Comparison of scar morphology by 3D multi-contrast late enhancement MRI, 3D DW-MRI and histology in a pig model of chronic infarct

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Introduction: Following a myocardial infarct, surviving bundles can form abnormal pathways for cardiac electrical waves that can trigger lethal arrhythmias; therefore an accurate assessment of the scar extent and tissue remodeling during healing is very important [1]. Currently, the gold-standard for clinical evaluation of myocardial viability in patients with prior infarct is late-enhancement LE-MRI [2]. An improved method (named multi-contrast late enhancement, MCLE) has proved to be superior to conventional LE in characterizing infarct areas [3]. That said; it still can suffer from partial volume effects (due to slice thickness of 5-8mm) and noise inherent to motion which can hamper accurate quantification of peri-infarct zones. Another approach is to use non-contrast MR methods; for instance, it was shown [4] that apparent diffusion coefficient (ADC) from diffusion-weighted (DW)-MRI could be considered as an alternative non-contrast method for mapping chronic infarct in patients (though the method has limited applications due to low spatial resolution and motion artifacts). Other authors demonstrated in an ex vivo porcine model that DW-MRI is suitable to evaluate the characteristics of infarct at different points in the healing process, with exquisite spatial resolution [5]. To better understand the scar morphology associated with chronic infarct in a porcine model, here we use (in an ex vivo study) a newly developed 3D pulse sequence based on multi-contrast late enhancement (MCLE) and a non-contrast 3D DW sequence, and compare the results against histopathology. This comparison is an intermediate step that could be later used to relate the signal behaviour obtained ex vivo with that in vivo and to provide valuable insights into the MR characteristics of potential arrhythmogenic foci.

Materials and Methods: Myocardial infarction was created in 5 swine (20-25kg) by a 90-minute balloon occlusion of either the left anterior descending artery (LAD, n=3) or of the left circumflex artery (LCX, n=2), followed by reperfusion (confirmed by angiography). Flow restoration creates heterogeneous scar which could become the substrate for arrhythmic events. All animals were sacrificed at 6 weeks; a bolus of Gd-DTPA was injected 10-15min prior euthanasia. The hearts were quickly explanted, placed in a box filled with fluorinert and further imaged using a GE 1.5T Signa Excite MR scanner. The 3D MCLE sequence is based on an inversion-recovery (IR) pulse with a multi-contrast SSFP readout, together with the following acquisition parameters: FOV=16cm, 256x256 matrix (yielding a 0.63x0.63mm in-plane resolution), slice thickness of approximately 0.6mm. Other MR parameters include: TR=4.26ms, flip angle=45 and variable inversion times, TI. The hearts were then gently preserved in formalin for a few days and re-scanned using a 3D DW-MRI sequence (with voxels of similar size as in the MCLE study); other MR parameters were: TR=700ms, TE=35ms, NEX=1, seven directions for diffusion gradients and b-values of 500. We next derived apparent-diffusion coefficient ADC maps and assessed infarct heterogeneity, and further compared these heterogeneous areas with those obtained using the 3D MCLE. Based on signal thresholding, K-means clustering algorithms and expectation-maximization schemes we classified the tissue in MR images into three zones: healthy myocardium, infarct (dense scar), and peri-infarct. Furthermore, whole-mount histopathology was performed in select heart samples cut to coincide with the short-axis MRI views. Several stains (Masson Trichrome and Picrosirius Red) were used to study the extent of collagenous scars and the alteration of fiber architecture. These large slides were digitally at 10 microns scanned and analyzed as in [6].

Results: Figure 1 demonstrates the high-quality identification of scar areas by the 3D MCLE sequence, in one heart with LCX-infarct: images presented in (a-d) correspond to four different inversion times out of 16 used, (all through the same short axis-view), whereas images in (e-h) are from the apex towards the base of the heart (for the same TI). Images comparing 3D MCLE to 3D ADC map through the same short-axis view and corresponding segmentation results are shown in Figure 2 (a-d); note that ADC values in the regions of infarct are elevated compared to healthy myocardium (2c). The quantitative analysis was straightforward since the MR signal in the explanted hearts arises only from healthy myocardium and scars. Two different stained slides obtained from the histopathology were used to assess core infarct and border zones, as a gold standard. For instance, Masson Trichrome, MT (Fig 2e) demonstrates myocardial tissue remodeling in the scar area, dramatic alteration of fiber architecture, fibrosis (in green) completely replacing dead myocytes in the core of the infarct, and finger-like damaged bundles protruding into the healthy tissue. Picrosirius red, PR, shows the collagen deposition in the scar area (in red) and healthy myocardium (in dark yellow), as well as islands of viable myocytes at the peri-infarct zone (black arrow in Fig. 2f - inset). Both histology samples showed very good agreement with the extent of the scar as depicted by the increased MR signal in the MCLE sequence and increased ADC values in the dense scar, and intermediate signal intensities in the peri-infarct areas (also known as “grey zones”).

Conclusions: 3D MCLE identifies fine heterogeneity of infarct scar in a porcine heart model, ex vivo, and compares well the classification of pathology to that from ADC maps using DW-MRI. Future work will aim to compare MR signal behaviour in 3D MCLE ex vivo to 2D MCLE in vivo, to provide clearer pathological interpretation of “gray zones”.

References:

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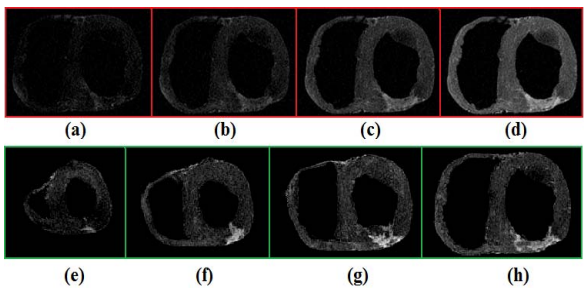

Figure.1 MR images of the chronic scar (bright areas) obtained in an LCX-infarct heart using the 3D MCLE sequence: (a-d) same slice with different inversion times; (e-h) same inversion time (TI=3.77ms) through different slices (from apex to base).

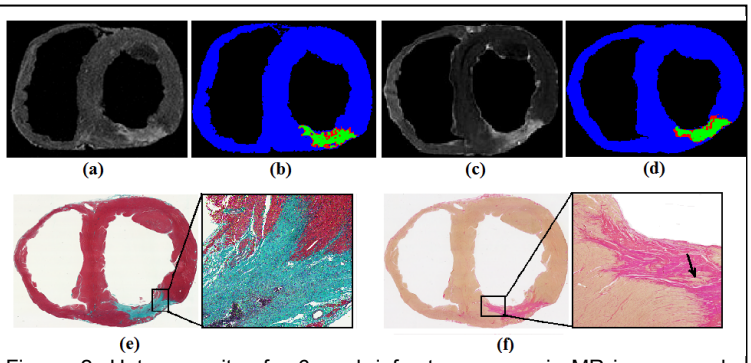

Figure. 2 Heterogeneity of a 6-week infarct scar seen in MR images and histology: (a) select MCLE image and (b) its corresponding segmentation (healthy myocardium in blue, core infarct in green and peri-infarct in red) as well as (c) select ADC image and (d) resulting segmentation (colors like in (b)); histological analysis: (e) MT stain and (f) PR stain (see text for details).