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Comparison of retinal thickness values and segmentation performance of different OCT devices in acute branch retinal vein occlusion

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CLINICAL STUDY

Abstract

Purpose To compare retinal thickness (RT) measurement and segmentation performance of time domain (TD, Stratus) and spectral domain (SD) optical coherence tomography (OCT) devices (Cirrus, Spectralis) for imaging macular oedema (ME) secondary to branch retinal vein occlusion (BRVO).

Methods In this study, 20 eyes of 20 consecutive patients with acute BRVO were included. A total of 18 unaffected fellow eyes served as control group. RT measurement was analysed in the five inner fields of the early-treatment diabetic retinopathy grid, and proportional segmentation errors were evaluated.

Results Central millimetre thickness (CMT) showed a mean difference of -64, -74, and $-18\,\mu m$ ($P < 0.001$) in the control group and $-31\,\mu m$ ($P = 0.107$), $-92\,\mu m$ ($P < 0.001$), and $-105\,\mu m$ ($P = 0.016$) in the BRVO group, between Stratus and Cirrus, between Stratus and Spectralis, and between Cirrus and Spectralis, respectively. Mean RT showed the highest variability between different devices in the area most intensively affected by BRVO-related ME. In eyes with BRVO, 14.6% of Spectralis, 20% of Stratus, and 36.6% of Cirrus scans demonstrated moderate and severe segmentation errors.

Conclusion RT measurement in eyes with BRVO, by TD and SD OCT, is compromised by a significant rate of segmentation errors. Deviations are most pronounced in the areas most severely affected by ME.

Introduction

Retinal venous occlusion (RVO) is supposed to be the most common retinal vascular disorder following diabetic retinopathy. Branch retinal vein occlusion (BRVO), in particular, affects approximately 1% of the population over the age of 48 years.[1] Acute BRVO has a characteristic clinical appearance with retinal haemorrhages, soft and hard exudates, retinal oedema, and dilated tortuous veins in a segmental distribution.[2]

Retinal thickness (RT) measurements are increasingly used to monitor macular oedema (ME),[3,4] and to assess the effectiveness of therapeutic interventions such as anti-angiogenic injections.[5]

With a vast spectrum of indications for treatment and the widespread presence of commercially available time domain (TD) and spectral domain (SD) optical coherence tomography (OCT) devices, the reliability and comparability of different OCT systems used in clinical practice have become a matter of interest. Although OCT software seems to be well adapted for healthy eyes,[6–8] several studies have shown that the accuracy and

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comparability of the data is reduced in cases involving retinal pathology.[8–12] It is hypothesised that the performance of OCT thickness measurements is also influenced by the type of macular pathology.[8,11]

The SD-OCT devices Cirrus and Spectralis provide a high number of scans and measurement points for the automatic thickness analysis. Stratus OCT provides only six radial scans, and may therefore be associated with a higher rate of thickness measurement errors because of a higher need for interpolation.[9]

Generally, accurate detection of retinal boundaries, which is the base for precise thickness determination, mainly depends on the quality of OCT software algorithms.

To provide more insight into the reliability of OCT procedures in specific macular pathologies, it was the aim of this study to compare RT measurements and segmentation performances of different TD- and SD-OCT devices in eyes with ME secondary to BRVO.

Patients and methods

Patient inclusion

In this prospective, comparative, and cross-sectional clinical study, 38 eyes of 20 consecutive patients (12 men, 8 women) were included. A total of 20 eyes with BRVO served as study group, and the unaffected fellow eyes served as control group. Two eyes of the control group were excluded because of the presence of macular pathologies.

The study was approved by the local Institutional Ethics Committee and written informed consent was obtained from all participants before inclusion. The study followed the tenets of the Declaration of Helsinki. We certify that all applicable institutional and governmental regulations regarding the ethical use of human volunteers were followed during this research.

Main inclusion criterion for the study group was the confirmed diagnosis of treatment-naive acute BRVO with a history of less than 3 months. Exclusion criteria for both groups were history of glaucoma, aphakia, or presence of an anterior chamber intraocular lens, significant cataract, rubeosis iridis, ocular infections, and any history of additional retinal pathologies (that is, age-related macular degeneration, diabetic retinopathy, ME for other reasons than BRVO) or previous vitreoretinal surgery.

