Pathology detection rate of spectral domain optical coherence tomography devices

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ABSTRACT

Background Spectral domain optical coherence tomography (SDOCT) allows for higher resolution scans and higher scanning speeds compared to time domain OCT (TDOCT). The purpose of this study is to compare the pathology detection rates of various SDOCT devices to the Stratus TDOCT.

Methods Patients with neovascular age-related macular degeneration were imaged on the Stratus and one of four SDOCT devices. The images were then analysed in a masked manner evaluating for the presence of epiretinal membrane (ERM), pigment epithelial detachment (PED) and subretinal fluid (SRF). After determining that low scan density with one of the devices was likely the cause of missed PED and SRF compared to the other SDOCT devices the study was repeated with a higher scan density.

Results 60 eyes from 60 patients with neovascular macular degeneration were imaged on each SDOCT device, for a total of 240 eyes from 240 patients imaged on Stratus. There were no instances where pathology was visible on Stratus but was missed on SDOCT. The highest incidence of missed pathology was with SRF, followed by ERM and PED.

Conclusions The increased resolution and image quality of SDOCT devices over TDOCT allows for finer discrimination of retinal structures. The increased speed of SDOCT allows for dense coverage of the macula resulting in the ability to see smaller areas of PED and SRF. There was a critical threshold for the distance between B-scans in the three-dimensional cube scan for detection of pathology.

BACKGROUND AND SIGNIFICANCE

Time domain optical coherence tomography (TDOCT) was the first commercialised OCT technology, and is currently in clinical use within the Stratus OCT III unit (Carl Zeiss Meditec, Dublin, California, USA). In TDOCT, each image is obtained by splitting the light wave and measuring the interference pattern of the light reflected from tissue compared to the light reflected from a moving reference arm with an interferometer.[1] The Stratus OCT produces images with 10 μm axial resolution and generates B-scans consisting of 512 A-scans in 1.28 s, allowing for the differentiation of at least seven retinal layers.[2] Unfortunately, the long time to capture an image with TDOCT results from having to compare the reflected light to the moving reference arm. During this time delay, there may be involuntary eye motions which have to be compensated for with motion correction and eye tracking algorithms. Although these algorithms do not affect relative measurements such as thickness of retinal layers, they alter the true topography of the retinal image and cannot correct for all eye movements.[3 4]

Since the reference arm has to move to obtain the scans in TDOCT, there is a limit to the speed with which images can be obtained with TDOCT. An alternative to this method is the use of spectral domain OCT (SDOCT). In SDOCT, a moving reference arm is not required, instead a spectrometer is used as a detector of the interference spectrum of the signal, and a Fourier transform is used to extract the frequency spectrum of the signal which is used to generate B-scans. With SDOCT it is possible to measure all echoes of light from different delays simultaneously allowing for significant increases in speed and sensitivity.[5]

There are several implications of the increased speed and sensitivity offered by SDOCT. SDOCT generates images with a lower signal-to-noise ratio compared to TDOCT[6] as well as higher resolution images. The higher resolution images obtained allow for better visualisation of disease processes and improve the ability to distinguish between retinal structures and disease entities. Faster acquisition times minimise artefacts from eye motion and make it such that motion correction algorithms are not required, further increasing the quality of the final images by preserving retinal topography.[7] SDOCT has also been shown to be able to image blood vessels as small as 10 μm, determine blood flow patterns, and distinguish between arteries and veins all of which were not possible with TDOCT.[8] Faster acquisition times mean that larger areas of the retina can be imaged. The faster acquisition times also have allowed for the acquisition of three-dimensional (3D) datasets, allowing for a view of the fundus as seen with traditional examination techniques and correlation of cross-sectional images to their location on the fundus as well as generating maps of retinal layer thicknesses.[8–10] An additional advantage of 3D imaging is that it allows for determination of areas of pathology which can then be chosen to be imaged at higher resolution. The purpose of this study is to compare the pathology detection rate between four different SDOCT devices and the Stratus TDOCT device.

