

High Resolution 3D 1H Contrast Enhanced MR Imaging in Reperfused Myocardial Infarction: A Histopathologic Correlation

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Introduction

Infarct size (IS, ratio of infarcted volume to muscle mass) defined by 3D contrast enhanced MRI is a known predictor of post-infarct complications¹. However, in vivo contrast enhanced 1H MRI with Gd-DTPA has been repeatedly shown to overestimate IS in comparison to the post mortem TTC gold standard¹⁻⁵. A possible explanation for this phenomenon is an increased volume of distribution for the extracellular contrast agent extending beyond the borders of myocardial infarction (MI). However, image resolution might have a considerable impact on the IS quantification and TTC stain may miss microinfarction. Therefore, we performed in vitro, high resolution contrast enhanced 1H MRI in reperfused MI and matched the MR images to post mortem Hematoxylin-Eosin stain (HE), to compare the spatial extent and patterns of MRI hyperenhancement with the incidence of myocyte necrosis in HE.

Methods

Experimental Protocol. The dataset was derived from eight myocardial slices, containing different degrees of infarcted tissue, generated by a 90 min. closed-chest coronary occlusion (ballon angioplasty). The reperfusion period was three days, then 20 cc of Gd-DTPA were injected 15 min before induction of cardiac arrest (KCl) and euthanasia. Two native slices were used for MRI and HE, four adjacent TTC slices were available for comparison with the high resolution MR images. The native slices were sutured to a template (a circle, being divided into 72 sections, each 5° wide). Two MRI visible markers (tubes containing blood, that was drawn after the contrast agent injection, image 1) were placed in the center of the template and on the 0° line. This setup was put on a 3 inch surface coil.

MRI. A 3D, T1 weighted spoiled GRASS sequence was used on a 1.5 T system. The 1H MR imaging parameters were: TR=17 msec, TE=4 msec, flip angle 60°, NEX=4, FOV 5 cm, matrix 512x512, slice thickness 0.5 mm, thus yielding a voxel size of 97µm x 97µm x 0.5 mm. Later, the slice thickness was stepwise increased from 0.5 to 5 mm, and pixel size from 97µm to 547µm, to evaluate the impact of resolution on IS assessment.

HE. After imaging, the slices (still fixed on the template) were cut in 19 pie-shaped transmural sections at various locations. These were further cut into a top, mid and bottom part. The template with the MR visible markers guaranteed that each section could be allocated to the MR image. Requirements for usable HE stains were that the whole transmural section from endocardium to epicardium was histologically preserved, no folding of tissue was allowed. Thus, 32 out of 57 sections were analyzed under the microscope: At a magnification of 400, a grid with 110 cross points was used to transmurally classify the histology as normal, necrotic myocytes or interstitial cells (IC, e.g. granulocytes, macrophages, fibroblasts). The 110 datapoints for each grid were normalized to 100%. Intramural vessels were neglected. In sum, 274 grids with 30140 data points were collected.

Results

MRI yielded three different hyperenhancement patterns: homogeneous, diffuse and heterogeneous (figure 1). The homogeneous pattern is associated with complete necrosis (figure 2A). However, diffuse (figure 2B) and heterogeneous hyperenhancement (figure 3) revealed normal myocytes interleaved with islands of necrosis. Signal intensities in homogeneous, diffuse and heterogeneous hyperenhanced areas were significantly higher than remote ($306\pm 34\%$, $208\pm 23\%$ and $245\pm 21\%$, resp., $p<0.01$, two-tailed unpaired Student's t-Test). IS increased with slice thickness (0.5 to 1, 2 and 5 mm) from 23.2% to 23.9%, 26.6% and 30.5%, resp.. There was no trend to an increasing IS with decreasing in plane resolution. IS in high resolution MRI still overestimated IS, when compared to TTC by $6.1\pm 2.5\%$ (mean, SD, $p<0.05$, two-tailed paired Student's t-Test).

Figure 1. Contrast enhancement in high resolution 1H MRI. Homogeneous hyperenhancement is associated with complete myocyte necrosis. Diffuse and heterogeneous hyperenhancement reveal normal myocytes with interleaved islands of necrosis.

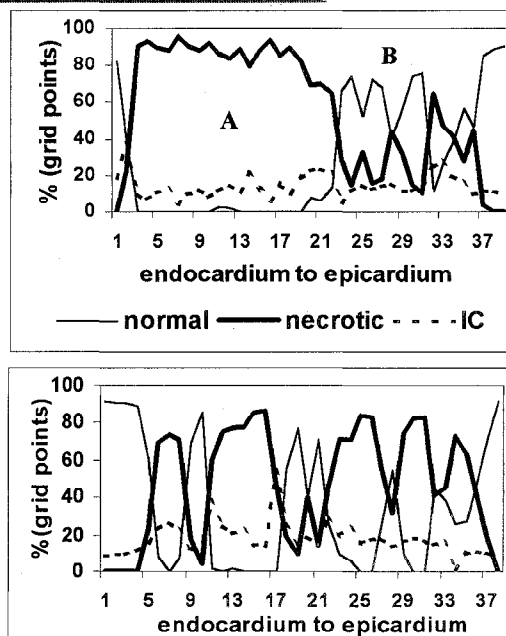
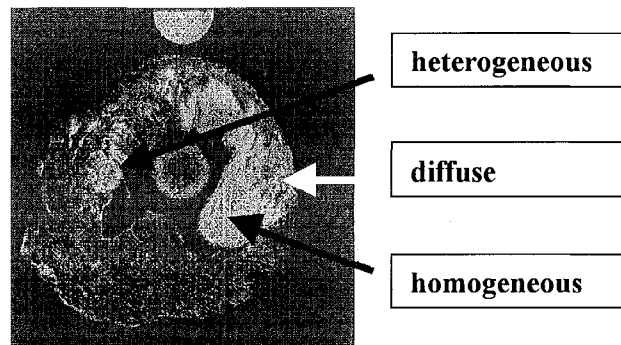


Figure 2 (top). Complete necrosis (A) and normal myocardium with islands of necrosis (B). The section was obtained from the region indicated by the white arrow in figure 1. **Figure 3 (bottom).** Histopathologic findings in regions of heterogeneous hyperenhancement.

Discussion

In reperfused MI three distinct hyperenhancement patterns of high resolution MRI correspond to characteristic histopathologic patterns of complete - or focal myocyte necrosis. These data indicate that hyperenhancement occurs only in non viable tissue. Further, IS measurement is a function of slice thickness. Therefore, if enough MR signal is available, slice thickness should be decreased. Thus, in comparison to the surface staining TTC, contrast enhanced MRI overestimates IS, but this is due to partial volume effects. However, as opposed to high resolution contrast enhanced MRI, surface staining TTC neglects the 3D morphology of MI within each slice. We believe that contrast enhanced 3D MRI is a powerful tool to accurately measure infarct size.

References

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