All patients underwent an initial standardised ophthalmic examination according to protocol, including measurement of best-corrected visual acuity with early-treatment diabetic retinopathy (ETDRS) procedures, and assessment of intraocular pressure, slit-lamp examination, ophthalmoscopy, and fluorescein angiography.

Optical coherence tomography imaging

After pupil dilation, OCT was performed in each eye by the same experienced examiner. Three different OCT technologies with the same settings described by Mylonas et al[12] were used:

The conventional TD Stratus OCT system (Version 4.0.1-0056, Carl Zeiss Meditec, Dublin, CA, USA) offers an axial image resolution of $\sim 10\,\mu m$, a transversal resolution of $15\,\mu m$, and a scanning velocity of 400 A scans/second using the 'fast macular thickness' pattern. RT is calculated from six individual B scans, arranged in a radial pattern, and displayed in a grid following the recommendations of the ETDRS study.

The Cirrus SD-OCT (Version 3.0.0.6.4, Carl Zeiss Meditec) is a high-resolution SD-OCT device with an axial image resolution of $5\,\mu m$, a transversal resolution of $15\,\mu m$, and a scan velocity of up to 25 000 A scans/second. Raster scans cover an area of $6 \times 6\,mm^2$. Two different types of raster patterns (512×128 and 200×200) were used for RT measurements.

The Spectralis HRA + OCT system (Version 3.2.1.0, Heidelberg Engineering, Inc., Heidelberg, Germany) is a high-resolution SD-OCT, allowing simultaneous angiographic, infra-red, autofluorescenc, and OCT measurements. It has an axial image resolution of approximately $7\,\mu m$, a transversal resolution of $14\,\mu m$, and a scanning velocity up to 40 000 A scans/second. The Spectralis is capable to perform raster scans of the central macula using an eye-tracking system. A scanning pattern consisting of 37 B scans per raster was used in our study.

OCT grid projection and segmentation analysis criteria

Each OCT scan was displayed using a grid projection introduced by the authors of the ETDRS trial. To allow for comparative imaging, in BRVO and control eyes, individual fields were labelled as shown in Figure 1.

Mean RT of central millimetre thickness field (CMT) and of fields 2, 3, 4, and 5 (F2–F5) was assessed using the automatic thickness analysis of the described OCT devices. The measurements obtained by the devices with respect to their retinal location were then compared for differences and specific characteristics.

All individual scans were analysed by a masked observer certified for OCT-reading procedures by the Vienna Reading Center.

Apparent errors in the automated identification of the inner boundary of the neurosensory retina as well as the outer subretinal boundary, consistent with retinal pigment epithelium (RPE) for all sub-fields of the performed raster and radial scans were identified as segmentation errors.

Segmentation errors were classified into three categories according to Mylonas *et al*:[12] negligible ($<50\,\mu m$), moderate ($50–200\,\mu m$), and severe ($>200\,\mu m$) for segmentation errors in the length scan and negligible ($<0.5\,mm$), moderate ($0.5–2\,mm$), and severe ($>2\,mm$) for artifacts in width scan. If more than one error was present in either direction, the documented error of the individual scan was defined as the severest error detected. Segments with a low signal because of ME, which are excluded from segmentation by the Spectralis OCT software (no segmentation line is visible in this area), were graded as segmentation errors based on the
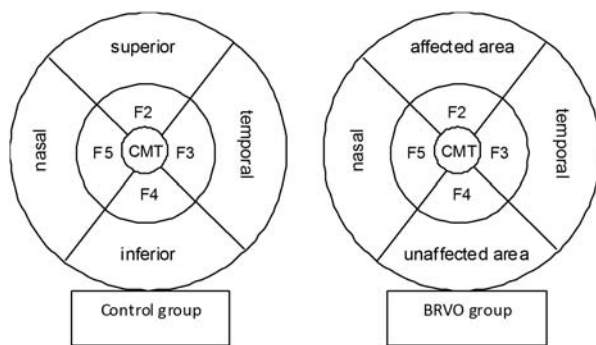
above-mentioned classification in width-scan direction. Figure 2 illustrates examples of all segmentation error categories.

