Introduction: feature issue on *In Vivo* Microcirculation Imaging

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Abstract: The editors introduce the *Biomedical Optics Express* feature issue, "*In Vivo* Microcirculation Imaging," which includes 14 contributions from the biomedical optics community, covering such imaging techniques as optical coherence tomography, photoacoustic microscopy, laser Doppler /speckle imaging, and near infrared spectroscopy and fluorescence imaging.

OCIS codes: (000.1200) Announcements, awards, news, and organizational activities; (170.3880) Medical and biological imaging; (170.4500) Optical coherence tomography; (110.5120) Photoacoustic imaging; (110.1080) Active or adaptive optics; (170.4580) Optical diagnostics for medicine

References and links

1. Z. W. Zhi, W. Cepurna, E. Johnson, T. Shen, J. Morrison, and R. K. Wang, "Volumetric and quantitative imaging of retinal blood flow in rats with optical microangiography," Biomed. Opt. Express **2**(3), 579–591 (2011).
2. Z. W. Zhi, Y. R. Jung, Y. L. Jia, L. An, and R. K. Wang, "Highly sensitive imaging of renal microcirculation in vivo using ultrahigh sensitive optical microangiography," Biomed. Opt. Express **2**(5), 1059–1068 (2011).
3. D. Y. Kim, J. Fingler, J. S. Werner, D. M. Schwartz, S. E. Fraser, and R. J. Zawadzki, "*In vivo* volumetric imaging of human retinal circulation with phase-variance optical coherence tomography," Biomed. Opt. Express **2**(6), 1504–1513 (2011).
4. F. Jaillon, S. Makita, E.-J. Min, B. H. Lee, and Y. Yasuno, "Enhanced imaging of choroidal vasculature by high-penetration and dual-velocity optical coherence angiography," Biomed. Opt. Express **2**(5), 1147–1158 (2011).
5. T. Schmoll, A. S. G. Singh, C. Blatter, S. Schriefl, C. Ahlers, U. Schmidt-Erfurth, and R. A. Leitgeb, "Imaging of the parafoveal capillary network and its integrity analysis using fractal dimension," Biomed. Opt. Express **2**(5), 1159–1168 (2011).
6. A. S. G. Singh, T. Schmoll, and R. A. Leitgeb, "Segmentation of Doppler optical coherence tomography signatures using a support-vector machine," Biomed. Opt. Express **2**(5), 1328–1339 (2011).
7. Y. M. Wang, A. A. Fawzi, O. Tan, X. B. Zhang, and D. Huang, "Flicker-induced changes in retinal blood flow assessed by doppler optical coherence tomography," Biomed. Opt. Express **2**(7), 1852–1860 (2011).
8. J. Enfield, E. Jonathan, and M. Leahy, "*In vivo* imaging of the microcirculation of the volar forearm using correlation mapping optical coherence tomography (cmOCT)," Biomed. Opt. Express **2**(5), 1184–1193 (2011).
9. T. Liu, Q. Wei, J. Wang, S. L. Jiao, and H. F. Zhang, "Combined photoacoustic microscopy and optical coherence tomography can measure metabolic rate of oxygen," Biomed. Opt. Express **2**(5), 1359–1365 (2011).
10. P.-H. Wang, J.-J. Luh, W.-S. Chen, and M.-L. Li, "*In vivo* photoacoustic micro-imaging of *microvascular changes for Achilles tendon injury on a mouse model*," Biomed. Opt. Express **2**(6), 1462–1469 (2011).
11. M. Leutenegger, E. Martin-Williams, P. Harbi, T. Thacher, W. Raffoul, M. André, A. Lopez, P. Lasser, and T. Lasser, "Real-time full field laser Doppler imaging," Biomed. Opt. Express **2**(6), 1470–1477 (2011).
12. O. Thompson, M. Andrews, and E. Hirst, "Correction for spatial averaging in laser speckle contrast analysis," Biomed. Opt. Express **2**(4), 1021–1029 (2011).
13. S. Kwon and E. M. Sevick-Muraca, "Mouse phenotyping with near-infrared fluorescence lymphatic imaging," Biomed. Opt. Express **2**(6), 1403–1411 (2011).
14. A. V. Patil, J. Safaie, H. A. Moghaddam, F. Wallois, and R. Grebe, "Experimental investigation of NIRS spatial sensitivity," Biomed. Opt. Express **2**(6), 1478–1493 (2011).

In many different physiological and pathophysiological conditions it is crucial to image the microcirculation that sustains the nutritive flow to and from the tissue. Therefore, there is a special demand in the community, both biological and physical, to develop imaging technologies that can provide both qualitative and quantitative information as to how microcirculation responds to certain injury and/or disease, and its treatment. In this quest,

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biomedical optics can play a critical role in meeting the biological and clinical requirements to monitor and image the blood perfusion, oxygenation and vascular anatomy within microcirculatory tissue beds. This special issue of *Biomedical Optics Express* was organized to reflect the recent developments to this important activity in the biomedical optics community.

We were very pleased with the overwhelming responses from the authors to the initial call for papers which was issued in September 2010. After undergoing rigorous review process to meet the high publication standard of OSA, we selected 14 papers to be included in this special issue, covering such areas as optical coherence tomography and its variants [1–8], photoacoustic microscopy [9,10], laser Doppler/speckle imaging [11,12], and near infrared spectroscopy and fluorescence imaging [13,14]. We believe that the assembled feature issue appropriately captures the current state of the art in the field, and will be a useful depository that serves to further advance the field of *in vivo* microcirculation imaging.

