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Comparison of SDOCT Scan Types for Grading Disorganization of Retinal Inner Layers and Other Morphologic Features of Diabetic Macular Edema

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Purpose: To assess grading reproducibility of disorganization of the retinal inner layers (DRIL) and other morphologic features of diabetic macular edema (DME) across spectral domain optical coherence tomography (SDOCT) instruments and scan types.

Methods: A cross-sectional study enrolled participants with current or recent center-involved DME. In group A (27 eyes), we obtained two Cirrus scans (512 × 128 macular cube [Cube] and high-definition five-line raster [HD 5-Line]) and two Spectralis scans (high-resolution [HR] and high-speed [HS]). In group B, 26 eyes underwent HR scans and Optovue AngioVue (OP) 3 × 3-mm scans. All scans were graded for type and extent of DRIL, intraretinal cysts, cone outer segment tip visibility, and subretinal fluid (SRF).

Results: In the total cohort, mean central subfield thickness was 342.9 ± 83.4 µm. Intraclass correlations were high for DRIL extent across the four different imaging settings (HR vs. HS, $r = 0.93$; HR vs. Cube, $r = 0.84$, HR vs. HD 5-Line, $r = 0.76$, HR vs. OP, $r = 0.87$) and ranged from good to excellent for intraretinal cyst and SRF area. There were significantly smaller mean normalized differences between HR/HS scans versus HR and all other scan modalities (HR/HS vs. HR/Cube, $P = 0.02$; HR/HD 5-Line, $P = 0.0005$; HR/OP, $P < 0.0001$).

Conclusions: Our data suggest that the reproducibility for SDOCT parameters of DRIL and intraretinal cysts was high across all five SDOCT scan types; thus, evaluation of DRIL is feasible using multiple SDOCT models in eyes with DME.

Translational Relevance: DME morphological changes can be evaluated on multiple SDOCT devices with good reproducibility, allowing clinicians and researchers flexibility in DME assessment for clinical care and research.

Introduction

Spectral domain optical coherence tomography (SDOCT) is a noninvasive imaging modality that delineates the neural retinal structure and provides high-resolution images of the retinal anatomy. Central retinal thickness measured via SDOCT is the gold standard for the evaluation and management of diabetic macular edema (DME).[1–3]

Previous studies have demonstrated that treatments that diminish central retinal thickening in eyes with DME can improve or stabilize visual acuity (VA); however, multiple investigations have demonstrated

that central retinal thickness is only modestly correlated with current VA or change in VA in eyes with DME.[4] A study from the DRCR Retina Network suggested that changes in central subfield thickness (CST) on SDOCT explained only 12% of the variation in changes in VA over 2 years in eyes undergoing anti-vascular endothelial growth factor therapy for DME.[5]

Our group previously described the SDOCT biomarker of disorganization of the retinal inner layers (DRIL), which has been highly associated with both current and future VA in eyes with both current and resolved DME.[6–8] Change in DRIL extent within the central 1-mm foveal zone during the first 4 months of follow-up was predictive of change in VA at 8- and 12-month follow-up.[8] The relationship between early change in DRIL extent and subsequent change in VA was the strongest and most consistent of all examined SDOCT parameters, including change in retinal thickness, external limiting membrane or ellipsoid zone disruption, and cone outer segment tips visibility.

