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Comparison of Enhanced Depth Imaging and Swept Source Optical Coherence Tomography in Assessment of Vogt-Koyanagi-Harada Disease

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Abstract

Objective: To compare enhanced depth imaging optical coherence tomography (EDI-OCT) and swept source OCT (SS-OCT) images in Vogt-Koyanagi-Harada (VKH) disease to determine the agreement of subfoveal choroidal thickness (SFCT) measurements between them.

Methods: SFCT of one eye of all consecutive VKH patients seen at the Singapore National Eye Centre during 2012 to 2013 was measured using both modalities by one masked trained observer. Charts were retrospectively reviewed for demographics, duration of disease and phase of disease. The acute phase was defined as being within the first 6 months of onset and the chronic phase any time thereafter.

Results: 137 SS-OCT and EDI-OCT scans were obtained from 48 patients. Mean age was 52 years. Majority were Chinese (31 patients, 65%) and females (29,60%). The quality of SS-OCT images were superior to EDI-OCT during the acute phase but were similar in the chronic phase. There was good inter-OCT correlation for both the acute and the chronic phase (Mean difference in SFCT ± 2 standard deviation of -22.7 ± 39.4 microns and -13.0 ± 42 microns respectively).The mean SFCT was greater the in acute phase (352.4 microns, SD 89.5) than in the chronic phase (221.5 microns, SD116.1, P<0.001) and became less with increasing age and duration of disease (Spearman's rho -0.60 and -0.64 respectively, P<0.001).

Conclusion: SS-OCT provides much better resolution images of the choroid than EDI-OCT resulting in more measurable images. There was good agreement of SFCT measurements between the two modalities when both sets of images were measurable.

Keywords Vogt-Koyanagi-Harada; Swept source and enhanced depth imaging optical coherence tomography

Introduction

The acute phase of Vogt-Koyanagi-Harada Disease (VKH) is characterized by diffuse choroiditis and focal or bullous serous retinal detachment. With immunosuppressive therapy, the height and extent of the serous retinal detachment reduces within weeks and this is fairly easily monitored clinically. On the other hand, monitoring of the underlying choroidal inflammation is challenging as mild choroidal swelling is difficult to detect on clinical examination and eyes with chronic subclinical inflammation may subsequently develop extensive fundal changes including sunset glow fundus, peripapillary atrophy (PPA) and chorioretinal atrophy [1,2] which can impair their visual function [3,4]. Indocyanine green angiography (ICGA) is one of the modalities used to detect any ongoing inflammation in eyes with chronic disease and hence guide therapy. However it is invasive, costly and is contraindicated in patients who are allergic to iodides.

B scan ultrasonography is able to demonstrate the grossly swollen choroid of the acute phase but its resolution is too poor for it to be used for monitoring changes in choroidal thickness during the chronic phase. Spectral domain optical coherence tomography, in particular the enhanced depth imaging mode (EDI-OCT), provides far better resolution of choroidal thickness. It is able to quantify the changes in the subfoveal choroidal thickness (SFCT) as the acute phase resolves and the eye becomes quiescent [5-8]. It has also been able to demonstrate a negative correlation between choroidal thickness and duration of disease as well as choroidal depigmentation in eyes with convalescent disease [6,9,10]. However despite its much improved resolution as compared to B scan ultrasound, it is still unable to measure choroidal thickness that is greater than 1000 microns and its utility in detecting any potential change in SFCT during episodes of recurrence in chronic disease is also limited.[9] This may be related to the resolution of the EDI-OCT scan or alternatively may be partly due to the fact that the magnitude of the change in SFCT during episodes of recurrences may be much lower than that occurring during the acute disease. In particular, Da Silva noted that the difference in

thickness between eyes with and without clinically active disease in convalescent disease may be as little as 16 microns [9].

The swept source OCT (SS-OCT) is a new generation Fourier-domain OCT which uses a probe light with a wavelength-sweeping laser of 1050 nm and 100nm tuning range, allowing higher penetration of tissues than conventional OCT (wavelength 850nm) and with an axial resolution of 8 microns. The high scan speed (axial scan rate of 100,000 Hz) and relatively lower sensitivity roll-off depth enables better visualization of the choroid [11-13]. This study aims to compare the quality of the images as well as the limits of agreement of measurements of SFCT obtained using the EDI-OCT with that of the SS-OCT.

