IMAGING MICROVASCULAR MORPHOLOGY AND FUNCTION USING LASER SPECKLE CONTRAST

by

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Abstract

Laser speckle contrast imaging (LSCI) is an optical imaging technique traditionally used to study relative regional blood flow changes in the brain. Based on preliminary evidence, I hypothesized that it would be possible to develop LSCI for obtaining detailed information about microvascular morphology and blood flow at a high spatial resolution; thereby enabling both short and long term assessment of vascular physiology and remodeling. Consequently, I report an LSCI-based imaging platform comprising various technological innovations and demonstrate its utility in two *in vivo* models of vasculature undergoing remodeling – murine ear model of wound healing and rat brain model of tumor angiogenesis.

Specifically, I demonstrate that LSCI is able to elucidate cross-sectional and axial blood flow profiles in individual microvessels; and utilize these profiles to estimate the distribution of blood flow in each arm of branching vascular trees. I also report a novel LSCI-based methodology for discriminating arterioles and venules. The methodology, validated using both dye injection and histology, can enhance a neurosurgeon's ability of classifying vessels as arterioles. Subsequently, I present two enhancements that I made to LSCI to make it suitable for both monitoring rapid physiological events (using an anisotropic scheme – aLSCI) as well as long term vascular remodeling (using a multi exposure approach – meLSCI). aLSCI requires only three acquired image frames for processing and was shown to image heart rate associated blood flow variability with higher signal-to-noise ratio than equivalent LSCI schemes. meLSCI

improves robustness of LSCI-based flow estimates across multiple imaging sessions, which is relevant when conducting comparative assessments in longitudinal in vivo experiments.

I use LSCI to monitor the murine ear vasculature over the course of wound healing and characterize the microvascular remodeling using metrics such as microvessel length and tortuosity; and the associated hemodynamic changes through the creation of wide-area maps of the entire wound periphery, including spatiotemporal information about micro and macro vascular perfusion. Finally, in a rodent glioma model, I demonstrate that LSCI is capable of imaging the tumor associated increase in microvessel density. The microvessel density fourteen days post tumor inoculation, is significantly elevated in the tumor group as compared to controls, providing preliminary evidence of LSCI's suitability for intraoperative monitoring of angiogenic changes during tumor resection neurosurgery.

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