Towards *In-Vivo* Characterization and Deep Imaging of the Cornea and Beyond

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Abstract: This talk reviews ongoing work towards *in-vivo* characterization and deep imaging of the human eye, primarily for the purpose of quantifying corneal transparency, for which to date no objective clinical tool exists. © 2018 The Author(s)

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1. Introduction

The diagnosis and management of ophthalmic diseases has been transformed in the last decade by the advent of optical coherence tomography (OCT) [1]. Ophthalmic OCT uses interference of broadband or tunable light to generate optical sections of the retina and anterior segment. However, conventional (time- or spectral-domain) clinical OCT systems generally suffer from limited lateral resolution and quantification capabilities.

This talk reviews ongoing work towards *in-vivo* characterization and deep imaging of the human eye, primarily based on full-field optical coherence tomographic microscopy (FF-OCT or FFOCM, a high-resolution variant of OCT) and for the purpose of quantifying corneal transparency, for which to date no objective clinical tool exists.

2. Methods and Results

Full-field optical coherence tomographic microscopy (FF-OCT or FF-OCM [2,3]), originally developed by Prof. Claude Boccara's group at the *Institut Langevin*, uses high numerical-aperture optics and acquires *en face* (parallel to the tissue surface) tomographic images without x-y scanning, thereby achieving a lateral resolution comparable to the resolution in depth. A spinoff from *Institut Langevin* (LLTech, SAS) has commercialized FF-OCT for *in-vitro* microscopy.

At the Quinze-Vingts National Eye Hospital (in collaboration with Prof. Vincent Borderie's anterior segment service), we have been investigating the device's potential for examining donor corneas before transplantation, as an addition and improvement upon current eye-banking procedures for graft quality control [4]. In fact, we have already demonstrated the capability of FF-OCT to provide structural information superior to histology and to identify more disease indicators as was possible with the combination of clinical OCT and confocal microscopy [5]. Further, the technique was able to identify new quantitative parameters in the assessment of human donor corneal stroma [4,5] (note that the transparency of the cornea largely relates directly to stromal structure [6,7]). Most notably, objective analysis of stromal light backscattering with FF-OCT (also in collaboration with Prof. Karsten Plamann from the *Laboratoire d'Optique et Biosciences*) has shown promise in the quantification of corneal transparency, as well as in differentiating abnormal from normal corneal tissues [8].

In collaboration with Prof. Boccara's group at the *Institut Langevin*, ongoing work [9] seeks to make FF-OCT suitable for *in-vivo* characterization of the cornea, with the development of a non-contact system that integrates an ultrahigh-speed CMOS camera. Contrary to confocal microscopy [10], axial resolution (determined by the light source bandwidth) and lateral resolution (determined by the resolving power of the objectives) are decoupled in FF-OCT. Thus, FF-OCT can achieve non-contact operation with moderate numerical aperture objectives, and at the same time high lateral and axial resolutions down to 1 μm along with a relatively large field-of-view.

To further enhance FF-OCT technology and enable deeper penetration into the corneal tissue and beyond, we are also exploring axial motion compensation (collaboration with Prof. Jin Kang, at the Johns Hopkins Whiting School of Engineering [11]) and light manipulation (collaboration with Dr. Alexandre Aubry, at the *Institut Langevin* [12,13], an expert in light manipulation techniques, in particular the backscattering matrix approach [14,15]) techniques.

3. Discussion and Conclusion

These advances will establish the foundation for and the development of new clinical tools and diagnostic procedures permitting the objective and quantitative characterization of corneal transparency. Loss of corneal

transparency is a major cause of visual handicap worldwide, affecting over 10 million people [16]. While early diagnosis and quantitative follow-up could improve clinical outcome and hence prevent loss of vision, means to assess corneal transparency are extremely limited and in current clinical and eye-bank practice usually involve a subjective and qualitative observation of opacities. Hence, the ability to objectively and quantitatively assess and monitor changes in corneal transparency will have a substantial impact in the study, prevention, diagnosis, treatment and monitoring of various pathologies as well as surgeries affecting corneal transparency.

Beyond the characterization of corneal transparency, the presented research will open the door to the characterization of transparencies of other ocular media (most notably of the crystalline lens, which will be important to understand the various aspects and factors in cataract development). In addition, the technological FF-OCT enhancements, specifically the implementation of a backscattering matrix approach for eye imaging [12,13] that takes advantage of recent advances in light-manipulation and wavefront-shaping techniques [14,15], have implications beyond that of ocular media transparency characterization, most notably for imaging through ocular media opacities (*e.g.*, imaging the retina when there is loss of ocular media transparency, such as imaging through cataract opacities).

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