Methods

This is a retrospective study conducted at the Singapore National Eye Centre. This study was approved by the Central Institutional Review Board of SingHealth. From July 2012 to October 2013, all consecutive patients with VKH seen at the Uveitis clinic underwent both EDI-OCT (Spectralis® HRA+OCT, Heidelberg Engineering, Germany) and SS-OCT (Swept source imaging prototype; Topcon, Japan) imaging at every visit. Eyes with myopia greater than 6 dioptres were excluded from the study. The scans were performed by the same trained ophthalmic technician within minutes of each other, starting with the EDI-OCT. The SFCT of the right eye was measured by one masked trained observer (NSWC) on both the EDI-OCT and SS-OCT images. The SFCT measurements on the SS-OCT images were repeated after at least 72 hours to obtain the intra-observer agreement. The SFCT on the SS-OCT images were also measured by another masked trained observer (SPC) in order to determine the inter-observer agreement. The SFCT measurements were taken from the retinal pigment epithelium/Bruch reflective complex to the sclerochoroidal interface using manual callipers. If either of these interfaces could not be defined even with enhancement, the image was considered to be unmeasurable. The limits of agreement of the 2 OCT methods as well as intra- and inter observer agreements were determined by the mean of the difference between the 2 measurements ± 2 standard deviation [(SD), Bland Altman analysis)]. The intraclass correlation coefficient (ICC) was also calculated.

Charts were reviewed for patient demographics, duration of disease and phase of disease (acute or chronic). The diagnosis of VKH was made based on the revised diagnostic criteria of Read et al [14]. Acute disease was defined as active inflammation within an interval of 6 months or less from onset of symptoms and chronic disease was defined as an interval of more than 6 months from onset of symptoms. During the study period, ICGA was not routinely performed at every visit. Hence SCFT was not correlated with disease activity during the chronic phase since subclinical disease cannot be confidently excluded.

Results

A total of 137 pairs of concurrent SS-OCT and EDI-OCT images were obtained of the right eye of 48 patients with VKH during the study period. 32 of the pairs of images (23.36%) were acquired during the acute phase. The mean age of the patients was 52.2 years (SD 15.6). The majority was females (29, 60.4%) and Chinese (31, 64.6%). Of the remainder, 5 were Indians (10.4%), another 5 (10.4%) were Malays and 7(14.6%) were of other ethnic groups. The median duration of disease in the chronic phase was 79 months (range 7.30 to 358).

Qualitative anaylsis

The EDI-OCT images were more likely to be unmeasurable than the SS-OCT images during the acute phase. [20(62.5%) and 15 (46.9%) respectively, P<0.001 Fisher's Exact test)] (Figures 1A and 1B).

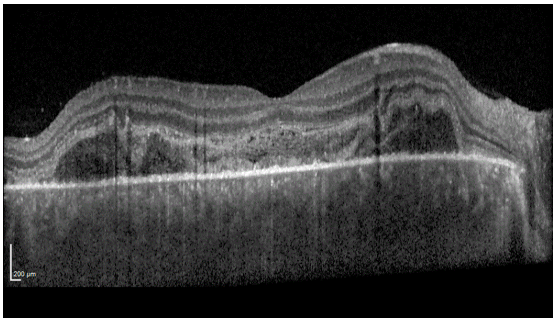

Figure 1A: Enhanced depth imaging optical coherence tomography scan (edi-oct) of a patient with acute Vogt-Koyanagi-Harada Disease obtained 5 days after onset.

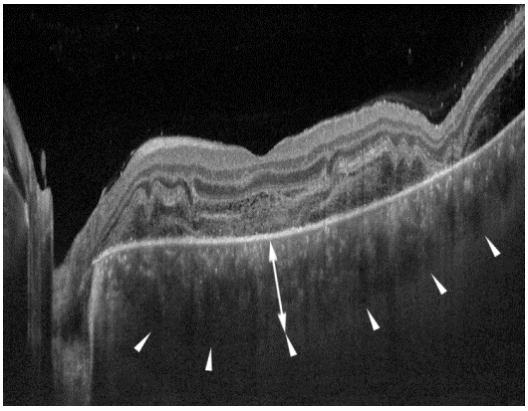

Figure 1B: Swept source optical coherence tomography scan (SS-OCT) obtained at the same time of the same eye. The sclerochoroidal interface of the EDI-OCT scan is poorly defined whereas that of the SS-OCT is clearly defined. The subfoveal choroidal thickness measured on the SS-OCT is 532 microns. The sclerochoroidal interface is indicated by white arrowheads.

Unmeasurable images	Acute phase (N=32 pairs)	Chronic phase (N=105 pairs)
Swept Source No. (%)	15(46.9)	10(9.5)
Enhanced Depth Imaging No. (%)	20(62.5)	33(31.4)
P*	<0.001	0.068
*Fisher's Exact test		

Table 1: Comparison of the quality of images obtained with swept-source (SS) and enhanced depth imaging (EDI) optical coherence tomography.

