PhD Thesis Defense TANJA DRAGOJEVIC 'Translation Of Speckle Contrast Optical Techniques From Bench-Top To In Vivo Applications'

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Friday, May 10, 11:00. ICFO Auditorium

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Cerebral blood flow (CBF) feeds the brain tissue with oxygen and clears the by-products of its metabolism to maintain healthy functioning. There are many contexts in the clinics, in biomedical sciences and in the wellness industry where retrieving information about CBF has important potential applications. Ideally, these methods would be non-invasive, continuous, portable, bedside or even wearable. Diffuse optical methods are currently the front-runners that promise to fill this gap.

In particular, laser speckle based techniques are able to measure CBF directly without the need for any exogenous agents or surrogate parameters. However, their current implementations such as diffuse correlation spectroscopy (DCS) and laser speckle contrast imaging (LSCI) are either limited in penetration depth (LSCI) or scalability (DCS).
In this thesis, new methods and instrumentation were developed for speckle contrast optical spectroscopy and tomography (SCOS/SCOT). These methods allowed for measuring deep tissue blood flow with a relatively high spatial and depth resolution.

In particular, previously, speckle contrast optical spectroscopy, which has been introduced by our group, was developed to exploit multi-exposure and multi-distance speckle contrast measurements to retrieve deep tissue (_ 1 cm) flow information.
However, the application of the technique was limited to phantoms or single subject measurements with a multi-distance approach.

On the other hand, in the case of multi-exposure time, the temporal resolution was low, thus not allowing recovery of fast changes.
To improve the temporal resolution, therefore to allow imaging of faster blood flow changes and also for the improvement of the signal-to-noise ratio by averaging, faster detectors with negligible inter-frame dead time, low or no readout noise and with high photon sensitivity needed to be implemented. It this case, a continuous acquisition of the frames (one after the other) could be done and in post-processing images could be summed to get desired exposure times, giving higher temporal resolution than in already used detectors. I have implemented this approach and named it single-shot acquisition multi-exposure speckle imaging (sMESI) and is demonstrated here. To verify the method, a comparison between standard and the single-shot acquisition was done in same conditions in phantoms and in vivo, showing high agreement between the methods. Thus allowing to move from phantom-based measurements to measuring deep tissue blood flow in the adult human brain.

This allowed us to envision high-density tomographic measurements with SCOT and, also an ultra-portable, low-cost, compact point measurement system with SCOS. The latter was implemented with a custom single-photon avalanche photodiode (SPAD) array, where sixty-four detectors were embedded in a small tube. I have demonstrated and validated real-time deep tissue blood flow measurements with this system paving the way towards the development of wearable cerebral blood flow monitors.

On the other hand, high-density tomographic measurement of CBF was previously prohibitively complex and expensive.

However, my work has introduced this both in small animalmodels with tens of housands of source-detector pairs through the intact skull and using a 32x64 SPAD camera on the adult human brain.

Overall, these contributions demonstrated the development of a new class of diffuse optical CBF measurement technologies by breaking the scalability and cost barriers. The next step is to introduce these technologies to pre-clinical and clinical research.

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