Statistics

All data were entered into a Microsoft Excel spreadsheet. Statistical analysis was performed using Microsoft Excel and SPSS 12.0 software (SPSS, Chicago, IL, USA). The levels of statistical significance and correlation coefficients between the different devices were calculated using Wilcoxon's matched-pairs signed-rank test, χ^2 test, and Pearson's correlation coefficients. Bland–Altman plots were used to identify a potential correlation between the differences and the mean results of two measurements. *P*-values of less than 0.05 were considered to be statistically significant. In the case of multiple comparisons, the Bonferroni–Holm correction was performed.

Figure 1 Optical coherence tomography grid projection introduced by the authors of the ETDRS trial. In this study, fields within the central 3 mm diameter were evaluated. In control group, fields were named as follows: CMT, central millimetre thickness; F2, superior inner macula; F3, temporal inner macula; F4, inferior inner macula; F5, nasal inner macula. In branch retinal vein occlusion (BRVO) eyes, fields were named as follows: CMT, central millimetre thickness; F2, area most intensively affected by BRVO-induced oedema; F3, temporal macula; F4, area relatively unaffected by BRVO-induced oedema; F5, nasal macula.

Results

Demographic data

The mean age of all participants was 68.7 ± 7.8 years (range: 56–84 years). The mean duration of symptoms was at 1.9 ± 1.5 months.

The oedema affected the superotemporal macular area in 15 eyes and the inferotemporal macular area in 5 eyes.

Mean signal intensity of analysed OCT images was 5 ± 1.7 by Stratus OCT and 6 ± 0.7 by Cirrus OCT ($P = 0.02$).

Mean visual acuity was 52 ± 11.5 and 68 ± 4.2 ETDRS letters in the study group and in the control group, respectively ($P < 0.001$).
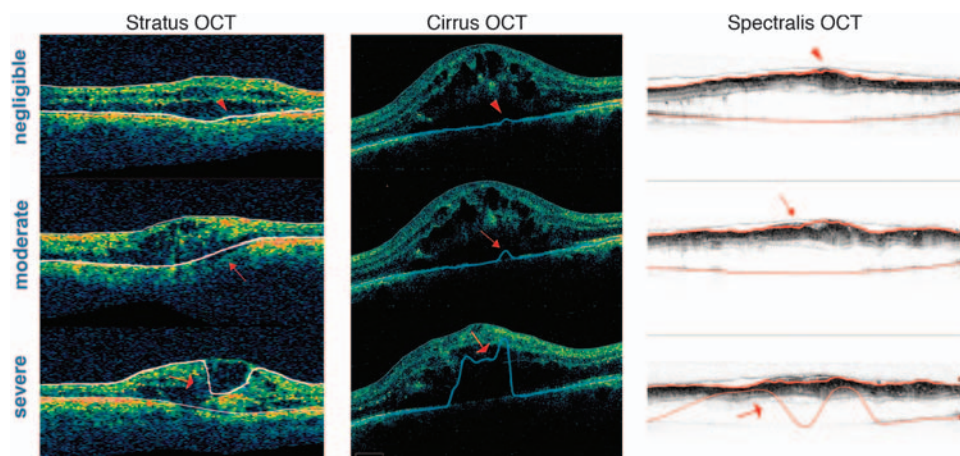

Figure 2 Images obtained from Stratus OCT, Cirrus OCT, and Spectralis OCT showing negligible (▶), moderate (→), and severe (——▶) segmentation errors.

Quantitative OCT analysis

Control group. In the control group, the Stratus data showed the lowest mean thickness values for all fields. The highest mean values were obtained by Spectralis (Table 1).

The mean difference in CMT between Stratus and Cirrus 512×128, between Stratus and Cirrus 200×200, and between Stratus and Spectralis was -64 ± 24, -57 ± 10, and $-74 \pm 8.4\,\mu m$, respectively ($P < 0.001$). The mean difference in CMT between Spectralis and Cirrus in the 200×200 pattern was $18 \pm 7.0\,\mu m$ ($P = 0.001$).