In cross-sectional analysis, other researchers have confirmed that in eyes with DME the presence of DRIL evaluated on Cirrus cube scans (Carl Zeiss Meditec, Jena, Germany) is positively correlated with increased retinal thickness and ellipsoid zone disruption when compared with eyes without the presence of DRIL.[9] The relationship of DRIL extent with additional aspects of functional vision has also been explored in eyes with and without diabetic macular edema by using contrast sensitivity and visual field tests. These results show that eyes with DRIL have reduced retinal function compared to those without DRIL.[10] The association of DRIL with visual outcomes is also seen in other retinal vascular diseases. A longitudinal study of eyes with cystoid macular edema from central retinal vein occlusion demonstrated that changes over a 3-month period in DRIL extent and ellipsoid zone disruption were predictive of 1-year VA, independent of baseline central retinal thickness and vision.[11] Another study showed that the tissue integrity of the inner retinal layers, more specifically of the plexiform layers, measured on SDOCT is correlated with visual function at baseline in patients with cystoid macular edema.[12] A cross-sectional study demonstrated an association between DRIL and outer retinal layer disruption, as well as a positive correlation with DR severity worsening in eyes DME.[13] The presence of DRIL has been associated with macular ischemia on fluorescein angiography, decreased perfusion of superficial and deep capillary plexus, and enlargement of foveal avascular zone area on SDOCT angiography in eyes with and without center involved DME.[14–17]

Although DRIL is a potential biomarker for assessing retinal morphology and visual acuity changes in these eyes, most previous studies assessing DRIL have done so on SDOCT imaging via a Heidelberg Spectralis system (Heidelberg Engineering, Heidelberg, Germany), using a standard imaging protocol of 49 B-scans spanning a 20 × 20 frame, with a mean of 16 automatic real-time tracking (ART) images per scan in high-resolution mode.[6–8,16] However, there are other commercially available SDOCT imaging systems and scan protocols that are widely used to visualize the neural retina. This study evaluates the reproducibility of DRIL measurements and other SDOCT variables across five different SDOCT imaging protocols across the Cirrus, Spectralis, and Optovue AngioVue (Optovue, Inc., Fremont, CA) systems to gain insight into the comparability of morphologic assessments via these modalities and machines.

Materials and Methods

This single-site, prospective study was performed at the Beetham Eye Institute of Joslin Diabetes Center in Boston, a tertiary referral center for diabetes care. The study design was consistent with the tenets of the Declaration of Helsinki and was approved by the Joslin Diabetes Center Institutional Review Board.

Eligible participants were at least 18 years old, had a history of diabetes mellitus type 1 or type 2, and had current or recently resolved center-involved DME (CI-DME). CI-DME was defined as retinal thickening within 500 µm of the macular center, confirmed by gender- and machine-specific values equivalent to time-domain central subfield thickness greater than 250 µm.[18] Eyes in which CI-DME had resolved within the last 3 months were categorized as having recently resolved DME.

Exclusion criteria included significant media opacity (such as dense cataract or vitreous hemorrhage), poor-quality images with artifacts from motion or blinking that led to segmentation error or central foveal subfield displacement, or poor patient compliance that precluded good-quality imaging. In addition, patients with history of retinal vein occlusion, uveitis, and other nondiabetic retinal pathology that might affect VA were excluded.

Study Procedures and Image Analysis

All imaging was performed following pupillary dilation by clinical study-certified imagers. In group A, for each study eye, four total consecutive scans

