

Exploring revascularization using fluorescence angiography: going with the flow

Zorina S. Galis, Dept. of Medicine, Emory University, Wallace Coulter Dept. of Biomedical Engineering, Georgia Tech/Emory University, and the Parker Petit Institute of Bioengineering and Biosciences, Georgia Institute of Technology, Atlanta, USA

The growth of new capillaries from the existing vasculature is necessary for the development and growth of existing tissues, wound healing, and revascularization of tissues supplied by non-functional arteries. Similarly, angiogenesis is essential for the *in vivo* integration and survival of tissue engineered constructs. However, angiogenesis also assists pathological processes such as tumor progression and metastasis, macular degeneration, or complications of atherosclerotic disease. Thus therapeutic regulation of angiogenesis offers attractive opportunities for clinical management of these important conditions. Obtaining functional information regarding perfusion of microvasculature is essential in detecting experimental pathological conditions and monitoring therapeutic interventions. A major limitation is the current status of methods used to monitor interventions. Most of these provide limited functional or morphological information, or are extremely resource intensive. We developed the use of fluorescent microangiography, as a versatile, sensitive, and rather simple explorative technique to obtain accurate functional and visual information from the microvasculature. We imaged microvascular networks of multiple organs, including three-dimensional reconstructions, and we exemplify quantification of vascular hierarchy and angiogenic branching. The technique was also tested for quantitative monitoring of physiological and pathological changes of microvascular perfusion, by monitoring the angiogenic response induced by ischemia or development of experimental atheroma. We also examined the possibility of simultaneous imaging within the tissue of other fluorescent biological markers. We will also exemplify how the use of this method allowed us to identify the specific role of matrix metalloproteinase-9 (MMP), specialized in degradation of the endothelial basement membrane and known to be involved in angiogenesis. Thus, fluorescent microangiography can be used to monitor the experimental regulation of the angiogenic response to obtain both quantitative functional and microstructural information.

Acknowledgements: These studies have been supported partially through funds from NSF award ERC-9731643, NIH R01 HL 64689 and NIH R21 HL7203