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Anterior segment optical coherence tomography angiography

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Chapter 8

Discussion and Future Perspectives

CHAPTER 8: DISCUSSION AND FUTURE PERSPECTIVES

Summary and Overview

In this thesis, I have described a novel application of OCT angiography (OCTA), an emerging technique for imaging ocular vasculature, as a rapid, non-contact method for imaging the corneal vascularisation. This application of OCTA may be useful for a diverse range of clinical applications, from the objective delineation of corneal vessels to monitoring treatment of corneal inflammatory disorders. First in Chapter 2, I described a technique for adapting a retina OCTA system to use in the cornea, and found that it was possible to produce OCT angiograms of the corneal and limbal vasculature with substantial consistency in healthy human eyes. I then described a method of performing image analysis to quantify corneal vascularisation and the technique of analyzing en face images with accurate segmentation in the abnormal human cornea in vivo (Chapter 3). In Chapter 4, I elaborated on how in vivo OCTA images were comparable to the current gold standard for vessel visualisation, ICG angiography (ICGA). Here, we found that although the agreement between OCTA and ICGA scans was good, the OCTA overestimated vessel density compared with the ICGA, which needs to be noted in future studies. Next, in Chapter 5, I described how OCTA was used successfully in serial imaging of abnormal corneal vascularisation in vivo to monitor changes in vessel density in a longitudinal study. Following this, I executed a study of OCTA imaging of corneal vascularisation in an animal model and found that OCTA was able to detect smaller vessels compared to slit-lamp photography (SLP) and ICGA (Chapter 6). Finally in Chapter 7, I compared two different OCTA systems to scan the cornea, one based on split-spectrum amplitude decorrelation angiography (SSADA) and one based on spectral domain OCTA (SD OCTA), and found that although correlation was moderately good, SSADA compared with SD OCTA reported a consistently greater vessel density. This needs to be taken into consideration when using different imaging systems.

Discussion

Specifically in the anterior segment, OCTA has many potential advantages over current imaging techniques. Firstly, OCTA can rapidly acquire images in a non-invasive and dye-free way, thus saving time in busy clinics and avoiding dye-related side effects and offering a more patient-friendly alternative to invasive dye-based angiography such as ICGA (Chapter 2).¹ The absence of leakage also ensures that deeper vessels are not obscured (Chapter 3).² Secondly, OCTA can produce high-resolution cross-sectional images, which can be segmented into different layers, allowing visualization of vessels at different depths and in different planes, including “en face” - Figure 4 (Chapter 4).³ These features can provide accurate localisation of the pathology, which will be helpful for diagnosis or during planning for surgery or other treatment (Chapter 5).^{4,5} Thirdly, OCTA has shown to detect vascularisation even in cases with severe corneal opacification, which would not have been visible by SLP (Chapter 6).⁶ Nonetheless, it is also important to note the current limitations of OCTA. This includes restricted field of view, lack of information on flow speed, lack of information on vessel maturity due to absence of leakage, projection and motion artefacts caused by scattering and lack of motion tracking system, inability to differentiate afferent and efferent vessels, and the need for careful examination of artefacts that might be mistaken as vessels, such as from hyper-reflective structures like corneal fibrosis (Chapter 7).^{1, 2, 5}