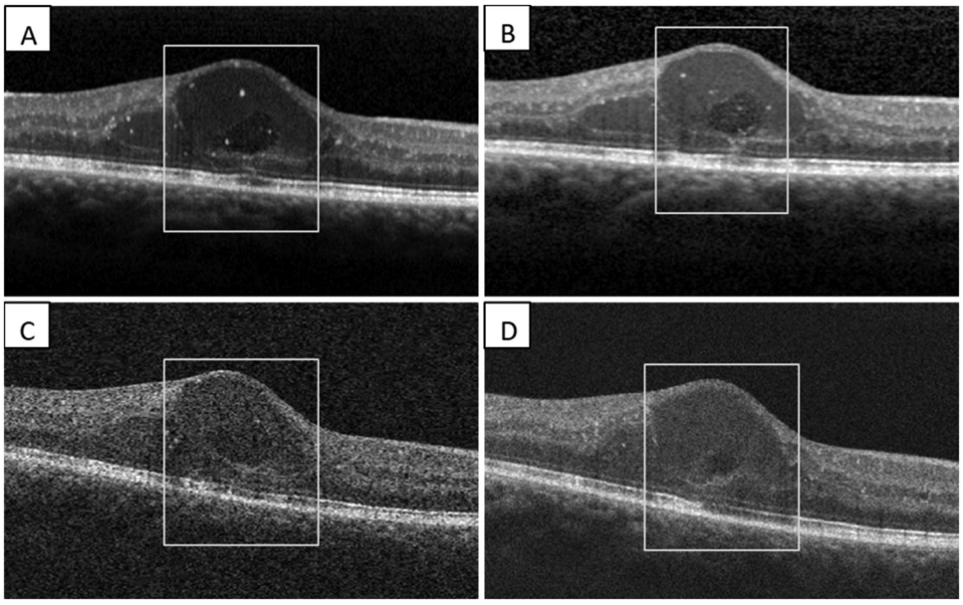

Figure 1. Representative B-scans of the same eye for each SDOCT modality in group A: (**A**) Spectralis HR, (**B**) Spectralis HS, (**C**) Cirrus Cube, and (**D**) Cirrus HD 5-Line Raster.

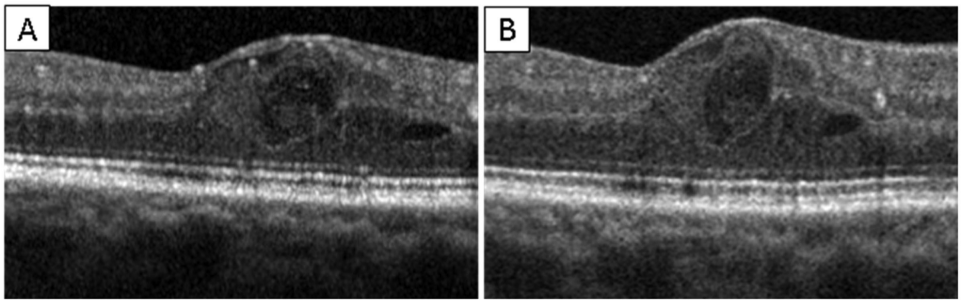

Figure 2. Representative B-scans of the same eye for each SDOCT modality in Group B: (**A**) Spectralis HR, and (**B**) Optovue AngioVue.

within a single visit were obtained: two scans on Cirrus, including 512 × 128 macular cube (Cube) and high-definition five-line raster (HD 5-Line), and two scans on Spectralis, including 20° × 20°-frame, 49 B-scans, 16 ART images per scan, high-resolution (HR) and high-speed (HS) (Fig. 1). In group B, for each study eye, two total consecutive scans within a single visit were captured: one scan in Spectralis HR mode as described for group A and one scan on the AngioVue (OP), with 300 raster scans in the 3 × 3-mm macular area (Fig. 2). Transverse spacing between B-scans for Spectralis HR and HS was 120 µm; for the Cirrus Cube, 47 µm; for the Cirrus HD 5-Line, 250 µm; and for the AngioVue OP, 10 µm.[19–21]

Assessment of DRIL on Spectralis HR has been considered the gold standard[1–3] and has been used in the majority of previous studies to explore the relationship between retinal morphology and function in eyes with DME by producing the highest resolution SDOCT scans. B-scans that passed through the foveal center were selected so that certified graders could examine roughly equivalent areas of neural retina approximating a 1-mm-square box of retina centered on the foveal depression, as previously described.[6–8] Table 1 provides details of the seven central B-scans selected for each protocol and a comparison of the scan protocols.