METHODS

This project was approved by the Cleveland Clinic Institutional Review Board. Consecutive patients presenting to the Cleveland Clinic Cole Eye Institute retina service that were sent for OCT imaging were enrolled in the trial. Following written informed consent, patients were imaged on Stratus and one or more SDOCT device using the protocol described below.

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SDOCT imaging

Four different SDOCT devices were used in this study: SOCT Copernicus (Copernicus; Optopol Technology SA, Zawiercie, ulŻabia, Poland), Heidelberg Spectralis HRA+OCT (Spectralis; Vista, Heidelberg, Germany), Cirrus HD-OCT (Cirrus; Carl Zeiss Meditec, Dublin, California, USA) and Topcon 3D OCT-1000 (3D OCT-1000; Topcon, Paramus, New Jersey, USA). Each of these devices has different acquisition protocols and analysis packages, the methods for each device are described below. The specifications of each of the devices are compared in table 1.

SOCT Copernicus (Copernicus)

The Copernicus employs a superluminescent diode with a wavelength of 840 nm. The axial resolution of the Copernicus is <6 μ with a data-acquisition speed of 25 000 A-scans/second. Patients were imaged using a single high-resolution B-scan image centred on the fovea (7427 A-scans, scan length 7.0 mm) and a 3D cube scan pattern (50 B-scans×743 A-scans, covering a retinal area of 7.0×7.0 mm). Centre point thickness was automatically evaluated using the software within the Copernicus and was defined as the distance between internal limiting membrane (ILM) to the inner segment/outer segment junction (IS/OS) junction. It was measured on a single B-scan and a foveal B-scan that was selected from 3D volume scan image. Retinal thickness for central subfield (CSF) was also defined as the distance between ILM to the IS/OS, and measured automatically from the 3D volume scans by the automated software within the central 1 mm circle.

Heidelberg Spectralis HRA+OCT (Spectralis)

The Spectralis employs a superluminescent diode with a wavelength of 870 nm. The axial resolution of the Spectralis OCT is <7 μ with a data acquisition speed of 40 000 A-scans/s. Patients were imaged using a single, horizontal B-scan image centred on the fovea (1536 A-scans, scan angle 30°, scan length 9 mm) and a 3D cube scan (19 B-scans×384 A-scans, covering a retinal area of 30×20°). The scans were obtained using the automated retinal tracking system (ART) turned on to amplify the signals and reduce noise within the images. Eight images were averaged using ART for all scans. Center point thickness (CPT) was defined as the distance between ILM to the bottom of the retinal pigment epithelium (RPE) by the automatic segmentation algorithms of the Spectralis software. CPT was measured on a single B-scan and a foveal B-scan that was selected from 3D image.

Cirrus HD-OCT (Cirrus)

The Cirrus employs a superluminescent diode with a wavelength of 840 nm. The axial resolution of the Cirrus is <5 μ with a data acquisition speed of 27 000 A-scans/s. Patients were imaged using a '5 line raster' scan centred on the fovea (4096 A-scans, scan length 6.0 mm), which consists of five closely spaced horizontal lines, a 'Macular Cube 200×200' scan (200 B-scans× 200 A-scans, covering a retinal area of 6.0×6.0 mm) and a 'Macular Cube 512×128' scan (128 B-scans×512 A-scans, covering a retinal area of 6.0×6.0 mm). Automated measurement of CPT was not available, so CPT was measured manually using the software calipers on a foveal B-scan image that was selected from 3D image as the distance between ILM to the top of RPE. CSF was measured automatically by the software and defined as the distance between ILM to the middle of RPE on 3D cube scans.

