Delayed Enhancement of the Peri-Infarct Border Zone is Significantly Affected by Partial Volume Averaging: Insights from ex vivo Rat Heart Images at a Near-Cellular Resolution

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Introduction: Delayed contrast enhancement MRI is a widely used technique to depict myocardial infarction [1]. There is an increasing interest in measuring the peri-infarct border zone using intermediate signal intensity between normal and hyperenhanced infarct voxels [2,3]. At least two distinct but related mechanisms can explain the intermediate signal intensity in the border zone: 1) simple partial volume errors at distinct borders between normal and infarcted myocardium, or 2) biological complexes that represent a mixture of normal and abnormal cardiomyocytes (which manifest as intermediate singal intensity due to partial volume averaging in limited imaging resolution). We hypothesized that the intermediate signal intensity in the peri-infarct border zone between normal and infarcted myocardium maybe explained by partial volume averaging. Using 3D ex vivo rat heart MRI at an isotropic voxel resolution equivalent to 3 cardiomyocytes, we quantified the volume of peri-infarction on the acquired isotropic 3D high resolution images and on post-hoc slab averaged low resolution images.

Methods: 8 week old Sprague Dawley rats (n=6) were submitted to 60-minutes of coronary ligation to create myocardial infarct model. Ex vivo MRI was performed on a 7T scanner (Bruker, Billerica, MA) 2 months later. All animals were given Gd-DTPA (0.3 mmol/kg) through a tail vein catheter and euthanized 10 minutes later to lock in the physiological distribution of gadolinium at that time point. A T1-weighted 3D gradient echo sequence was used: TR/TE=20/3.0 ms, flip angle 30 degree, FOV 1.3x1.0x1.0 cm, matrix 256x192x192, resolution 50x52x52 microns, 3 averages, 36 minutes of acquisition time per dataset. Histological slices were stained by Masson's trichrome to indicate the regions of myocardial infarction. Corresponding MR images were resliced in 3D to match the histological slices for qualitative comparison. Low resolution images were reconstructed post-hoc by using only 32 k-space lines and averaging 16 image slices to produce a voxel 2048 times larger than the original high resolution images (which is still >100 times better than current clinical resolution). Quantification of infarct volume was performed by an automated program using a 50% intensity threshold between dark normal and bright enhanced voxels [4]. Additional volume measurements of contrast enhancement were performed by using a two standard deviations (2xSD) threshold above the normal voxel intensity. The peri-infarct border zone was defined as the voxel space between 2xSD and 50% threshold regions. Both high resolution raw image and reconstructed lower resolution image dataset were processed with the same settings.

Results: The average volume of the rat hearts was 1165±187mg based on a 0.00014 mg per voxel weight. Fibrosis associated with myocardial infarction (blue zones on Mason's trichrome histology, Figure-1a) correspond well with ex vivo high resolution delayed enhancement images (Figure-1b; correlation r^2=0.96 and y=1.01x+0.01 now shown). The corresponding low resolution image (Figure-1c) shows blurry infarct edges that look similar to the intermediate signal intensity seen in the border zone around in vivo human infarcts. In the color overlay MR images (Figure-1d and Figure-1e), the blue zone represents myocardial infarction defined as voxels brighter than the 50% intensity threshold (between the mean of normal voxels and the 95th percentile of bright infarct voxels), while the red zone represents the peri-infarct border zone defined by the 2xSD. The apparent size of the border zone on the low resolution image is twice as large as that seen on the high resolution image. In analysis of the whole dataset, infarct size measured using the 50% threshold was similar for both high and low resolution volume dataset (n=NS) while the border zone increased by a factor of 2 in the low resolution dataset (p=0.02).

Discussion: With a spatial resolution equivalent to about three myocytes per voxel, we show that contrast enhanced regions in ex vivo rat heart model details myocardial fibrosis and infarction corresponding closely with the histology. Degrading the effective image resolution increases the size of the peri-infarct border zone which is a result predictable by partial volume averaging. While the in vivo distribution of Gd-DTPA accurately depicts regions of myocardial infarction at nearly a cellular level, clinicians need to be cautious about over-interpreting the significance of delayed enhancement and consider the effect of non-isotropic voxel due to thick imaging planes.

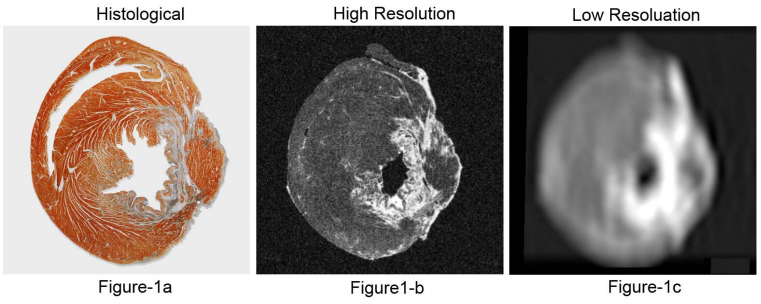

Figure-1a Figure1-b Figure-1c

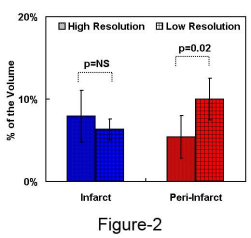

Figure-2

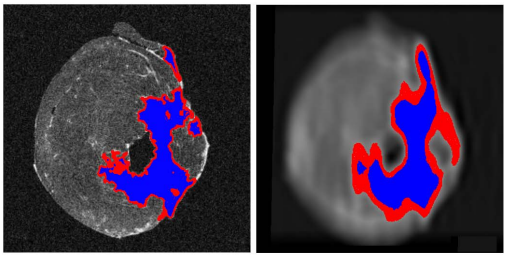

Figure-1d Figure-1e

References

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