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Editorial: *In vivo* opto-physiological imaging

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Editorial on the Research Topic
In Vivo Opto-Physiological Imaging https://www.frontiersin.org/researchtopic/12898

This edition of Frontiers in Physics is focussed on the research topic "*In Vivo* Opto-Physiological Imaging" and emphasises the value of delivering high performance multi-functional *in vivo* imaging and its dependence on the development of sophisticated electronics, executive software and, increasingly, the application of machine learning (ML) techniques to a diverse range of signal processing algorithms.

Over the last half century there has been a steady increase in the diversity of optical techniques used to distinguish normal from pathological function, and these have provided an ever-widening range of diagnostic means for monitoring treatment effectiveness. In this special edition of Frontiers in Physics, two papers from Arrigo and co-workers Arrigo et al., Arrigo et al. show how developments in optical coherence tomography (OCT) hardware and image processing are making it possible to quantify neovascularisation associated with age-related macular degeneration (AMD); thus affording new ways to investigate its pathogenesis, development and likely outcome. This troubling disease, with a prevalence in Europe of over 2% [1], is an increasing burden in countries with ageing populations [2].

The basic idea in Arrigo et al. is to understand why OCT does not reveal the full extent of neovascular lesions in AMD, especially in the type I variant. The performance of OCT in this context is also limited by differences between manufacturers and experimental protocols. Given these constraints, the aim of this study was to distinguish between high and low reflectivity lesions (as a measure of well or poorly detected blood flow) and to see the relationship between OCT performance and blood flow when compared to the gold standard of angiography, (either using fluorescein or indocyanine green, ICG). By measuring average lesion area from images of 50 eyes (beautiful images judging by the representative examples presented), the authors show that the agreement between lesion areas measured by OCT and angiography is remarkably close for type II lesions, while for type 1 lesions, the agreement is good only when using early ICG angiography data. The reflectivity measurements provide a valuable means of assessing differences in regional blood flow, a variable unavailable from gold standard fluorescence angiography.

The second paper by Arrigo et al., a preliminary prospective cohort study on 28 patients with AMD, again focussing on the retinal microvasculature, considers correlations between variables such as vessel tortuosity reflectivity and lesion area; and the growth of the lesions during a year in which they were treated with anti-VEGF to suppress blood vessel growth and lesion size. The results of this small study, while not providing conclusive evidence that the effectiveness of the treatment can be reliably monitored by OCT, demonstrate how differential growth of capillaries, their morphology and blood flow rate can be reliably and repeatably quantified. Such information is essential for a better understanding of the pathogenesis of AMD and demonstrates the potential of OCT to monitor progression and treatment effectiveness.

Moving from the softest tissues in the body to the bones, the review by Zhang and McCully Zhang et al. on quantifying blood flow in limb bones by near infra-red spectroscopy (NIRS) is a tantalising addition to the sparse literature on this subject. At first glance one might think that the opacity of bony tissue and its depth below the skin surface, would provide only the weakest of back scattered signals; and to a great extent this is true. However, by careful signal processing and limiting measurements to superficial bones, such as the tibia, it is possible to obtain a pulsatile signal and to separate this from microvascular flow in the soft tissue between the bone and the skin; although it is not entirely clear how this is achieved. Absolute measurement of blood flow is not yet possible but is accessed by tracking the rate of change in tissue oxygenation during the induction of ischaemia with a restricting cuff inflated to suprasystolic pressure and during hyperaemic flow following the cuff release. Whether it is possible to assess differences in this response between healthy and diseased subjects remains to be seen. A second type of intervention, again with the potential to distinguish between healthy and diseased, or young and old bone, is to record the effect of exercise on the NIRS signal. Again, studies in human subjects are urgently needed.

By contrast, the report by Yoshida et al. shows how echo Doppler is able to estimate the magnitude of pulse wave reflection, arterial stiffness and most importantly central pressure, in the pulmonary circulation. The presence of reflected waves in the vascular system, especially near the heart, has a marked effect on cardiac load, pumping efficiency and systolic pressure. In general, positive reflections lead to hypertrophy of the major systemic and pulmonary arteries, which increases their stiffness, thus augmenting cardiac load and setting up a positive feedback loop which can ultimately lead to heart failure and, in the systemic circulation, to stroke. Unfortunately, central pressure and wave reflection cannot easily be measured non-invasively so the report by Yoshida et al., albeit in an animal model, is both timely and welcome. By comparing several haemodynamic variables obtained invasively using a catheter (the tip equipped with a pressure and flow sensor) placed in the pulmonary artery near its origin with the same variables derived indirectly from ultrasound images using wave intensity analysis [3], it was shown that this non-invasive ultrasound technique was able to estimate systolic and diastolic pressures, reflection coefficient and pulse wave speed. Furthermore, when pulmonary hypertension was induced by injection of microspheres, the agreement between the catheter based and ultrasonic measurements was maintained. These elegant experiments suggest that non-invasive diagnosis and quantification of pulmonary hypertension are within the grasp of clinicians, although much validation is needed to ensure accuracy and precision in human subjects.

The four papers included in this special edition provide only a glimpse of the possibilities available to the research and clinical communities of advanced imaging techniques for the diagnosis and treatment-monitoring of an ever-widening range of diseases, as well as more general health assessment. With recent advances in optoelectronic hardware together with novel embedded signal processing algorithms enhanced with ML techniques; real-time opto-physiological imaging will be realised as an *in vivo* tool not only for front-line clinical professionals but also suitable for individual personalised home-based healthcare.

Author contributions

All authors listed have made a substantial, direct, and intellectual contributions to the editorial work and approved it for publication.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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