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Percutaneous delivery and non-invasive imaging of gene and cell therapy in a porcine model M. Rodriguez-Porcel[*1], T. J. Brinton[2], O. Gheysens[1], I. Y. Chen[1], F. Ikeno[2], J. C. Wu[3], P. G. Yock[2] and S. S. Gambhir[1]; 1. Molecular Imaging Program at Stanford, Stanford University, Stanford, California; 2. Department of Medicine, Division of Cardiovascular Medicine, Stanford University, Stanford, California; 3. Dept of Radiology, Stanford University, Stanford, California; 4. Department of Bioengineering, Stanford University, Stanford, California and 5. Department of Medicine, Division of Cardiovascular Diseases, Mayo Clinic and Foundation, Rochester, Minnesota

Objectives: Gene and cell therapy are powerful potential treatments for ischemic heart disease. We previously showed the feasibility of using PET for non-invasive monitoring of such therapies, using reporter genes, in rodents. Before these therapies are ready for clinical applications, they need to be tested in clinically relevant large animal models. However, most preclinical studies in large animals have utilized direct intra-myocardial injections of genes in an open chest model. In the current study, we evaluated the feasibility of combined minimally invasive percutaneous endomyocardial delivery and monitoring of gene and cell therapy, using PET-CT, in a porcine model.

Methods: In a porcine model, we delivered genes (Adenovirus expressing a mutant herpes simplex virus type 1 thymidine kinase reporter gene, Ad-CMV-HSV1-sr39tk, $1.5x10^{10}$ pfu, n=2), cardiomyoblasts (24 hours after infection of $4x10^{7}$ cells with Ad-CMV-HSV1-sr39tk, 100 multiplicity of infection, n=1), or saline (control, n=1) to the antero-septal wall of the myocardium using an endomyocardial delivery system (BioCardia, South San Francisco, CA), via an arterial retroaortic approach. 72 hours (genes, control) or 6 hours (cells) after percutaneous delivery (Figure, left), animals were imaged after the administration of 10±2 mCi of ^{18}F-labeled 9-[4-fluoro-3-(hydroxymethyl)butyl]guanine ([^{18}F]-FHBG), with a clinical PET-CT system.

Results: There were no complications associated with the procedure. A myocardial focal signal was seen only in experimental animals and was localized to the antero-septal wall, by either clinical PET-CT scanner (Figure 1, middle and right) or microPET-CT (only the heart was scanned). In experimental animals, [^{18}F]-FHBG myocardial uptake was 4-fold higher than background (0.54±0.1 vs. 0.14±0.04 SUV, respectively). No focal uptake was observed in the control group. Activity of HSV-1 sr39tk was confirmed by digital autoradiography, and immunohistochemistry.

Conclusions: Gene and cell therapy can be performed using percutaneous endomyocardial delivery and monitored using PET-CT. The combination of minimally invasive delivery and non-invasive monitoring will play a critical role in the advancement of the field of gene and cell therapies.