Consistently, there was a significant difference of mean CMT and macular thickness in all other fields (F2–F5) between the different OCT devices ($P < 0.05$), except between the Cirrus 512×128 and the Cirrus 200×200 raster pattern ($P > 0.05$).

Study group. In eyes with BRVO, the lowest mean CMT value ($470\,\mu m$) was measured by Stratus and the highest mean RT value ($572\,\mu m$) was measured by Spectralis,

similar to the findings in the control group. Table 2 summarises the mean RT values for all OCT devices in the BRVO group.

The mean difference in CMT between Stratus and Cirrus 512×128, between Stratus and Cirrus 200×200, and between Stratus and Spectralis was $-31 \pm 89\,\mu m$ ($n = 19$, $P = 0.107$), $-5 \pm 139\,\mu m$ ($n = 19$, $P = 0.882$), and $-92 \pm 87\,\mu m$ ($n = 17$, $P < 0.001$), respectively. The mean difference in CMT between Spectralis and Cirrus 200×200 was $-105 \pm 155\,\mu m$ ($n = 16$, $P = 0.016$).

A statistically significant difference in CMT was only observed between Stratus and Spectralis ($P < 0.001$) and between Cirrus and Spectralis ($P = 0.016$). There was no statistically significant difference in CMT between Stratus, Cirrus 512×128, and Cirrus 200×200 ($P > 0.05$).

With regard to mean RT values of the area most intensively affected by BRVO-induced ME (F2), a statistically significant difference was observed between all three OCT devices ($P < 0.01$).

Table 1 Mean retinal thickness values of unaffected fellow eyes obtained from all OCT devices

Control group	Mean	Median	SD	Min	Max	95% CI	Upper LOA	Lower LOA
CMT								
Stratus	210	216	24	172	258	5	257	164
Cirrus 512	274	277	27	218	329	6	326	222
Cirrus 200	267	273	22	222	302	5	310	223
Spectralis	284	286	21	244	322	4	326	242
F2								
Stratus	269	274	18	231	299	4	304	233
Cirrus 512	322	327	16	294	351	3	352	291
Cirrus 200	321	324	14	298	347	3	348	294
Spectralis	340	341	16	319	369	3	372	309
F3								
Stratus	268	273	18	230	298	4	303	232
Cirrus 512	324	326	18	288	351	4	359	290
Cirrus 200	325	326	16	295	350	3	356	293
Spectralis	343	345	19	307	372	4	379	307
F4								
Stratus	270	272	13	242	293	3	295	244
Cirrus 512	320	321	12	297	342	2	343	298
Cirrus 200	320	321	12	294	344	3	344	296
Spectralis	339	340	14	313	360	3	366	311
F5								
Stratus	262	265	14	238	287	3	289	235
Cirrus 512	315	317	13	291	331	3	341	289
Cirrus 200	314	316	13	288	329	3	339	289
Spectralis	334	338	14	307	351	3	361	307

Abbreviations: CI, confidence interval; CMT, central millimetre thickness; F2, superior macula; F3, temporal macula; F4, inferior macula; F5, nasal macula; LOA, limit of agreement; SD, standard deviation.

Table 2 Mean retinal thickness values of eyes with branch retinal vein occlusion (BRVO) obtained from all OCT devices

BRVO group	Mean	Median	SD	Min	Max	95% CI	Upper LOA	Lower LOA
CMT								
Stratus	470	457	142	289	767	30	749	191
Cirrus 512	501	463	138	362	869	29	772	231
Cirrus 200	475	455	131	241	753	27	731	220
Spectralis	572	572	165	364	817	35	896	247
F2								
Stratus	531	501	125	317	842	26	776	285
Cirrus 512	377	358	173	70	620	36	716	38
Cirrus 200	347	433	183	58	600	38	705	-11
Spectralis	598	558	138	362	825	29	868	329
F3								
Stratus	424	390	107	285	636	22	634	214
Cirrus 512	412	406	107	186	624	22	622	203
Cirrus 200	370	371	95	174	545	20	556	185
Spectralis	505	496	115	342	686	24	731	279
F4								
Stratus	320	308	48	241	421	10	415	225
Cirrus 512	379	339	93	282	652	19	561	198
Cirrus 200	385	342	108	287	763	23	596	173
Spectralis	387	376	56	304	502	12	496	277
F5								
Stratus	401	380	103	273	673	22	603	198
Cirrus 512	438	409	99	319	706	21	632	244
Cirrus 200	405	392	66	298	532	14	534	275
Spectralis	475	452	107	344	696	22	686	265