Optical coherence tomography (OCT) represents the most important development in biomedical optical imaging that has revolutionized the current ophthalmic practice. Based on the optical scattering as its contrast mechanism, OCT has been demonstrated from its outset as a label free imaging tool (i.e., Doppler OCT) to image and monitor dynamic blood flow within tissue beds *in vivo*. Recent developments has seen exciting movement towards using OCT to image microcirculations, with the major efforts paid to improve its sensitivity to slow blood flows, such as in the capillaries within microcirculatory tissue beds that support the normal tissue functions. Thus it is no surprise that the papers in OCT constitute the majority portion of this feature issue, representing the trend of this development. Zhi *et al.* introduced optical microangiography imaging technique for imaging and quantifying the volumetric blood flow, down to single capillaries, within retina [1] and kidney [2] in small animal models. Kim *et al.* [3] used phase-variance OCT to characterize the human retinal circulation. Enhanced imaging of human choroidal vasculature was made possible by Jaillon *et al.* [4] with the use of the high-penetration wavelength of 1050 nm together with the dual-beam setup of conventional Doppler OCT. The imaging speed is one of the key factors that may mitigate the inevitable problems of subject movement; Schmoll *et al.* [5] reported the use of 100 kHz ultrahigh-resolution spectral domain OCT to image the parafoveal capillary network without significant motion artifacts. With the help of the phase values in the Doppler signals (i.e., phase variance OCT) as well as the available texture information, Singh *et al.* [6] introduced a method that uses a support-vector machine classifier for segmenting the retinal blood flow networks, while Huang *et al.* [7] examined the use of Doppler OCT to investigate flicker-induced changes of total retinal blood flow. Yet, another recent development in using OCT to image the microcirculations is a method that uses correlation mapping of conventional OCT signals, by the use of which Enfield *et al.* [8] reported the results of vasculature network within the volar forearm. It is clear that the use and further development of OCT technology will continue increasing our ability to image the intact microcirculations within tissue beds *in vivo*, providing critical information, both qualitatively and quantitatively, as to how microcirculation responds to certain injury and/or disease, and its treatment.

Photoacoustic microscopy (PAM) departs from OCT in that it is based on the absorption properties of biological tissue to provide the imaging contrast; thus it is inherently sensitive to microcirculation within tissue beds, because hemoglobin is one of the major absorbers among the tissue constituents. Included in this feature issue, Liu *et al.* [9] proposed to measure the metabolic rate of oxygen (MRO_2) in small animals *in vivo* using a multimodal imaging system that combines laser-scanning optical-resolution PAM and spectral-domain OCT. With the scattering contrast provided by OCT and the absorption contrast by PAM, the complementary information delivered by their combined system enabled the MRO_2 within blood vessels to be evaluated. Another study by Wang *et al.* [10] reported *in vivo* photoacoustic micro-imaging of microvascular changes for Achilles tendon injury on a mouse model, demonstrating that photoacoustic imaging can potentially be a complementary tool for high sensitive diagnosis and assessment of treatment performance in tendinopathy.

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Two additional papers are devoted to laser speckle imaging (LSI) and laser Doppler imaging (LDI) of the microcirculations *in vivo*. Leutenegger *et al.* [11] introduced a full-field laser Doppler imaging instrument, which enabled real-time *in vivo* assessment of blood flow in dermal tissue and skin. Thompson *et al.* [12] presented a method to allow for correcting spatial averaging in laser speckle contrast analysis, which is necessary because practical laser speckle contrast analysis systems face a problem of spatial averaging of speckles, due to the pixel size in the cameras used. LSI and LDI are two important imaging modalities that have been used extensively in both preclinical and clinical investigations. The simplicity and cost effectiveness of their nature would no doubt continue contributing a great deal to our improved understanding of the vascular involvements in a number of dermatological and neurologic diseases.

The final two papers applied near infrared spectroscopy (NIRS) and fluorescence imaging to measure and image the hemodynamics and lymphatic systems in small animal models. Kwon and Sevick-Muraca [13] reported an exciting approach that uses near-infrared fluorescence to nondestructively and quantitatively image the lymphatic system and its contractile function for mouse phenotyping, with the help of injecting indocyanine green in normal and transgenic mice. This study can be useful for quantifying lymphatic function for future studies designed to discern differences in lymphatic function in murine models of human lymphatic disease. Last, Patil *et al.* [14] investigated the spatial sensitivity of near-infrared optical measurements by using an experimental approach in order to understand the relationship between spatial changes in optical properties and corresponding changes in the NIRS signal. This is important because proper understanding of the origin of NIRS signals would improve its clinical interpretation in the investigations of hemodynamic changes.

All papers included in this feature issue have resulted from a rigorous peer review process, and we are indebted to the referees for their efforts in ensuring that the Optical Society of America's standards for quality and integrity were met, and more importantly for their timely responses to the reviewing requests that resulted in expressed decision made on the submitted papers. We are also especially gratefully to Joseph A. Izatt (Editor-in-Chief), Gregory W. Faris (Deputy Editor), and the publication staff at the Optical Society of America (Joe Richardson, Miriam Day, Kelly Cohen and many others) for their hard work and dedication to this feature issue.

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