However during the chronic phase, the images obtained by two devices were similar in terms of interface quality [33 (31.4%) and 10 (9.5%) respectively, P=0.068 Fisher's Exact test)] (Table 1). The majority of the unmeasurable SS-OCT images [16, (61.5%)] were obtained during the first two months of onset when the choroid was excessively swollen. In contrast amongst the 53 unmeasurable EDI OCT images, images obtained during the first 2 months [17 (32.1%) accounted for only one-third of the cases (Figures 2A and 2B), and more than half [31 (58.5%)] were scans obtained from eyes that had ill-defined interfaces even beyond the first 6 months (Table 2).

Unmeasurable images	Swept Source (N=25 images)	Enhanced Depth Imaging (N=53 images)
Swollen Choroid within two months of onset	15	17
Small pupil	4	5
Poorly defined interfaces more than 2 months after onset	6	31

Table 2: Reasons for unmeasurable swept-source (SS) and enhanced depth imaging (EDI) optical coherence tomograms.

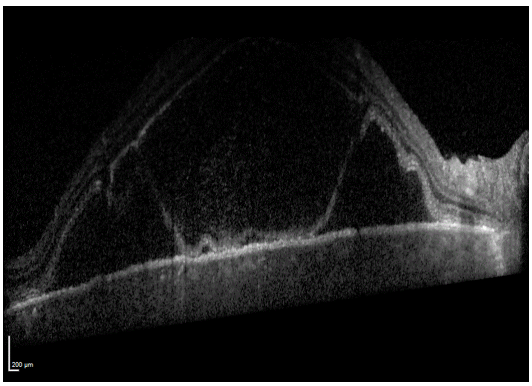

Figure 2A: Enhanced depth imaging optical coherence tomography scan of a patient with acute Vogt-Koyanagi-Harada Disease obtained 2 days after onset.

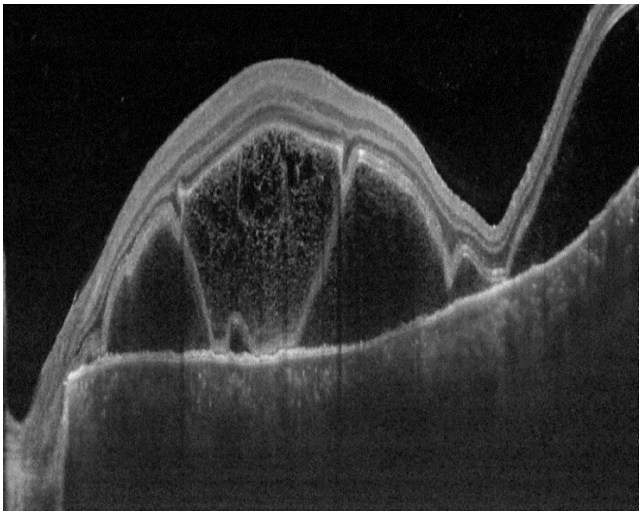

Figure 2B: Swept source optical coherence tomography scan obtained at the same time of the same eye. Both images are unmeasurable as the choroid is extremely swollen with an indistinct sclerochoroidal interface despite enhancement.

Quantitative analysis

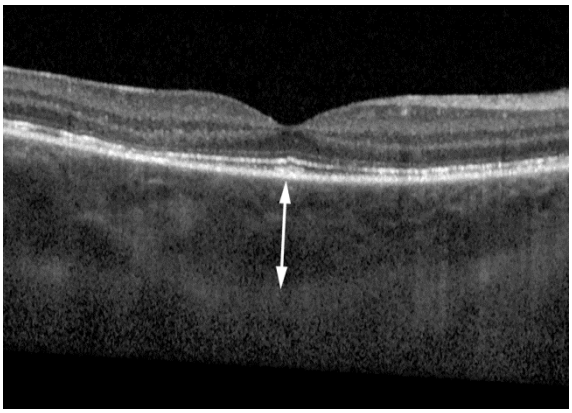

Figure 3A: Enhanced depth imaging optical coherence tomography scan (edi-oct) of a patient with acute Vogt-Koyanagi-Harada Disease obtained 10 weeks after onset.

