Visualization of a Passive Intra-Myocardial Needle with Off-Resonance Positive Contrast FLAPS Imaging for Regenerative Myocardial Therapy

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Introduction Magnetic resonance image-guided delivery of therapeutic agents for regenerative tissue repair may determine the overall efficacy of treatment. In interventional MRI, while active devices seem to be the method of choice, potential tissue heating and altered mechanical properties are also their well known limitations [1]. Alternatively, passive (conventional) interventional devices, to date, have been considered unattractive since these methods tend to use T_2*-weighting to visualize the interventional devices as large signal voids [2]. Recent off-resonance positive contrast imaging approaches may be used to improve the visualization of the devices by generating signal enhancements (positive contrast) surrounding the susceptibility-shifted interventional devices [3-5]. Among these methods, Fast Low Angle Positive contrast Steady-state free precession (FLAPS) imaging has been proposed for time-efficient acquisition of off-resonance positive contrast images [6]. The FLAPS technique takes advantage of the unique spectral response of the steady-state free precession (SSFP) signal to generate signal enhancement from off-resonant spins while suppressing signal from on-resonant spins at relatively small flip angles. In this work we investigated whether a passive, MR compatible needle used for intra-myocardial delivery of cell therapy can be visualized with FLAPS imaging in an *ex-vivo* heart and with a swine model *in vivo*.

Methods *Ex-vivo Tissue Studies:* A 7F steerable catheter typically used in conjunction with cell therapies (Boston Scientific, USA) fitted with a MR compatible, 22-gauge, 15 mm (full length) and 8 mm (exposed length) needle (Lufkin, E-Z-EM, USA) was advanced into the left ventricular (LV) chamber of a freshly excised lamb heart, placed in blood bath and scanned at 1.5T using FLAPS. Long and short axis images were acquired prior to and post insertion of the needle into the LV myocardium. The scan parameters were: field of view (FOV) = 30 x 30 cm^2; acquisition matrix = 192 x 192; T_R/T_E = 3.3/1.65 ms; flip angle (α) = 20^o (prior to myocardial insertion) and 10^o (post myocardial insertion); slice thickness (ST) = 5 mm; 4 averages; acquisition time (TA) = 2.8 s. Choice of flip angle was based on contrast characterization studies [4]. *In-vivo Swine Studies:* Pigs (n=2) were sedated, intubated, and the common femoral artery was accessed using a 5-F micro-puncture set and exchanged for an 8-F groin vascular sheath. Under x-ray guidance, the steerable catheter was advanced into the (i) descending aorta, (ii) ascending aorta, (iii) LV chamber and (iv) LV myocardium. In between each spatial advance of the injector (catheter/needle) unit, the animal was transferred to the MR scanner bed, ventilated and a breath-held scan using FLAPS was prescribed in cine mode. Scan parameters were: FOV = 29 x 38 cm^2; acquisition matrix = 144 x 192; T_R/T_E = 3.38/1.69 ms; spatial resolution = 1.8 x 1.8 mm^2; flip angle (α) = 20^o (prior to myocardial insertion) and 10^o (post myocardial insertion); slice thickness (ST) = 5 mm; 2 averages; acquisition time (TA) = 18 s; and 18 cardiac phases. *Data Analysis*: Respective contrast-to-noise ratios (CNR), computed as signal differences between signal-enhanced regions and the background normalized by the standard deviation of noise, were computed from the images acquired with the needle in the aorta, LV chamber, and following insertion into the heart muscle. The background signals used for CNR calculation in the aorta and LV chamber were taken as the signal values of surrounding blood in the vasculature and LV chamber not affected by the off-resonance induced by the needle, respectively. The background for the signal measurements in the muscle is computed from the surrounding heart muscle not affected by the needle. CNR values averaged from four different cine phases acquired at evenly spaced trigger times. Results are reported as mean $\pm$ standard error all measurements.