Abbreviations: CI, confidence interval; CMT, central millimetre thickness; F2, area most intensively affected by BRVO-induced oedema; F3, temporal macula; F4, area relatively unaffected by BRVO-induced oedema; F5, nasal macula; LOA, limit of agreement; SD, standard deviation.

Table 3 Pearson correlation coefficients of thickness measurements in unaffected fellow eyes

Control group	CMT	F2	F3	F4	F5
Stratus—Cirrus 512	0.51	0.93	0.93	0.94	0.90
Stratus—Cirrus 200	0.91	0.87	0.93	0.93	0.91
Cirrus 512—Cirrus 200	0.68	0.96	0.98	0.97	0.98
Spectralis—Cirrus 512	0.56	0.95	0.95	0.93	0.95
Spectralis—Cirrus 200	0.95	0.95	0.97	0.93	0.96
tratus—Spectralis	0.94	0.89	0.91	0.93	0.88

Abbreviations: CMT, central millimetre thickness, F2, superior macula, F3, temporal macula; F4, inferior macula, F5, nasal macula.

Table 4 Pearson correlation coefficients of thickness measurements in eyes with branch retinal vein occlusion (BRVO)

BRVO group	CMT	F2	F3	F4	F5
Stratus—Cirrus 512	0.85	−0.18	0.46	0.69	0.71
Stratus—Cirrus 200	0.50	−0.50	−0.19	0.62	0.56
Cirrus 512—Cirrus 200	0.54	0.81	0.19	0.93	0.50
Spectralis—Cirrus 512	0.75	−0.43	0.28	0.65	0.59
Spectralis—Cirrus 200	0.50	−0.72	−0.25	0.54	0.55
Stratus—Spectralis	0.85	0.81	0.82	0.84	0.91

Abbreviations: CMT, central millimetre thickness; F2, mostly affected by BRVO-induced macular oedema; F3, temporal macula; F4, relatively unaffected by BRVO-induced macular oedema; F5, nasal macula.

Only between Stratus and Spectralis did the thickness values of all five investigated fields differ significantly.

Correlation of retinal thickness measurements

In healthy eyes, the thickness values of all corresponding fields showed a high correlation between the different OCT devices (Pearson correlation coefficients ranging between $r = 0.51$ and 0.98, Table 3).

In eyes with BRVO, correlations varied largely between the investigated OCT devices, ranging from -0.72 to $+0.93$. In the sub-field, most intensively affected by BRVO (F2), the Pearson correlation coefficients showed the lowest values, ranging between $r = -0.72$ and $+0.81$. As expected, correlations in F4 (unaffected area) were higher than in the other fields, ranging between $r = 0.54$ and 0.93 (Table 4).

Figures 3 and 4 show Bland–Altman plots comparing mean values and mean differences of the CMT between the three OCT devices.

Segmentation performance

No substantial segmentation errors were found in Stratus scans of healthy eyes. However, in 25 of 2176 (1.1%) Cirrus scans and in 9 of 629 (1.4%) Spectralis scans, moderate or severe alignment errors were detected ($P > 0.05$). In most cases, the segmentation errors were

caused by incorrect identification of the internal limiting membrane due to a partial detachment of the vitreous body.

In eyes with BRVO, segmentation errors occurred in the performance of all OCT devices. Severe alignment errors were detected in 9 of 120 (7.5%) of Stratus scans, in 56 of 629 (8.9%) of Spectralis scans, and in 758 of 2432 (31.2%) of Cirrus scans ($P < 0.001$, χ^2 test between Cirrus 512×128 and Stratus, as well as between Cirrus 512×128 and Spectralis, $P = 0.617$ between Stratus and Spectralis).