Topcon 3D OCT-1000 (3D OCT-1000)

The 3D OCT-1000 employs a superluminescent diode with a wavelength of 830 nm. The axial resolution of the 3D OCT-1000 is <6 μ with the data acquisition speed of 18 000 A-scans/s. Patients were imaged using a single 'line-scan' centred on the fovea (4096 A-scans, scan length 6.0 mm) and a '3D-scan' (128 B-scans×512 A-scans, covering a retinal area of 6.0×6.0 mm). Automated measurement of CPT was not available, so CPT was measured manually using the built-in calipers on a single B-scan and a foveal B-scan that was selected from 3D image as the distance between ILM to the top of RPE. CSF was measured automatically on 3D image by the software and defined as the distance between ILM to the top of RPE.

Patients with neovascular macular degeneration were imaged on Stratus and then immediately imaged on one of the four SDOCT devices. Each of the SDOCT and Stratus scans were than analysed by one grader (SS) to determine the presence/absence of epiretinal membranes (ERM), the presence/absence and maximum height of pigment epithelial detachments (PED), and the presence/absence and maximum height of subretinal fluid (SRF). In scans with more than one PED or SRF, the maximum height of the largest area of pathology was recorded.

An ERM was defined as a highly reflective line along the inner retinal boundary. PED was defined as any upward deviation of the normal counter of the RPE with an optically empty area underneath. SRF was defined as the presence of an optically empty area directly above the RPE/Bruch's membrane complex and below the outer retina. On Stratus, the size of a PED was measured from the OCT scans by estimating the distance from the RPE/Bruch's membrane complex to the optically

Table 1 Comparison of axial resolution, scan speed and imaging capabilities of the devices in this study

Device	B-Scan	3D-OCT number of scans	Axial resolution (μm)	Scanning speed (A-scans/s)	Imaging
Zeiss Stratus OCT III	Yes	N/A	10	400	Near-infrared
Reichert/Optopol SOCT Copernicus	Yes	50	6	25 000	Near-infrared
Heidelberg Spectralis HRA+OCT	Yes	19	3.5*	40 000	Scanning laser ophthalmoscope Fluorescein angiography Indocyanine green angiography Autofluorescence
Topcon 3D-OCT 1000	Yes	128	6	18 000	Near-infrared Color Fundus
Zeiss Cirrus HD-OCT	Yes	128	5	27 000	LSLO

*The Heidelberg Spectralis HRA+OCT has an axial resolution of 7 μm, but the manufacturer claims that by using image compositing it can produce an 'effective' axial resolution of 3.5 μm.
3D, three-dimensional.

Table 2 Total number (percentage) of scans showing the specified pathology along with the percentage of scans which were found on one of the SDOCT devices but missed by Stratus

Device	ERM (%)	PED (%)	SRF (%)
Stratus	66 (27.5)	85 (35.4)	45 (18.7)
SDOCT	97 (40.4)	111 (46.3)	76 (31.7)
Per cent missed	32.0	23.4	40.8
p Value	0.001	0.008	0.0006

ERM, epiretinal membrane; PED, pigment epithelial detachment; SDOCT, spectral domain optical coherence tomography; SRF, subretinal fluid.

empty bowl-shaped depression produced when the software eliminates the true PED during processing. On the SDOCT devices the software does not eliminate the PED during processing, so the size of the PED was directly measured from the top of the RPE/Bruch's membrane complex to the top of the choroid. For Stratus and SDOCT, SRF was measured from the top of the optically empty area to the top of the RPE/Bruch's membrane complex.

The Stratus scans were analysed first, and after all the scans were completed, the SDOCT scans for each device were analysed. The order in which scans from each device were analysed was randomised to ensure that the grader was not biased in examining the scans. The number of scans with each pathology was then quantified and compared between Stratus and the SDOCT device on which the patient was imaged. Groups were compared using χ^2 analysis. All statistical analysis were performed in GraphPad Prism V.5.02 (Graphpad Software, La Jolla, California, USA).

