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The potential for evaluating the effects of intensified antithrombotic therapy using retinal optical coherence tomography angiography

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ABSTRACT

Oral anticoagulants are widely used in the treatment and prevention of both venous and arterial thromboembolism. They are classified into vitamin K anticoagulants (VKAs) and non-vitamin K antagonist oral anticoagulants (NOACs). The main advantage of NOACs over VKAs is the absence of the need for continuous monitoring. However, there are concerns about their effectiveness and safety in certain clinical situations. In this manuscript, I discussed the possibility of using optical coherence tomography angiography [OCTA] in the monitoring of the activity of NOACs. The rapid development of OCTA technology is very promising. Further research and development will extend its use beyond the realm of ophthalmology.

Background

Oral anticoagulants are widely used in the treatment and prevention of both venous and arterial thromboembolism. They are classified into vitamin K anticoagulants (VKAs) and non-vitamin K antagonist oral anticoagulants (NOACs). Warfarin was approved by the United States Food and Drug Administration [US FDA] in 1954 [1]. It acts by inhibiting the synthesis of vitamin K-dependent clotting factors [Factors II, VII, IX, and X] via inhibition of the C1 subunit of vitamin K epoxide reductase [VKORC1] enzyme complex. Warfarin also inhibits the synthesis of anticoagulant proteins C and S.

NOACs was first introduced in 2010. Currently, there are four NOACs in the market; dabigatran [Praxada], rivaroxaban [Xarelto], apixaban [Eliquis] and edoxaban [Savaysa]. Dabigatran and its acyl glucuronides are competitive, direct thrombin inhibitors [factor IIa]. On the other hand, rivaroxaban, apixaban and edoxaban activities involve factor Xa and prothrombinase activity.

Monitoring of oral anticoagulants

The main advantage of NOACs over VKAs is the absence of the need for continuous monitoring. For warfarin, there is a need to maintain the patient within a therapeutic window by dose adjustment. NOACs have wide therapeutic window due to their predictable pharmacokinetics and pharmacodynamics, a rapid onset and offset of action, and a short half-life.

Currently, there are few haematological methods to monitor the activity of oral anticoagulants. Activated partial thromboplastin time [aPTT] and prothrombin time/International Normalised Ratio [PT/INR] are used to monitor the activity of VKAs.

The tests for the monitoring of NOACs are less widely used at the moment. Thrombin clotting time [TCT], Ecarin clotting time [ECT] and Thrombin Inhibitor Assay [Hemoclot ®] can be used for dabigatran. However, these tests do not predict the "in vivo" bleeding risk for an individual [2,3]. Anti-factor Xa assay has been used to monitor rivaroxaban, apixaban and edoxaban [4,5]. Thrombin generation assay [TGA] has also been used to assess the influence of NOACs on coagulation [6]. Global coagulation assays [PT, aPTT, TGA and thromboelastography] have been studied and found to be influenced by both VKAs and NOACs [7].

Although routine monitoring of NOACs is deem unnecessary, there are concerns about their effectiveness and safety in certain clinical situations. Therefore there is a need to explore a non-invasive method to evaluate the anticoagulant effect of these agents.

Optical coherence tomography [OCT] and optical coherence tomography angiography [OCTA]

The use of OCT for the human eye was first presented at the International Conference of Optics in Life Sciences in 1990 [8]. Since then, the technology has evolved tremendously. The current OCT machines are able to provide resolution details of retinal images in the order of few micrometers.

OCTA is a non-invasive imaging technique that provides angiographic information of the retinal blood vessels. Gao et al. and de Carlo et al. have discussed extensively on the history and principles of OCTA

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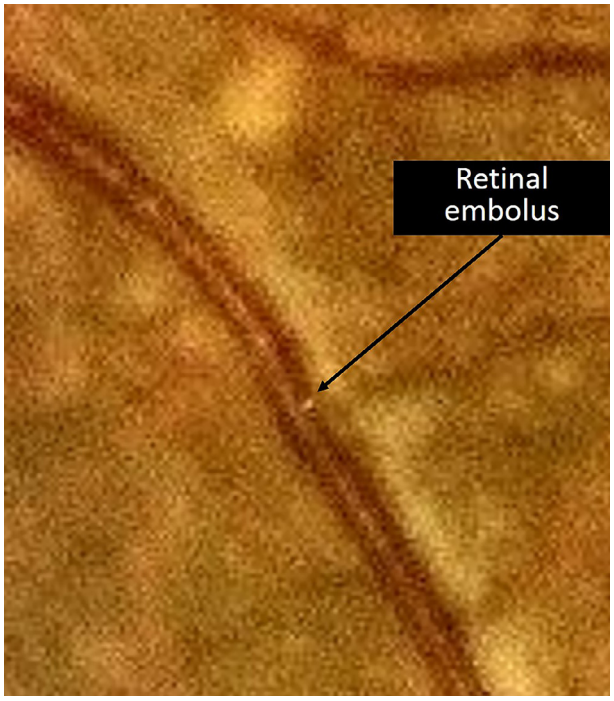

Fig. 1. Retinal embolus.

