Analyzing Phenotype Changes during Coronary Bypass Graft Remodeling

Reece Fratus, Thomas Fair, Lucas Schmidt, and Bruce Z. Gao
Graduate Researcher, Clemson University, Graduate Researcher, Clemson University, Post-Doctoral Fellows, Clemson University, Professor, Clemson University

Statement of purpose: When a saphenous vein is used as a coronary artery bypass graft, it undergoes a change in environment. This causes the vein to begin remodeling to act like an artery because it must adapt to the high pressure and high flow conditions. One issue with the remodeling process is that if there are zones with low flow resulting in low shear stress, the endothelial cells and smooth muscle cells of the graft can change phenotype which can initiate the neointima formation process. Unfortunately, areas of low flow are common in bypass grafts due to the geometry of the graft and the altered entry and exit of blood flow through the graft. With flow recircularization zones so common, 30-40% of vein grafts have significant occlusion after 1 year and up to 50% fail after 10 years. These number have remained nearly unchanged over the past 50 years. With recently developed imaging modalities, it is possible to study vein graft remodeling and attempt to understand how vein graft failure can be reduced. Optical coherence tomography (OCT) is an imaging modality discovered in the past 30 years and has clinical significance in ophthalmology. Recently, OCT has been shifting towards other fields of study including cardiovascular. OCT's unique ability to optically section samples at resolutions equal to microscopy provide it with a niche among certain areas of research. The optical sectioning ability of OCT allows for the observation of phenotype changes of cells within the vessel wall while simultaneously observing blood flow near those cells to correlate shear stress to phenotype.

Methods: To image both blood flow and cells in the vessel wall, a high depth of field is required which is achieved with a custom OCT design. The incident beam is a gaussian produced by a super-continuum laser which can be filtered to ranges in the near IR. The beam is split into two arms using a rod mirror which allows a ring-shaped beam to pass by the mirror while the center portion of the beam is reflected 90 degrees by the 45-degree reflective surface of the mirror. The ring beam is labeled as the sample arm while the reflected beam is labeled as the reference arm. The reference is reflected off a pair of mirrors fastened to a translational stage. Moving the stage changes the optical path length of the reference so it can be matched to the sample beam. The sample beam is scanned across a sample using a 2D galvo scanner and the beam is focused onto the sample using a 4f lens pair in combination with an objective lens. When the ring-shaped beam is focused, it creates a Bessel illumination near the focal plane which provides a higher depth of field. The reference and the sample are then recombined using a pellicle beam splitter after the rod mirror. In addition to the custom OCT system, a flow perfusion system was also constructed to mimic blood flow through vein samples. A peristaltic pump is used to generate a constant flow while a custom air pressure pump uses a membrane to provide a pulsatile flow. The prefusion system is set up in an incubator to keep the tissue alive and the media warm.

Results: Images of onion slices and glass beads imbedded in PDMS were captured with the custom OCT system. The beam profile was also obtained by capturing an image of beads imbedded PDMS from the side. The distribution of intensity spreads out more as the outer aperture of the sample arm is closed. This matches MATLAB simulations that show the Bessel length increases as the outer diameter of the beam decreases. The prefusion system has been constructed only recently, but initial testing shows proper pressure waveforms.

Conclusions: The desired imaging parameters are met by the constructed OCT system, but issues remain with the image processing. Ghost images appear for reflective samples making the true sample more difficult to discern. Processing algorithms should be able to remove these artifacts. The next step is to begin imaging tissue samples to get a baseline before testing veins in the perfusion system. Hopefully, the information gained from the study can provide information on how to best implant bypass grafts and potentially how to manufacture successful artificial grafts.