RESULTS

Sixty eyes from 60 patients with neovascular macular degeneration were imaged on each device SDOCT device, for a total of 240 eyes from 240 patients imaged on Stratus. There were no instances where pathology was visible on Stratus but was missed on SDOCT. There were a significant number of cases where Stratus missed the pathology, but it was seen on SDOCT (table 2). The highest incidence of missed pathology was with SRF (40.8% detected by SDOCT but missed by Stratus) followed by ERM (32.0%), and PED (23.4%). Stratus showed an ERM in 27.5% of patients versus 40.4% detected by SDOCT (p value 0.0029). Stratus showed a PED in 35.4% of patients versus 46.3% detected by SDOCT (p value 0.0201). Stratus showed a PED in 18.7% of patients versus 31.7% detected by SDOCT (p value 0.0011).

Segregating the results by SDOCT device shows differences in detection rate by device (table 3). The devices that met statistical significance for detection rate for ERM versus Stratus were the Copernicus and the Spectralis, but the Spectralis had the lowest detection rate compared to the other SDOCT devices for PED and SRF. This was expected due to the fact that ERM detection ability is related to the quality of the scan. None of the devices achieved statistical significance comparing Stratus to SD-OCT when evaluating for PED. All the devices, except for the Spectralis, achieved statistical significance in detecting SRF versus Stratus. Small PED and SRF are likely missed by this device compared to the others due to the low B-scan density and large distance between scans (table 4).

Table 4 Comparison of number of B-scans in three-dimensional (3D) cube scans of each device and distance between adjacent B-scans on SDOCT

Device	B-scans in scan	Distance between B-scans (μm)
Stratus	6	N/A
Copernicus	50	140
Spectralis	19	240
3D-OCT 1000	128	47
Cirrus	128	47

SDOCT, spectral domain optical coherence tomography.

Table 5 Spectralis scan density comparison showing characteristics of the three-dimensional (3D) cube scan with increased B-scan density

Protocol	Images averaged	Total images	Distance between B-scans (μm)
19	8	152	240
37	6	222	120

To test this hypothesis, we repeated this study with an increased number of B-scans per scan on Spectralis. To compensate for the increased time to perform the exam, the number of images averaged by ART was reduced to six. The number of B-scans per scan, total images taken, and distance between B scans is shown in table 5. A total of 60 eyes from 60 patients were imaged on Stratus and then on Spectralis using 19 B-scans and 37 B-scans in the 3D cube scan. By increasing the scan density the detection rate for PED and SRF increased to being similar to the other SDOCT devices with PED approaching significance and SRF achieving significance comparing the Spectralis detection rate versus Stratus (table 6).

DISCUSSION

The increased resolution and image quality of SDOCT devices over TDOCT allows for finer discrimination of retinal

Table 3 Pathology detection rate results by device

Device	ERM				PED				SRF			
	Stratus	SD-OCT	Per cent missed	p Value	Stratus	SD-OCT	Per cent missed	p Value	Stratus	SD-OCT	Per cent missed	p Value
Copernicus	20	29	31.0	0.04	22	30	26.7	0.07	9	16	43.8	0.05
Spectralis	14	22	36.3	0.05	25	30	16.7	0.17	15	22	31.8	0.08
3D OCT-1000	20	28	28.8	0.07	20	27	25.9	0.10	9	16	43.8	0.05
Cirrus	12	18	33.3	0.10	18	24	25.0	0.13	12	22	45.4	0.02
Total	66	97	32.0	0.0029	85	111	23.4	0.0201	45	76	40.8	0.0011

Showing total number of scans demonstrating each type of pathology by Stratus and by SDOCT. Per cent missed specifies percentage of scans which were found to have pathology on the specified SDOCT device but was not visible on Stratus.
3D, three-dimensional; ERM, epiretinal membrane; PED, pigment epithelial detachment; SDOCT, spectral domain optical coherence tomography; SRF, subretinal fluid.