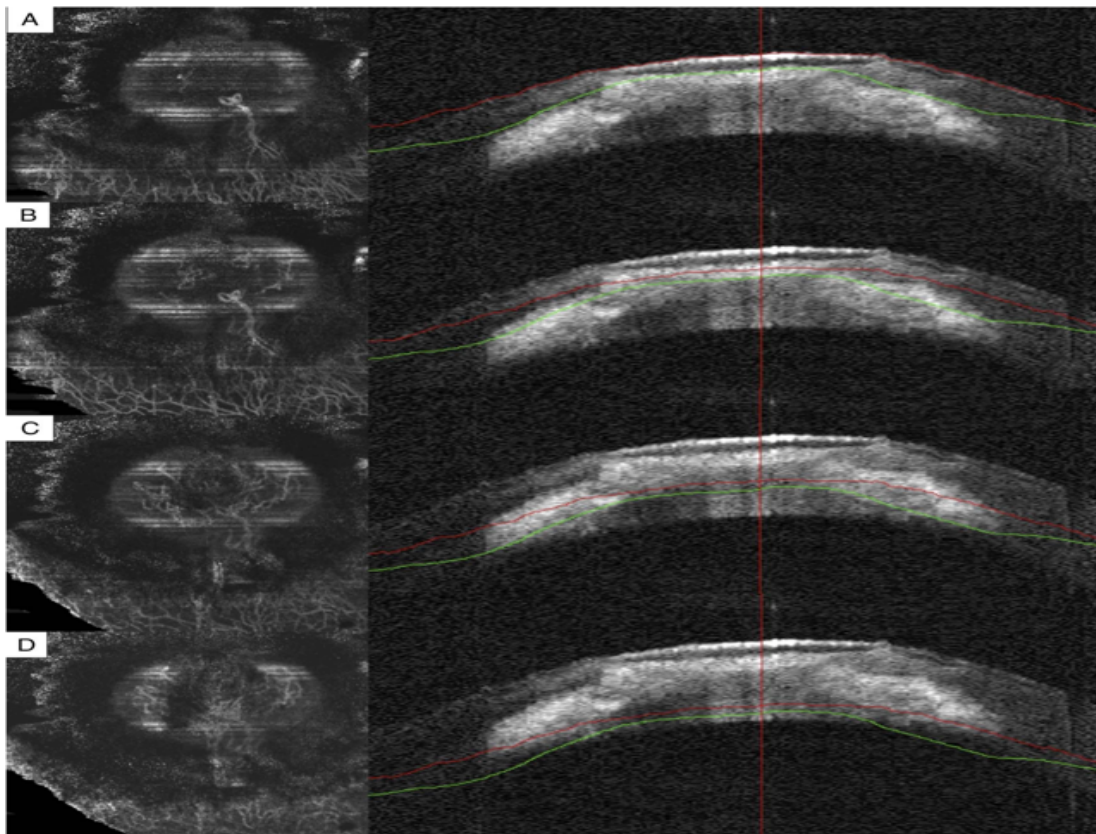


Figure 4. Example of cross-sectional OCTA images demonstrating the size and depth of a corneal scar (right) and corresponding en face OCTA images showing the location of the feeder blood vessel (left).

Although OCTA is currently not yet extensively used in clinics for corneal assessment, this thesis suggests that there may be already some useful clinical indications such as detecting vascularisation that are not visible due to reasons such as scarring (Chapter 3).⁷ Images of good quality and repeatability have been obtained for normal avascular corneas; as well as abnormal corneal vascularisation due to herpetic keratitis, corneal transplantation, bacterial keratitis, limbal stem cell deficiency, and pterygium (Chapter 5).³ In addition, studies suggested that OCTA might be able to visualize early corneal vascularisation more clearly than SLP.^{6,7} Also, OCTA may reveal fine abnormal vessels that in cases with corneal opacification, would have gone undetected by SLP.^{6,7}

I would like to acknowledge the limitations of the studies and experiments presented in my thesis. Firstly, many of the human in vivo studies were performed in a small number of eyes and in cross-sectional studies – as these were pilot studies using an imaging system that was not yet validated for the cornea. Second, a learning curve is required before consistent and good quality OCTA images can be obtained. This needs to be taken into consideration when it comes to generalizability of the results and actual application in the clinical setting. Third, image analysis, segmentation, and vessel measurements are still subjective, although we made efforts to be as objective as possible with images that were analysed by two or more masked observers. Therefore, many of our observations should be repeated in future studies once cardinal limitations of the current systems have been solved.

Nonetheless, I believe this thesis supports that the role of OCTA for the cornea is promising in future clinical applications. With the combined structural and vascular information, OCTA can potentially aid diagnosis of corneal pathologies, preoperative surgical planning and prognostication of diseases such as early limbal stem cell deficiency (Chapter 7).

Current Limitations of OCTA Technology for the Anterior Segment

The most important current limitations of OCTA technology for the cornea and other parts of the anterior segment arise due to the fact that OCTA systems are designed specifically with the intention of imaging the posterior segment. Thus, adapting OCTA for the anterior segment has resulted in some issues. Firstly, there is a need to make adjustments to scanning protocols and to use an anterior segment adaptor lens (Chapter 2).^{1, 7} Since the internal software of these systems are calibrated for the posterior segment, there can be non-parallel segmentation and artefacts caused by light scatter due to the cornea curvature, resulting in inaccurate vessel density calculations during depth-resolved analysis (Chapter 3).^{5, 8}

Secondly, the in-built eye-tracking systems cannot be used for the anterior segment. Also, anterior segment OCTA (AS OCTA) is unable to register patients and provide localization clues required for comparison of serial scans (Chapter 5).^{3, 9} While current studies on serial OCTA have shown that adjunct software for post-hoc registration for image analysis have helped manage this difficulty, an eye-tracking system is still desirable, also because it can help to reduce motion artefacts, which in turn will improve image quality.^{2, 10}

