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Visualizing the Microcirculation

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The microcirculation comprises the "terminal end" of the systemic circulation[1] and is the interface via which tissues receive oxygen and metabolites, as well as dispose of waste products. It maintains homeostasis and has been implicated in an array of diseases ranging from cancer[2] to COVID-19.[3] Therefore, there is an exigent need for imaging tools capable of characterizing the structural and functional heterogeneity of the microcirculation. However, imaging and visualizing the microcirculation do pose inherent challenges. For example, the spatial scale of the systemic circulation spans several orders of magnitude, from a few microns (e.g., endothelial cells) to several hundred microns (e.g., large blood vessels), which are difficult to span with a single imaging technique.[1] Moreover, tissue elements such as adipose deposits, bone, and collagen fibers can interfere with the image contrast mechanisms traditionally employed for structural imaging.[4] Analogously, since microcirculatory changes occur on time scales ranging from seconds (e.g., blood flow changes) to hours or days (e.g., wound healing and angiogenesis), characterizing them often requires the use of multiple imaging methods or techniques with a large dynamic range of sampling frequencies. The studies included in this SI address many of these challenges via a host of innovatively designed experimental models, imaging methods, and analytical approaches.

This SI begins with two studies describing new experimental assays for interrogating the microcirculation. The first, by Francis et al, describes an in vitro fibrin-based assay for studying angiogenesis that the authors combine with high spatial resolution live and fixed-cell microscopy to characterize endothelium-dependent vesicular trafficking in 3D.[5] The second, by Hodges et al.[6] describes an experimental rat mesentery culture model amenable to imaging, for investigating the de novo formation of blood vessels after stromal cell transplantation.

These studies are followed by four reports describing the development of novel hardware and software tools for characterizing structural and functional changes in the microcirculation. The first by Senarathna et al.[7] describes a fast, multicontrast imaging approach to characterize dysregulation of the gut microcirculation in an experimental model

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CONFLIC T OF INTEREST

None.

of necrotizing enterocolitis. The second by Li et al.[8] reports a fractal analysis approach for quantifying the complexity of microvascular networks, and demonstrate its utility by characterizing the spatiotemporal dynamics of vascular network formation in the yolk sac membrane. The third by Christie et al.[9] describes an analysis pipeline based on high-resolution in vivo optical imaging to characterize morphological and functional aspects of capillary networks in skeletal muscle. The fourth by Hu et al, provides a comparison of metrics derived from microcirculation-sensitive laser speckle contrast imaging for quantifying functional activation in the brain.[10] Next, the SI includes two studies on the lymphatic microcirculation. The first by Wang et al.[11] characterizes the dysregulated vasomotor dynamics of the collecting lymphatics during hypertension in an experimental model of spontaneously hypertensive rats. The second by Russel et al.[12] describes a new R-based software tool called “Vmeasur” for quantifying lymphatic contractility dynamics over extended length scales.

The final three reports of this SI focus on clinically applicable imaging techniques. The article by Wikslund et al.[13] describes the characterization of microvascular remodeling following skin injury. This is followed by an article by Abdelmaksoud et al.[14] describing the utility of nailfold capillary endoscopy as a potential noninvasive method for detecting microvascular changes in patients with adolescent type I diabetes. The article by Aghabaglou et al.[15] reports on the efficacy of clinically available ultrasound probes for detecting and quantifying the status of the microcirculation via a combination of in vitro and in vivo studies. The SI concludes with two comprehensive reviews: one on photoacoustic imaging by Mirg et al.[16] and another on techniques for imaging the lymphatic system by Banerjee et al.[17] covering preclinical and clinical applications.

Collectively, the articles in this special issue cover a broad range of approaches that make visible the myriad aspects of microcirculation and represent a burgeoning frontier in microcirculatory research. We are grateful to all the authors for their contributions and cannot wait to see what new innovations emerge at the intersection of imaging and the microcirculation.

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