Moderate and severe segmentation errors were detected in 14.6% of Spectralis scans, 20% of Stratus scans, and 36.6% of Cirrus scans. With regard to moderate and severe segmentation errors, there was a significant difference between Cirrus 512×128 and Spectralis ($P = 0.012$).

In all 99.6% of the described moderate and severe segmentation errors by Cirrus and 86% by Spectralis were caused by incorrect identification of the RPE. By Stratus, this boundary was only affected in 56.5% of moderate and severe segmentation errors.

Figure 5 illustrates the proportion of segmentation errors of varying degree.

Discussion

In this study, three different OCT devices comprising one TD- and two SD-OCT types were compared. The comparison was carried out by examining healthy eyes and eyes with ME because of BRVO, focusing on RT measurement and segmentation performance.

Regarding RT measurements, our results are similar to those of previous studies, which describe comparable baseline values in eyes with BRVO, assessed by a single OCT device (mainly Stratus)[13,14] and normal eyes.[7,15,16] We therefore conclude that the population of our study group is representative for the pathology.

To our knowledge, this is the first comparative clinical study analysing RT measurements of TD- and SD-OCT devices in eyes with BRVO. Yamaike *et al*[4] described the pathomorphological features of cystoid ME secondary to retinal vein occlusion using 3D OCT and Stratus OCT.[5] In contrast to our study, they included eyes with both BRVO and CRVO, focusing on morphological features of affected retina without comparative RT measurements.

Mean RT differed significantly in healthy eyes throughout all investigated sub-fields between Spectralis, Cirrus, and Stratus OCT, whereas Spectralis provided reproducibly the highest and Stratus the lowest thickness values.

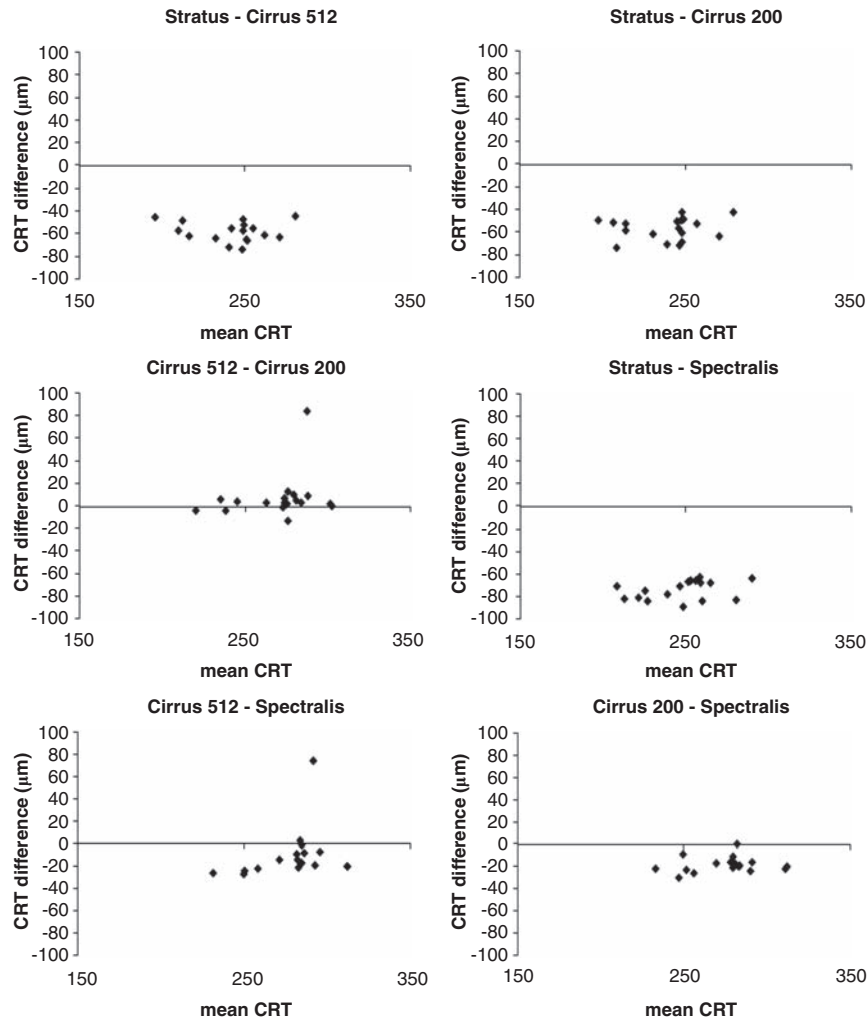Obviously, the discrepancies between the three devices are the result of various segmentation algorithms.