Results In the *ex-vivo* heart, the intra-myocardial injector with a short needle tip was easily visualized in the left ventricular chamber and muscle in long and short axis views (Fig. 1). The blood within the cardiac chambers, heart muscle, full length of the needle, tip, and the spatial location of the needle in relation to the myocardial surface were readily visible. In the *in-vivo* animal model, it was possible to visualize the intra-myocardial needle in the aorta (descending and ascending), in the chamber of the left ventricle, following insertion of the needle into the myocardium (Fig. 2). Results from CNR measurements: *Ex-vivo* studies: 24 $\pm$ 2.1 (pre-injection) and 18 $\pm$ 2.7 (post-injection); *In-vivo* studies: 22 $\pm$ 3.9 (aorta), 16 $\pm$ 4.1 (pre-insertion of the needle into the LV myocardium), and 13 $\pm$ 0.9 (post-insertion of the needle).

Discussion and Conclusion MRI-guided delivery of cells into the infarct zones within an organ may be valuable in regenerative medicine, since an accurate delivery of the therapeutic cells to the infarct zone may determine the prognosis of treatment. Guided by this goal, this work investigated whether the FLAPS technique can be used for the visualization of a passive intra-myocardial needle in an *ex-vivo* heart and *in-vivo* using a live pig. Based on the images and CNR analysis, results show that the passive intra-myocardial needle can be visualized ex- and in-*vivo* using the FLAPS method. These findings may be of interest to investigators seeking to accurately deliver therapeutic agents into the myocardium with passive injection devices fitted with a MR-compatible needle.

References [1] Ozturk C, Top MRI 2005;5:369**;** [2] Seppenwoolde JH, MRM 2003;50:784-790; [3] Cunningham CH, MRM 2005;53:999; [4] Stuber M, 13th ISMRM p. 2608; [5] Mani V, MRM 2006;55:126; [6] Dharmakumar R, Phys Med Biol. 2006;51:4201.

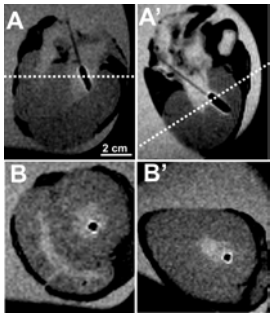

Fig. 1 Visualization of the intra-myocardial needle injection device in the cardiac chambers and heart muscle of an *ex-vivo* lamb heart placed in blood with FLAPS imaging at 1.5T. Long axis (A / A') and corresponding short axis (B / B'; both along the dotted lines) before (A / B) and after (A' / B') injection of the needle into heart muscle.

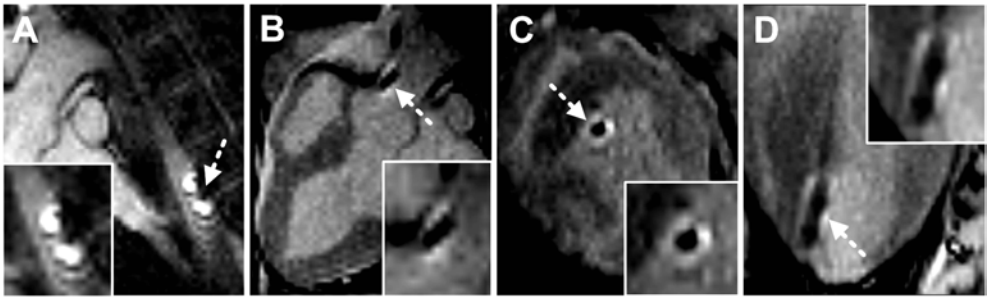

Fig. 2 Visualization of the intra-myocardial injection device in the descending (A) and ascending (B) aorta, LV cardiac chamber (C), and heart muscle (D) in a live pig using FLAPS imaging. Note that the needle is visualized as a signal enhancement (arrows) surrounding a signal void, consistent with the signal behavior of FLAPS surrounding susceptibility-shifted media [6]. Inserts in each image shows an enlarged view of the needle. Also note that the location of the needle within the chambers and the heart muscle can also be clearly visualized.