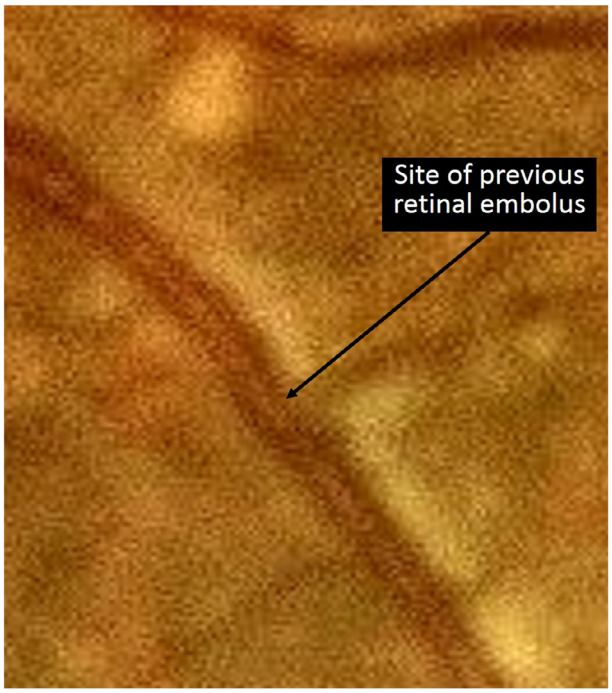

Fig. 3. Disappearance of retinal embolus.

[9,10].

Basically, OCTA is based on low-coherence interferometry to acquire volumetric angiographic information. It requires less than 10 seconds to perform and does not require the use of intravenous contrast agents. Blood cells movement within the blood vessels causes decorellation signals which are then used by the OCTA to create angiograms. This process of angiogram creation by the OCTA relies on the change between consecutive OCT b-scans [cross-sectional image where the amplitude of reflections are represented in a gray scale or a false-color scale]. Blood vessels with slow flow, where blood cell movements are not detected by the consecutive OCT b-scans will not be visualised [10].

Case study

A 75 year old gentleman with chronic atrial fibrillation was on maintenance therapy apixaban 5 mg twice daily. He was admitted for left acute brachial artery thrombosis. The condition was successfully

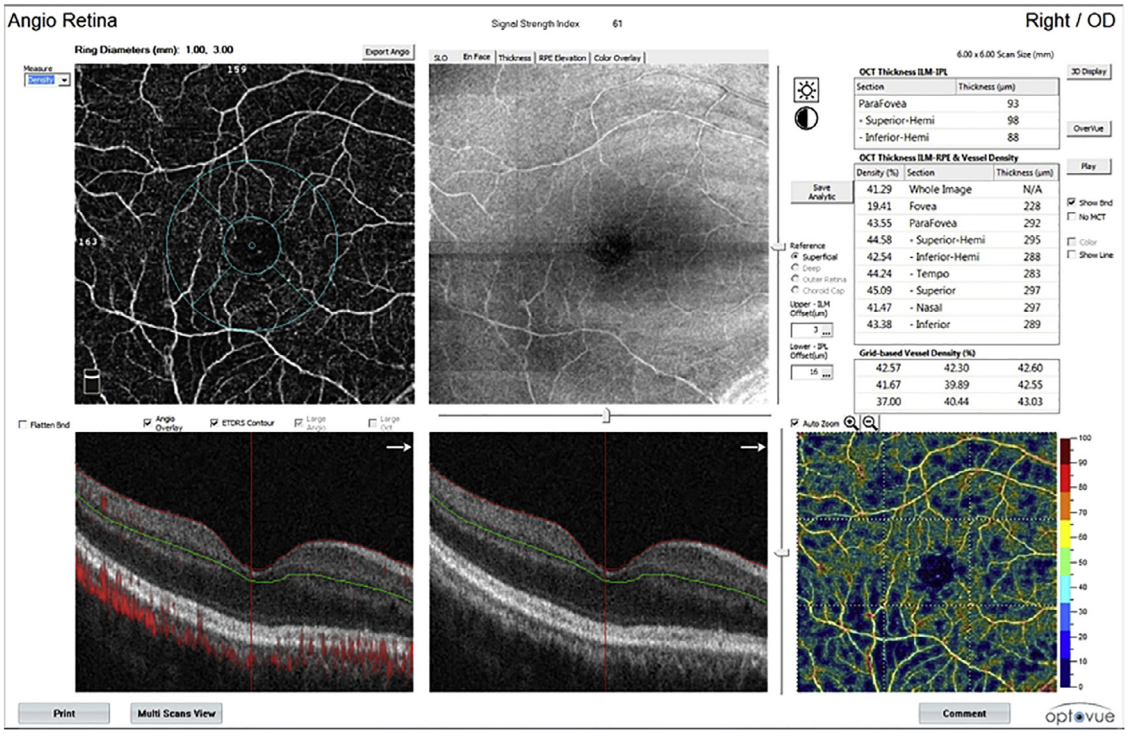

Fig. 2. A. OCTA at presentation.