A numerical approach for predicting the impact of vascular architecture on blood flow during ischemic repair

**Stephanie Ann Wood1, Shilpi Ghosh1, Kevin Jones1, Gabriel Gruionu2, & Trevor R. Cardinal1**

1. Department of Biomedical and General Engineering
   California Polytechnic State University, San Luis Obispo, CA
2. Biomedical Engineering Program, The University of Arizona, Tucson, AZ

---

**Introduction**

Chronic ischemia is associated with changes in vascular caliber and number. In addition to the vascular remodeling response, there is also a decrease in both resting blood flow and hyperemia in skeletal muscle during ischemic repair. Understanding the mechanisms underlying the reduction in skeletal muscle blood flow ischemia has important implications for comprehensive treatment in ischemic disease.

Determining the cause of blood flow reduction during ischemic repair requires investigation into how vascular network architecture properties affect the distribution of flow throughout the tissue. Numerical models can be used to provide quantitative assessments of network architecture and predictions of hemodynamics.

In this study we examined one mouse skeletal muscle (gracilis) sample that undergoes structural remodeling following ischemic surgery. The vessel network characteristics in muscle in control and ischemic muscle were recorded. The data was then analyzed using numerical models such as the diameter–defined Strahler method and the Hagen-Poiseuille flow equation to obtain organized information on connectivity, branching characteristics and hemodynamics.

**Hindlimb Ischemia Surgery**

The gracilis artery, the main blood supply to the gracilis muscle on the medial side of the thigh, is fed by two arteries, the muscular branch of the femoral artery and the saphenous artery (Fig. 1). The muscular branch along with the saphenous artery and the gracilis artery forms an arcade system that supplies blood to the tissue. The blood supply to the gracilis artery was disrupted by removing a portion of the saphenous artery in the experimental group mice. The saphenous artery of the sham control mice was exposed but maintained intact.

**Vascular casting using India ink**

India ink was used for visualization of the vascular network in the mouse gracilis muscle. The left ventricle of the mouse was cannulated with a catheter and the blood was flushed with PBS containing heparin and sodium nitroprusside. Ink solution was immediately perfused into the vasculature. The gracilis muscles from both hindlimbs were carefully dissected and placed flat on a microscopic slide to maintain their original length. The muscle was dehydrated in a graded series of alcohol solutions for 12 hours in each solution. Subsequently, the muscles were cleared in 100% methyl salicylate. The vasculature was then analyzed using a stereomicroscope after the muscle was sandwiched between two microscope slides and transilluminated.

**Morphometric Analysis**

Morphometric data such as length and diameter of blood vessel segments were obtained from digital photomicrographs. The vascular tree patterns typically found in vascular networks was a key feature used to identify arterioles in the image. Blood vessels were traced manually and each segment was labeled (Fig. 4). A vessel segment was defined as a vessel between two vascular bifurcation points called nodes, as illustrated in Fig. 3.

**Numerical models used for morphometric analysis**

Horton's Law was originally developed to describe the branching networks observed in streams in nature. This approach has since been modified and applied to vascular networks to describe the branching patterns in the cardiovascular system. Horton’s Law states that characteristics (type of branching level) will form an inverse geometric sequence with order number. Although applying Horton’s Law provides useful information on the overall network characteristics, it falls short in a few areas, namely that it only describes patterns between adjacent orders. Consequently, various adjustments have been made to the Horton's Law approach, resulting in what is called the diameter-defined Strahler system.

**Network Architectural Properties**

The vessel quantity and vessel diameter show good agreement with Horton’s Law. The vessel length in the control muscle vasculature is consistent with Horton’s Law, however, the remodelled vasculature shows substantial discrepancy. The overall consistency with Horton’s law tells us that vessel quantity, length and diameter increase geometrically with decreasing order number, which is an expected feature of tree-type structures.

**Summary & Discussion**

- The branching pattern in both the control and remodelled vasculature is consistent with Horton’s law in mouse gracilis muscle.
- The diameter-defined Strahler method aids in characterizing the asymmetric branching pattern found in the vasculature.
- The overall flow was calculated to be less in the remodelled vasculature and the lower flows in order 2 and order 3 vessels in the remodelled vasculature contributed largely to this change.

**Future Studies**

- Incorporate effects of branch angle on flow resistance into existing numerical model.
- Analyze more muscle samples that have undergone ischemic remodeling using the current numerical model.

**References/Acknowledgements**


**Additional Information**

Trevor R. Cardinal - tcardin@calpoly.edu
Shilpi Ghosh - sghosh@calpoly.edu