Thirdly, AS OCTA may not delineate well deeper vessels in eyes with corneal opacities or dense iris pigmentation, or vessels in thick iris tumors.^{7, 11, 12} The system also may have poorer detection of vessels with minimal flow since motion of erythrocytes is much slower in those vessels with small diameters.⁵ Since internal system algorithms of OCTA are optimized for the posterior segment with mainly transverse flows in those vessels, anterior segment vessels with axial flow may not be well detected.⁴

Lastly, image artefacts are common in AS OCTA scans. As AS OCTA systems do not yet have motion correction for saccadic eye movement, these movements often result in motion artefacts.² Also, vessels in the superficial layers can cause projection artefacts on the deeper layers as a result of multiple scattering. This can be misinterpreted by image analysis software as abnormal or additional vessels, resulting in inaccurate vessel density calculations. However, this problem can be mitigated by performing multiple scans and comparing these consecutive scans in en face function, or correlating with images from other techniques such as SLP.^{7, 10} In addition, with improvements in image analysis software, automated segmentation ability, better filtering techniques and threshold analysis, artefacts can be better managed.¹⁰

To summarize, further developments are needed as AS OCTA imaging is a new field and there are still many areas that require optimisation for the accurate imaging and clinical application in the cornea. Optimisation requires updates in both software and hardware. Software enhancements are needed to improve image resolution, reduce artefacts, and enhance the depth of field in the cornea.^{7, 18, 19} With further upgrading in scanning speed, improved wide-field imaging OCTA and automated montage functions by the internal software, this will become more realisable.² Improvements in segmentation are needed as it currently done manually for AS OCTA scans, because built-in automated segmentation is optimized for the posterior segment. Manual segmentation may result in artefacts due to non-parallel segmentation.⁸ Automated programs which already exist for AS OCT may be further developed to include AS OCTA segmentation in the future.²⁰ It would be useful to include a reliant eye tracker and image registration for AS OCTA imaging, as movements introduces motion artefacts that may lead to loss of detail and inaccurate vessel measurements in the images. However, this problem can be mitigated with developments in eye tracking and image registration.^{1, 8} Image processing algorithms that can reduce projection, shadow and motion artefacts could help to mitigate these limitations as well.⁵

Future Perspectives

From this thesis, we have demonstrated that there are many potential clinical applications of AS OCTA. Currently, AS OCTA would probably be useful objectively delineating corneal vascularisation in a variety of conditions, including ocular inflammatory diseases, limbal stem cell deficiency, anterior segment tumor vascularity, secondary or neovascular glaucoma, iris neovascularisation, and assessing episcleral venous flow in glaucoma.^{8, 10} Furthermore, with structural information from OCT scans, OCTA could aid in treatment or surgical planning, such as surgical treatment of corneal vascularisation, or planning of corneal transplantation surgeries in vascular lesions or scars.¹³ The quantitative information about the depth of pathology makes OCTA useful for evaluating the effectiveness of intervention, such as subconjunctival vascularity associated with bleb morphology after trabeculectomy.⁹

However, due to the above-mentioned technical limitations, further improvements and studies are needed before OCTA can be used for imaging the sclera, conjunctiva, and iris vasculature.¹⁴ Recently, one study revealed that OCTA successfully visualized intrascleral and conjunctival vessels, with a denser vasculature presented than conventional angiography. However, though episcleral and conjunctival vessels have been imaged by imaging modalities such as FA, non-invasive evaluation of vessels at a specific depth and imaging of intra-scleral vessels have been challenging.¹⁵ The ability to image scleral and conjunctival vessels separately will be beneficial to understanding conditions such as scleritis or uveitis, or the effect of the sclera and conjunctiva on glaucoma filtration surgery once the technique is optimised.¹⁴ Advancements in AS OCTA are also needed for reliable imaging of iris vasculature, which could provide multiple clinical applications in the future.¹⁶ The role of the iris and its vasculature have been increasingly recognized in homeostasis of the anterior chamber and pathogenesis of some eye diseases, including glaucoma and cataracts.¹⁷

Furthermore, it is postulated that iris vasculature studies can shed light on pathophysiology of developmental anomalies, degenerative diseases, diabetes microangiopathy, glaucoma and uveitis.¹¹ Iris vasculature is currently studied using FA and ICGA, with their invasive nature.¹⁶ Hence, non-invasive OCTA has become a potentially appealing alternative for the future.¹¹ Preliminary reports suggest that OCTA has been found to produce comparable images of differently pigmented healthy iris with FA, and with significantly more detail.^{11, 16} Apart from the applications mentioned above, OCTA may also be useful in diagnosis of ischemic conditions in systemic disease, or vascular changes secondary to uveitis, diabetic retinopathy or obstructive conditions.¹¹

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