Figure 3 Bland–Altman plots comparing mean and difference central millimetre thickness (CMT) values between optical coherence tomography (OCT) devices in control group.

Although the segmentation algorithm of Stratus defines RT as distance between the inner/outer segment of the photoreceptor layer and the internal limiting membrane (ILM), the algorithm of Cirrus defines it as the distance between the RPE boundary and the ILM. Spectralis detects the RPE layer slightly deeper than the Cirrus software. This difference of segmentation localisation leads to reproducible and well-defined discrepancies of thickness values under physiological conditions when boundaries are intact.

In contrast to the highly correlating measurements in healthy eyes, there was a substantial variability of RT values in eyes with BRVO with lower correlation. The variability between the three devices was most pronounced in retinal areas most intensively affected by ME. Only F4, the sub-field that was relatively unaffected by ME, showed a higher correlation.

The fact, that there was a high correlation of all corresponding sub-fields in our control group, but a low

correlation in eyes with BRVO, indicates a limited comparability of RT measurements between the three OCT devices in eyes affected by BRVO.

A limited interchangeability between Stratus and Cirrus OCT has also been demonstrated in other pathologies, such as neovascular age-related macular degeneration or diabetic ME.[3,12,17]

Several reasons for inaccurate measurements have been identified in recent studies. These include operator failure, decentration resulting from poor fixation, high foveal thickness standard deviation, and failure of accurate retinal boundary detection by the OCT software algorithms. In our study, all OCT images were taken by the same certified examiner, therefore operator failure could be ruled out.

Scan-by-scan analysis indicated that incorrect segmentation processes caused the errors in thickness measurement in affected eyes. Although almost no segmentation errors were found in the control group or
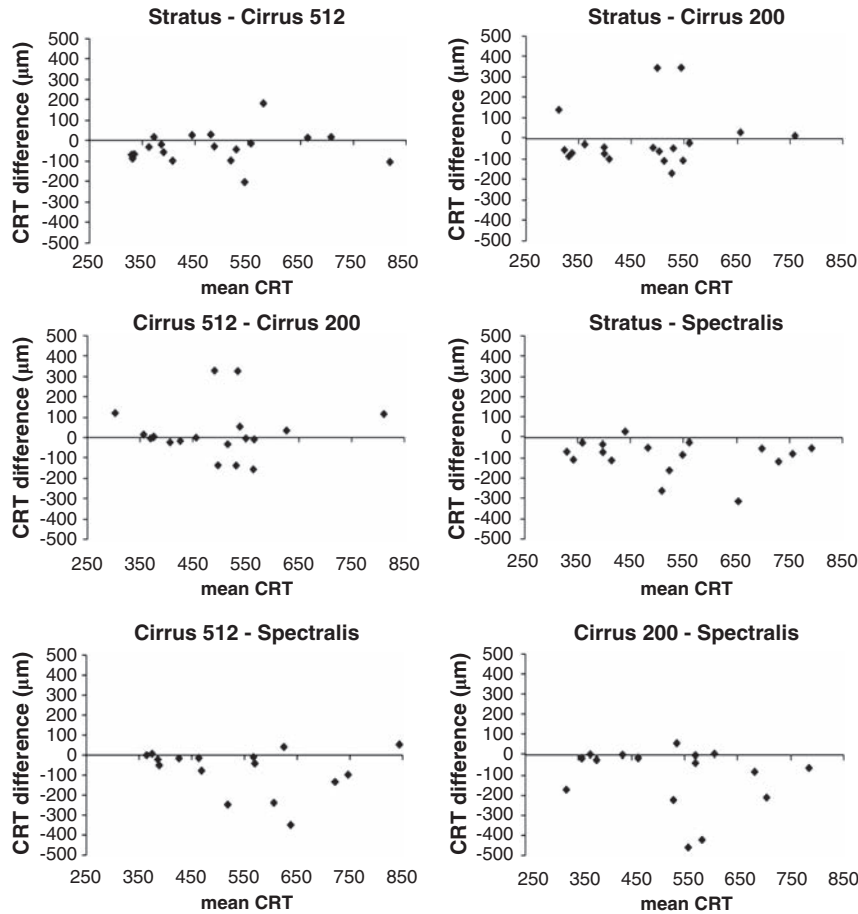
Figure 4 Bland–Altman plots comparing mean and difference central millimetre thickness (CRT) values between optical coherence tomography (OCT) devices in eyes with branch retinal vein occlusion.
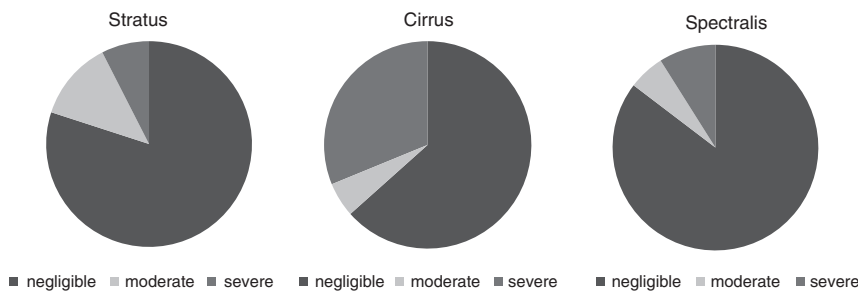

