Magnetic Capture of Endothelial Cells to Vascular Stents Within An Externally Applied Magnetic Field

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Statement of Purpose: Targeted delivery of drugs, contrast agents, and cells is highly desirable for an increasing number of medical diagnostic and therapeutic applications. Beneficial site-specific effects can be enhanced while harmful off-site effects can be minimized. Magnetic forces are a promising means of achieving targeted delivery. We have previously demonstrated the feasibility of using magnetic attraction to capture and retain magnetically-labeled endothelial cells to the surface of magnetized vascular stents (Pislaru SV. J Am Coll Cardiol. 2006;48:1839-1845). Targeted delivery of autologous endothelial cells to a stented artery may enhance healing, mitigate thrombosis and restenosis, and improve clinical outcomes. In the current study, we investigate the hypothesis that delivering magnetically-labeled endothelial cells to a ferromagnetic vascular stent within an externally applied magnetic field will enhance cell capture when compared to cell delivery in the absence of an externally applied magnetic field.

Methods: Ferromagnetic vascular stents were manufactured from 2205 duplex stainless steel. This material was chosen based on its magnetizability, biocompatibility, and suitable mechanical properties. Autologous endothelial outgrowth cells (EOC) were cultured from whole porcine blood as described in our previous report (Gulati R. Circ Res. 2003;93:1023-1025). Cells were labeled with superparamagnetic iron oxide nanoparticles (SPION) consisting of a magnetite core surrounded by a polymer shell. Stents were crimped onto a delivery balloon and implanted into the right coronary artery of a porcine model. Some stents were magnetized prior to implantation by holding in close proximity to a rare earth magnet and control stents were left non-magnetized. SPION-labeled EOCs were then delivered to the stented artery during 2 minutes of blood flow occlusion by means of an intravascular catheter. Pigs were sacrificed after 1 week of implantation and stented arteries were histologically processed. Magnetized stents were also placed within an externally applied magnetic field between two rare earth magnets or left unexposed to an externally applied magnetic field and SPION-labeled endothelial cells were delivered. Photographs of cell capture within and without the externally applied magnetic field were taken using a dissection microscope.

Results: The 2205 duplex stainless steel stents were all crimped and expanded without mechanical failure. Stent deployment was symmetrical and resulted in minimal damage to the arterial wall. Right coronary artery segments stented with both non-magnetized and magnetized stents were fully patent for all 4 pigs that survived to the 1 week time point. Histological examination demonstrated neointimal healing over most of the stent struts. Iron staining indicated the presence of SPION-labeled cells at the strut surface of both non-magnetized and magnetized stents, indicating that delivered cells were successfully captured and retained under arterial blood flow conditions. More SPION-labeled cells were observed on the struts of magnetized stents when compared to non-magnetized stents (Fig. 1).

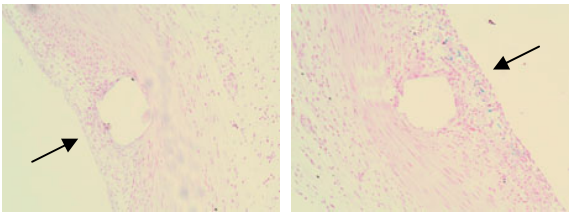

Figure 1. Cell capture and retention (blue) to a non-magnetized (left) and magnetized (right) stent.

Some magnetic stent struts exhibited significant cell capture while others exhibited none, indicating non-uniform cell capture. This may be in part due to the reduction of magnetic field strength in 2205 stainless steel stents upon plastic deformation during expansion. In addition, 2205 duplex stainless steel is only weakly magnetizable and the magnetic field induced within our stents never exceeded 1 G. Given the weakness of the induced magnetic field and the significant loss of magnetic field strength upon stent expansion, we tested the hypothesis that delivering cells to an expanded stent within an externally applied magnetic field will result in enhanced cell capture. SPION-labeled EOCs delivered to magnetized 2205 duplex stainless steel stents within an externally applied magnetic field demonstrated markedly better capture when compared to EOCs delivered to stents in the absence of an externally applied magnetic field (Fig. 2). Cells were preferentially captured to bends in the stent struts where magnetic poles form.

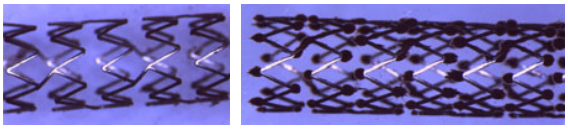

Figure 2. Cell capture (brown) without (left) and with (right) an externally applied magnetic field.

Conclusions: Magnetic targeting of endothelial cells to vascular stents is a promising means of cell capture and retention. The presence of autologous endothelial cells may enhance healing of the stented artery and improve clinical outcomes. Magnetizing stents prior to implantation and delivering cells without an externally applied magnetic field resulted in modest cell capture. Delivering cells in the presence of an externally applied magnetic field resulted in significantly enhanced cell capture. Studies are currently underway to test this strategy in a porcine model.