetic material (Figure 1). The outer guiding catheter can be bended from the outside by pulling a towing string (Figure 1). The needle catheter is completely covered by the outer catheter, when the system is directed into the left ventricle. When the target is reached, the needle catheter is pushed out of the guiding catheter and inserted into the myocardium. A lock-mechanism that unfolds as soon as the needle catheter is pushed out of the guiding catheter is integrated in the needle catheter, so that the needle can not be inserted deeper than 3 mm into the tissue.

The catheter was first tested in a simple phantom, consisting of a tube that represented the aorta and a pig heart. Real time imaging was performed using a radial steady-state free-precession sequence with a frame rate of 15/sec (TR 2.5 ms, TE 1.2 ms, 45° flip angle, 80 radials, 8 mm slice thickness, matrix 128 x 128, FOV 320 x 320 mm², sliding window reconstruction). The catheter was advanced into the heart, the tip bended and the needle inserted into the tissue. An improved catheter prototype was subsequently tested in vivo.

For this purpose, reperfused myocardial infarction was induced in 9 pigs, by occluding the left anterior coronary artery for 45 minutes using a balloon-catheter. Two hours after reperfusion MRI was started at a 1.5 T closed bore system (Intera, Philips, Best, The Netherlands), MS-325 (Vasovist, Schering, Berlin) a gadolinium-containing blood pool contrast medium was intravenously injected to delineate the infarct. An introducer sheath was placed in the right carotid artery. The catheter was advanced through the aorta into the left ventricle under real-time guidance and inserted into the myocardium at the border of the infarct. Next 2 ml of 0.4 mmol/ml Gd-DTPA-BMA (Omniscan) solution, mixed with blue dye for tissue staining, was injected intramyocardially. T1 values of the injection sites ischemically injured and remote myocardium were measured with the Look-Locker technique. After the interventions were finished, the hearts were excised and stained with 2,3,5-triphenyltetrazolium chloride (TTC), to delineate the infarct.

Results

The catheter was clearly visible on real time images in the phantom and in all animals (Figure 3), which made guiding the device into the heart and steering it into the target area possible . The catheter could be advanced into the hearts and inserted into two regions at the border of the infarct in all animals. Perforation of the myocardium did not occur in any of the animals. The injections could be differentiated from the infarct and from remote myocardium on real-time images. T1-values at the injection site (240±25ms), the infarct region (377±37ms), and the remote myocardium (645±28ms) were significantly different. Complications, such as cardiac arrest or haematoma did not occur. Postmortem analysis showed the blue tissue dye at the border of the infarct in all cases.

Discussion

The introduced catheter can be used for intramyocardial injection under MRI guidance. Perforation of the myocardium is prevented by the lock-mechanism. The interventionalist can actively steer the tip of the catheter into a preselected target area in the myocardium.

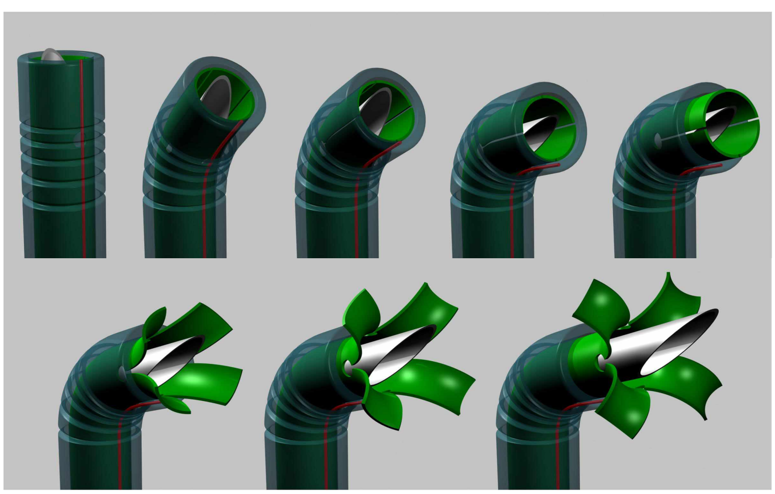

Figure 1: The catheter consists of an outer guiding catheter, which can be bend by pulling a towing string (red). The inner catheter contains a lock, which prevents insertion of the needle deeper than 3 mm.

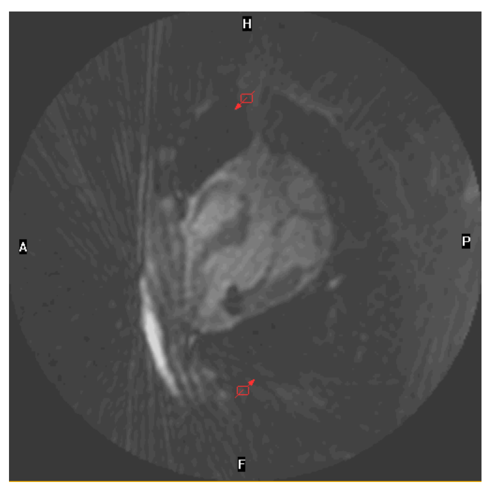

Figure 2: Selected real-time image. The bended catheter is visible. The needle tip generates a small susceptibility artifact, which allows for delineation of the needle tip