

ASSESSMENT OF THREE DIMENSIONAL LEFT VENTRICULAR STRAIN AFTER VEGF GENE THERAPY IN OCCLUSIVE INFARCTION ON MAGNETIC RESONANCE IMAGING

M. Saeed¹, M. Carlsson^{1,2}, D. Dicks¹, A. Martin¹, and D. Saloner¹

¹UCSF, Dep of Radiology and Biomedical Imaging, San Francisco, CA, United States, ²Lund University Hospital, Dep of Clinical Physiology, Lund, Sweden

INTRODUCTION: Vascular endothelial growth factor (VEGF) gene delivery has been proposed as a therapy to reduce left ventricular (LV) failure after myocardial infarction. MRI provides the means to quantify LV function in detail. Systolic wall thickening on cine MRI is a measure of radial strain, while tagging MRI provides information on circumferential and longitudinal myocardial strain during the cardiac cycle. Furthermore, a transendocardial technique to deliver gene and cell therapy (1, 2) using a percutaneous catheter under MR-guidance has been developed.

PURPOSE: To provide evidence that VEGF-gene delivered transendocardially under MR-guidance improves LV 3D strain (circumferential, longitudinal and radial) and reduce infarct transmuralty in permanent coronary artery occlusion in dogs.

MATERIALS AND METHODS: Approval was obtained from the Institutional Committee on Animal Research and the study was performed in concordance with the Guide for the Care and Use of Laboratory Animals. The left anterior coronary artery (LAD) was surgically ligated after the first diagonal in 12 dogs to create occlusive infarction. MRI was performed for delivery of therapy at 3 days after coronary artery occlusion. VEGF-gene (n=6, treated) or LacZ-gene (n=6, control) was transendocardially injected under MRI guidance. The effectiveness of therapy was determined using tagging, cine and delayed enhancement (DE)-MRI at 3 and 50 days after infarction. Tagging MRI was obtained in short and long-axis planes using a turbo-field echo-planar sequence (TR/TE=35/6.1ms, flip=25°) to evaluate changes in regional circumferential and longitudinal strain, respectively. A cine steady-state free precession sequence (TR/TE=8/5ms, flip=20°) was used to assess peak systolic radial wall thickening. Inversion-recovery gradient-echo (TR/TE/TI=4.4/2.1/270ms, flip=15°) DE-MR images for measuring infarct transmuralty and size were acquired 20 minutes after administration of 0.15mmol/kg Gd-DOTA. Short and long-axis tagging MR images were analyzed using the HARP software (Diagnosoft Inc., CA). Cine and DE-MRI images were analyzed using Segment v1.699 (<http://segment.heiberg.se/>)

RESULTS: The increase in circumferential and radial strain at 50 days compared to 3 days in the infarcted regions was significant in treated animals in short axis slices ($P<0.05$), but not in controls (Figure 1 and 2). In control animals there was a deterioration in radial strain in the infarcted region at 50 days as compared to 3 days ($P<0.05$). In contrast, treated animals showed significant improvement in radial strain at 50 days compared to 3 days in infarcted and peri-infarcted regions. VEGF-gene delivered under MR-guidance significantly also improved longitudinal strain (from $-1.8\pm1.0\%$ to $-5.7\pm1.0\%$, $p<0.05$). Decreased infarct transmuralty was found in both control and treated animals over 50 days, however, a greater decrease in infarct transmuralty and circumferential extent was noted in VEGF-gene treated animals compared to control animals.

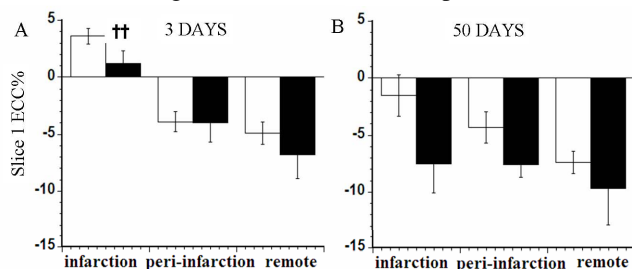


Figure 1. Peak circumferential strain (ECC%) in control (white bars) and VEGF-gene treated (black bars) animals at 3 (A) and 50 days (B) in one slice at the site of the infarction. At 50 days ECC% showed better function in VEGF-gene treated animals in the infarcted and peri-infarcted regions compared to controls. * signifies $P<0.05$ between control and treated animals; †† signifies $P<0.01$ between 3 days and 50 days within the same group.

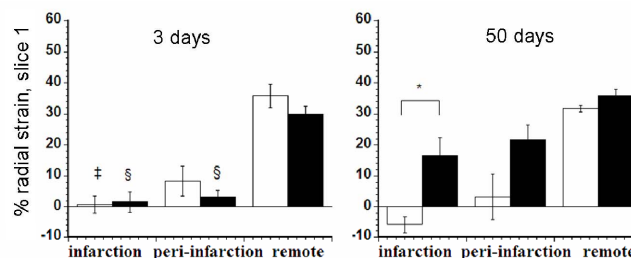


Figure 2. Peak systolic radial strain (wall thickening) in control (white bars) and VEGF-treated (black bars) animals. At 3 days, there was no difference in radial strain between control and VEGF-gene treated animals. Both groups showed a decline in infarcted and peri-infarcted regions compared to remote. Control animals demonstrate greater decline in radial wall thickening at 50 days as compared to 3 days, whereas improved radial strain was found in VEGF-treated animals.

CONCLUSION: Transendocardial delivery of VEGF-gene in infarcted and peri-infarcted myocardium under MR-guidance improved 3D (radial, circumferential and longitudinal) strain within 50 days and caused significant reduction in infarct transmuralty of treated animals compared to controls. Cine and tagging MRI are sensitive techniques for monitoring the effects of locally delivered therapies.

Acknowledgment. This study was supported by a grant from NIH (RO1HL072956).

References 1. Karmarker MR-trackable intramyocardial injection catheter. Magn Res Med 2004.

2 Saeed M et al. Permanent coronary artery occlusion: cardiovascular MR imaging is platform for percutaneous transendocardial delivery and assessment of gene therapy in canine model. Radiology 2008.