Table 6 Results from higher number of B-scans per scan on Spectralis

	ERM				PED				SRF			
Scan protocol	Stratus	SD-OCT	Per cent missed	p Value	Stratus	SD-OCT	Per cent missed	p Value	Stratus	SD-OCT	Per cent missed	p Value
Spectralis 19 B-scans	12	20	40	0.05	18	22	18.1	0.22	12	16	25	0.19
Spectralis 37 B-scans	12	20	40	0.05	18	26	30.7	0.06	12	20	40	0.05

ERM, epiretinal membrane; PED, pigment epithelial detachment; SDOCT, spectral domain optical coherence tomography; SRF, subretinal fluid.

structures. In order to test this hypothesis we examined the ability to discern the presence/absence of ERMs on SDOCT versus Stratus. The SDOCT devices were always able to see ERM when there was an ERM seen on Stratus. The device with the highest detection rate for ERMs compared to Stratus was the Spectralis followed by Cirrus, Copernicus and Topcon. Comparing these numbers to image quality scores seen in the above study shows a direct correlation of image quality to detection rate for ERM, but there is no correlation of detection rate to axial resolution. The ability to discern fine pathology in an image is related to the level of contrast between layers of the retina, resolution of the image, and overall quality of the image. Thus, the device with the best overall image quality results in the best detection rate of ERM.

Although SDOCT devices are able to discern the presence of ERMs that are missed by Stratus, the significance of this finding is unknown. Many of these patients had very fine ERM that were just barely visible, even on SDOCT. These very fine early ERMs are not very significant to the patient since they do not greatly impact their vision. Indeed, most physicians base the decision to surgically remove an ERM based on the visual acuity and not on appearance on OCT. There is also no non-surgical treatment for ERM, so earlier detection by SDOCT likely does not alter the treatment course.

The increased speed of SDOCT devices allows for '3D cube scans' of the retina, with multiple B-scans taken next to each other. This is a significant advantage over TDOCT since there is much denser coverage of the retina, resulting in more accurate retinal thickness maps, and also allowing one to see areas of pathology that may be occurring in between the radial line scans on Stratus. Totally, 40.8% and 23.4% of patients had SRF or PED, respectively, which was missed on Stratus but visible on SDOCT because it was occurring in between the radial lines used by Stratus. There seemed to be a critical threshold for the distance between B-scans in the 3D-cube scan for detection of this pathology. This is likely related to the average size of PED and SRF. The Spectralis had a lower detection rate for these pathologies initially due to the large space, 240 μm, between adjacent B-scans. Increasing the scan density resulted in a miss rate on Stratus similar to the other devices, although this was from preliminary data on a smaller number of patients.

The denser coverage of the retina by SDOCT devices resulted in a higher detection rate of pathology. This is significant for treatment decisions because many retinal physicians are basing the decision to treat AMD patients on whether or not there is fluid visible on OCT. These are patients who likely would not have been treated based on Stratus results, but would have treated based on findings on SDOCT. Whether or not the decision to treat based on OCT findings is the most appropriate therapy decision is not known. All the clinical trials evaluating drug therapy for neovascular age-related macular degeneration (AMD) have been based on results of OCT and have treated with a monthly schedule. There is no randomised clinical trial supporting the use of OCT to decide treatment, but trials are underway evaluating this. These trials are currently based on Stratus OCT and it is now known whether these results will be extendable to SDOCT.

A flaw in the design of this study is the same patients were not imaged on all the devices. This was not possible due to most patients' unwillingness to take part in five OCT examinations at the same time. Thus, we had to resort to comparing detection rates across different subsets of patients with neovascular macular degeneration under the assumption that the distribution and rate of pathology was similar across the different groups of patients. Ideally, we would like to examine the same patients on each device in order to draw conclusions in between devices. However, this is highly dependent on patient cooperation, and most patients have been unwilling to undertake five OCT examinations on the same day while also undergoing other tests for their visit.

Contributors All authors contributed to the work to a degree to warrant authorship per the BJO guidelines.

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