	Intraclass correlation coefficient (95% confidence interval) of inter-observer reliability for SS-OCT measurements	Intraclass correlation coefficient (95% confidence interval) of intra-observer reliability for SS-OCT measurements	Intraclass correlation coefficient (95% confidence interval) of the reliability of SS-OCT measurements as compared to EDI-OCT	Mean (Standard deviation) of the difference in subfoveal choroidal thickness (microns) measured by SS and EDI-OCT	Upper limit of agreement (microns)	Lower limit of agreement (microns)
Acute phase	0.983	0.978	0.950	-22.7(19.7)	16.7	-62.1

	(0.954 to 0.994)	(0.940 to 0.992)	(0.421 to 0.989)			
Chronic phase	0.992 (0.988 to 0.994)	0.994 (0.991 to 0.996)	0.983 (0.951to 0.992)	-13.0 (21.0)	29	-55

Table 3: Intraclass correlation coefficient and limits of agreement of subfoveal choroidal thickness measurements obtained with swept source optical coherence tomography (SS-OCT) and enhanced depth imaging (EDI) optical coherence.

There was good inter-OCT correlation and limits of agreement were acceptable when both the EDI and SS images were deemed measurable (Table 3) (Figures 3A, 3B and 3C). The mean SFCT was significantly thicker during the acute phase (SS-OCT 352.4 microns, SD 89.5; EDI-OCT 333.6, SD 65.5) as compared to the chronic phase (SS-OCT 221.5 microns, SD116.1; EDI-OCT192.4 SD 93.8, P<0.001 Mann Whitney Test) and became progressive thinner with increasing age as well as duration of disease (Spearman's rho -0.60 and -0.64 respectively, P<0.001) (Figures 4 and 5).

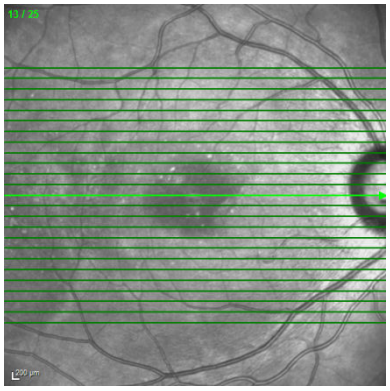

Figure 3B: Corresponding photograph of the fundus showing the location of the EDI-OCT scan.

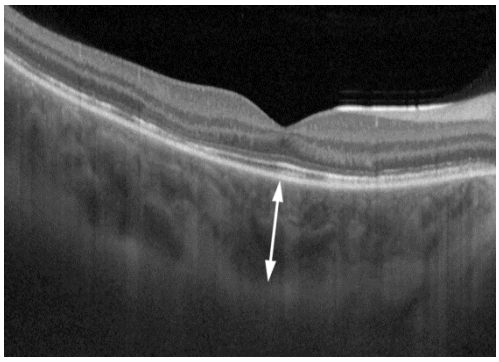

Figure 3C: Swept source optical coherence tomography scan (SS OCT) obtained at the same time of the same eye. The sclerochoroidal interface is clearly defined in both the scans. The subfoveal choroidal thickness measured on the EDI-OCT IS 415 microns and that measured on the SS OCT is 410 microns.

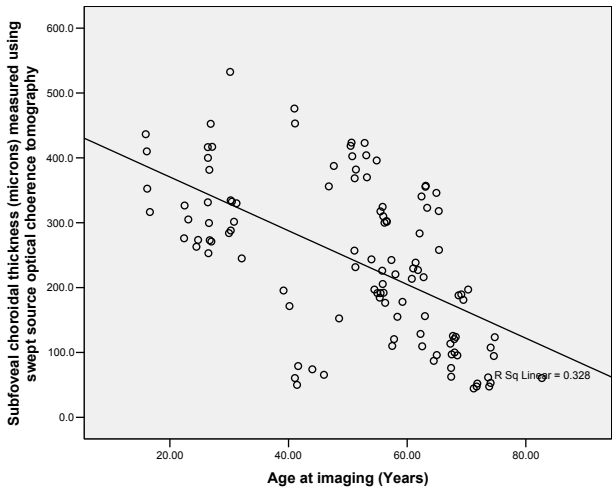

Figure 4A: Scatter plot of age at imaging against the subfoveal choroidal thickness measured on swept source optical coherence tomography showing a negative correlation between age and the subfoveal choroidal thickness.

