Quantification of No-reflow Zone using Semi Automated Approach

B. Ruzsics[1], P. Suranyi[2,3], P. Kiss[2,3], S. Singh[2], S. Litovsky[2], B. C. Brott[2], H. Gupta[2], and G. A. Elgavish[2,3]

[1]Biochemistry and Molecular Genetics, University of Alabama at Birmingham, Birmingham, Alabama, United States, [2]University of Alabama at Birmingham, [3]Elgavish Paramagnetics

Introduction:

The no-reflow phenomenon within the myocardial infarction is associated with poor functional and clinical outcomes. In the era of primary intervention, accurately identifying lesions at high risk of no reflow is of crucial importance. Myocardial contrast echocardiography revealed that the no-reflow phenomenon is observed in patients with a reperfused AMI, and those patients usually have poor functional and clinical outcomes. In the present study we investigated the role of DE-MRI and MDCT for microvascular obstruction quantification. We presume that if we could calculate the no-reflow zone that could represent a predictive value of future clinical outcome.

Methods and Materials

In four pigs (n=4), one week following reperfused infarction delayed enhancement imaging was carried out. Delayed Enhancement (DE) Imaging: Images were acquired using a 180º-prepared, segmented, fast gradient-echo sequence 15 to 20 minutes after the administration of Gd(DTPA). Imaging parameters were: FOV = 300 mm, image matrix = 256x256, slice thickness = 10mm, read out flip angle = 25°, echo time (TE) = 3.32 ms, repetition time (TRp) = 7.18 ms, and a recycle time (TR) of one or two R-R intervals. The inversion time (TI) was set to the optimal value (between 225-325ms) to null the signal in areas of healthy myocardium.

Cardiac MDCT imaging was performed in five pigs (n=5) one week after reperfused myocardial infarction using a 64-detector CT scanner (Philips, Best, Netherlands). After scout acquisition and slice prescription, a 5-mL/kg bolus of Iodixanol (Visipaque 320 mg iodine/mL, Amersham Health, Amersham, United Kingdom) was injected intravenously at a rate of 3 mL/s, followed by a 30-mL saline chaser. The bolus tracking sensor was positioned in the ascending aorta. When the signal in the ascending aorta reached a predefined threshold of 150 Hounsfield units, respiration was suspended and imaging performed with a retrospectively gated cardiac MDCT protocol (gantry rotation time = 400 ms, detector collimation= 0.64 x 0.625, pitch=0.2, tube voltage=140 kV, tube current=600 mA, scanning field of view=12 mm, 0.675 mm thick images at 0.33 mm interval). Post-contrast imaging protocol was done 15 minutes following the administration of Iodixanol.

After completion of the in-vivo MRI and CT session, pigs were eutanized. From each pig, an entire transverse cross section of TTC-stained left ventricle was submitted for histologic examination. Samples were divided into sections that fit a histology cassette, were paraffin-embedded, sectioned at 5µm, and stained with Hematoxylin-Eosin (H&E). Following microscopic photography, from the individual sections, a composite microscopic photograph was reconstructed encompassing the entire infarct and the surrounding 5-10 mm peri-ifarct region. The myocardial infarct was quantified by drawing the infarcted territory on each composites and at the center of the infarct region of microvascular obstruction (i.e no reflow zone) was defined. Microvascular obstruction (MO) was calculated as a percentage of the myocardial infarction, Percent area of MO per Infarct in microscopic slides ($PAMO_{MICRO}$). DE image analysis: the mean signal intensity (SI) of a remote, normal myocardial region was measured (SI_{remote}, about 100 pixels). Mean SI_{remote} plus two to six times the standard deviation (SI_{remote}+ 2 SD) were used to define threshold limits. Pixels with signal intensities over this threshold value were considered infarcted pixels. Within the infarct mean SI minus 2 SD was used to delineate subendocardially the lower signal intensity enhancement zone representing the area of MO. Percent area of MO per Infarct in DE-MRI ($PAMO_{DE-MRI}$) was calculated as number of MO pixels divided by the number of infarcted pixels multiply by 100. CT Image analysis True short axis cardiac slices 1.4 mm thick at 75% of cardiac phase were reconstructed on a Philips workstation. A 49-slice image stack was acquired, from which every 7th image was used for further analysis, representing the same image localizations that had been imaged with the 7 short axis MRI slices covering the whole heart. MDCT images were analyzed automatically after manual endo and epicardial contour tracing. Similar to MRI DE, myocardial hyperenhancement suggesting nonviable tissue was delineated by thresholding the images as before (SI_{remote}+2SD). Direct slice-by-slice comparisons of MDCT and TTC images were accomplished with multiplanar reconstructions of axial slices that matched the short-axis postmortem myocardial slices. In the thresholded MDCT images the center of infarct represented similar SI values as in the remote, healthy myocardium. Tracing that area within the infarct quantified the MO zone. And similarly to DE Image analysis, Percent area of MO per Infarct in MDCT ($PAMO_{CT}$) was determined.

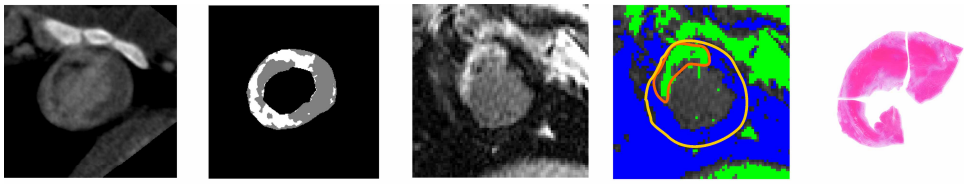

Figure 1. Corresponding images. A. MDCT raw image B. Thresholded MDCT image MO zone can be seen within the infarct. C. DE-MRI raw image. D. Thresholded DE image subendocardially delineates the MO zone similarly to MDCT image. E. H&E microscopy from the same slice huge no reflow zone (i.e MO) was surrounded by necrotic infacted tissue.

Results

At the center, all infarcts (n=5) showed coagulation necrosis with loss of nuclei and striations, and (usually small) areas of hemorrhage. No reflow zone was seen in raw images after contrast agent administration in all animals. Both DE-MRI and MDCT was underestimated the area of MO compared with MO determination in post mortem microscopy ($PAMO_{MICRO}$ vs. $PAMO_{DE-MRI}$ r=0.64, y=0.53x+0.7 and vs. $PAMO_{CT}$ r=0.75, y=0.64x+5.3). The MO area was shown in Figure 1 in different image modalities.

Conclusion

Microvascular obstraction can be visualized and quantified in vivo. H&E microscopy can serve as gold standard for MO, no-reflow zone determination. CT lacks of partial volume effect and gives better visualization form the surface of the slice so simple 2SD thersholding delineates the territory of MO at the center of the infarct.