Figure 5 Proportion of segmentation errors in eyes with branch retinal vein occlusion. 1: Stratus OCT, 2: Cirrus OCT, 3: Spectralis OCT.

unaffected sub-fields, the BRVO group, and particularly sub-fields, most intensively affected by ME, demonstrated segmentation errors of varying degree, depending on the OCT device. The most segmentation errors were detected in Cirrus scans and the fewest in Spectralis scans.

In all devices, segmentation errors occurred more frequently and more pronounced in areas affected by ME. Segmentation errors increased with the level of

ME and were mainly caused by incorrect identification of the RPE. Overlying ME may lead to a lower scanning signal in the underlying areas. This may complicate the correct identification of limiting structures such as the RPE. The Spectralis software excludes areas with very low-signal quality because of extensive ME from analysis. In such case, no segmentation line is visible in the affected area. Many of the severe detection errors with this system were related to incorrect identification

of the ILM because of a partial detachment of the vitreous.

As axial resolution and scanning speed are similar between Cirrus and Spectralis, the higher rate of segmentation errors with the Cirrus system seems to be a consequence of the different segmentation algorithms.

TD OCT systems may be expected to cause a higher rate of measurement failures because fewer measurement points are recorded. In our study, the TD Stratus OCT showed surprisingly few segmentation errors. It is also reported that Sadda *et al*[11] investigated risk factors for measurement errors by Stratus OCT, and reported that retinal cysts and the diagnosis of a retinal vascular disease were less likely to cause severe segmentation errors than other pathologies, such as the presence of subretinal fluid.

In conclusion, the three examined OCT devices are not comparable for imaging eyes with ME secondary to BRVO. Overall, SD-OCT provided more detailed images and superior visualisation of intraretinal structures because of a high-resolution technology as reported previously.[18]

Nevertheless, in eyes with BRVO, SD Cirrus scans showed significantly more segmentation errors than (TD) Stratus scans. Accurate thickness measurement without segmentation errors is rather a matter of segmentation software than of OCT scanning technology.

Summary

What was known before
- It was known before that the accuracy of retinal thickness measurements in affected eyes depends on the type of retinal pathology and on the OCT device.

What this study adds
- This study offers knowledge about the reliability of different OCT devices (time domain and spectral domain) in eyes with untreated acute BRVO.

Conflict of interest

The authors declare no conflict of interest.

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