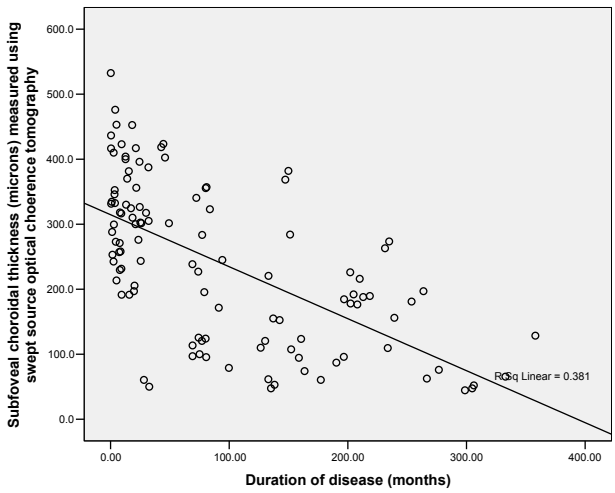

Figure 4B: Scatter plot of duration of disease against the subfoveal choroidal thickness measured on swept source optical coherence tomography showing a negative correlation between duration of disease and the subfoveal choroidal thickness.

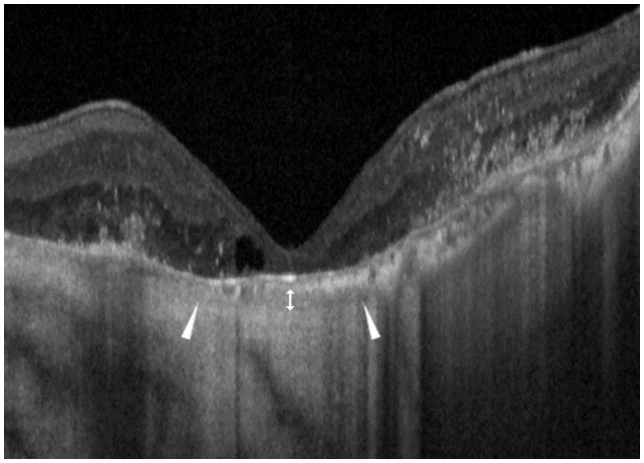

Figure 5: Swept source optical coherence tomography scan (SS-OCT) scan of a patient with chronic recurrent VKH obtained 300 months after onset showing thin choroid with a subfoveal thickness of 47 microns and the presence of cystoid macula edema and epiretinal membrane. The sclerochoroidal interface is indicated by white arrowheads.

Discussion

Both the EDI and the SS OCT gave comparable measurements of the SFCT in eyes where the interfaces are well defined despite the fact it is often impossible to measure exactly the same location when using two different modalities. However, due to its improved resolution the SS-OCT was much less likely to produce unmeasurable images than the EDI-OCT [25 (18.2%) and 53(38.7%) and respectively, P<0.001 Fisher's Exact test]. This is consistent with the findings in normal eyes where choroidal thickness was measurable in all eyes with the SS OCT, in contrast to only 70% with EDI-OCT [11,12]. Similarly a comparison of OCT images obtained with SS and EDI OCT in eyes with pathological myopia showed that choroidal as well as retinal details were better visualized with the SS-OCT not only due to its better resolution but also due to the greater width of its images [13]. This improved ability to obtain SFCT measurements with the SS-OCT could enable its use in detecting recurrences in VKH. There are various possible reasons for ill-defined interfaces beyond the first two months such as lens opacities, eye movements as well as the limits of resolution of each machine.

There was a negative relationship between the SFCT and age as well as with duration of disease. These findings are consistent with what has been shown by other studies on SFCT in VKH [5-10] and the Beijing eye study [15].

The limitations of this study are its retrospective nature, the lack of adequate images per eye as well as the lack of concurrent ICGA to allow for longitudinal analysis of any change in SFCT measurements with recurrent disease which may help to elucidate the ability of SFCT to monitor disease activity in chronic VKH.

Nonetheless since all quantitative measurements of choroidal dimensions are subject to confounding from other variables such as circadian rhythm, blood pressure and age, [16-18] an additional potential benefit of SS-OCT is its ability to image the choroid and its vasculature in much greater detail [19,20]. Hence multimodal imaging techniques whereby SS-OCT images are obtained in combination with simultaneous ICGA and fundus autofluorescence [21,22] may enable us to identify the presence of granulomas and thus monitor disease activity non-invasively in future.

In conclusion, SS-OCT provides much better resolution images of the choroid than EDI-OCT resulting in more measurable images. Where both SS-OCT and EDI-OCT images are measurable, the measurements are comparable.

Conflict of Interest StatementAll authors certify that they have no financial support or benefits from commercial sources for the work reported in this manuscript, or any other financial interests that could create a potential conflict of interest or the appearance of a conflict of interest with regard to the work.

Contributorship Statement

Each author meets the uniform requirements of the Journal of Clinical and Experimental Ophthalmology criteria for authorship.

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