Grading was performed by two certified, experienced graders masked to clinically relevant information using custom MATLAB software (MathWorks, Natick, MA). A 1-mm-wide box overlay was centered on the foveal depression of each B-scan to define the grading area. B-scans were graded for a variety of SDOCT parameters such as overall horizontal extent of DRIL, intraretinal cyst area (determined by the widest vertical and horizontal dimensions of each cyst), subretinal fluid (SRF) horizontal extent, and cone outer segment tip (COST) visibility. The

Table 1. Comparison of SDOCT Scan Protocols

SDOCT Scan Protocols	Spectralis HR	Spectralis HS	Cirrus Cube	Cirrus HD 5-Line	AngioVue OP
B-scan spacing (µm)	120	120	47	250	10
Scan area	20° × 20°	20° × 20°	6 × 6 mm	6 × 6 mm	3 × 3 mm
B-scans (*n*)	49	49	128	5	300
A-scans/s	40,000	40,000	27,000	27,000	70,000
B-scans superior and inferior to the foveal scan for DRIL grading (*n*)	3	3	3rd, 5th, 8th	3rd, 5th, 8th	12th, 24th, 36th

Table 2. Demographic and Ocular Characteristics of the Study Population

Characteristics	Total	Group A	Group B
Demographic			
Eyes/participants, *n*	53/38	27/20	26/18
Age (y), mean ± SD	55.6 ± 16.7	64.4 ± 15.1	45.8 ± 12.6
Gender (female), *n* (%)	17 (44.8)	11 (55)	6 (33.3)
Type 1 diabetes, *n* (%)	15 (39.5)	4 (20)	11 (61.1)
Duration of diabetes (y), mean ± SD	22.8 ± 9.5	23.3 ± 8.8	22.3 ± 10.4
Hemoglobin A1c (%), mean ± SD	7.9 ± 1.1 ($n = 30$)	7.8 ± 1.2 ($n = 16$)	8.2 ± 0.9 ($n = 14$)
Ocular (based on Spectralis HR scans)			
CST (µm), mean ± SD	342.9 ± 83.4	366 ± 100	320.3 ± 53.4
DRIL extent (µm), mean ± SD	264.2 ± 221.8	728 ± 216.6	152.8 ± 177.6
By blurriness	48.6 ± 120.1	602.9 ± 154.5	2.9 ± 8.9
By cysts	183.3 ± 179.1	673.9 ± 173.4	128.3 ± 178.0
By hyperreflective foci	36.4 ± 50.8	267.2 ± 65.8	22.4 ± 19.7
Cyst area (µm^2), mean ± SD	20,155.5 ± 18,545.3	73,031.5 ± 20,443.2	10,125.2 ± 14,906.0
COST visibility extent (µm), mean ± SD	517.6 ± 370.1	876.5 ± 237.8	647.8 ± 360.3
SRF horizontal extent (µm), mean ± SD	37.0 ± 153.2	540.0 ± 130.7	0.0 ± 0.0

Group A: comparison of Spectralis HR versus Spectralis HR, Cirrus Cube, and Cirrus HD 5-Line; group B: comparison of Spectralis HR versus Optovue AngioVue.

horizontal extent of each finding was graded in microns on each B-scan and then averaged across the seven B-scans for each eye. Specific causes of DRIL were also assessed as generalized inner retinal layer boundary blurring (blur), intraretinal cysts crossing boundary lines (cysts), or hyperreflective foci obscuring layer demarcations.

Statistical Analysis

Analysis was performed using SAS 9.4 software (SAS Institute, Inc., Cary, NC). We used intraclass correlation coefficients (ICCs) between respective SDOCT parameters of Spectralis HR and the four other scan modes and 95% confidence intervals (CIs) of the within-scan coefficient of variation.[22] The level of reliability was interpreted as moderate, good, or excellent based on ICC values of 0.50 to 0.75, 0.76 to 0.90, or 0.91 to 1.00, respectively, based on previously described guidelines.[23] $P < 0.05$ was considered significant for these exploratory analyses.

Results

Patient and Ocular Characteristics

In the total cohort, we enrolled 53 eyes of 38 participants. Study population characteristics are displayed in Table 2. Overall, participants had a mean age of 55.6 ± 16.7 years, mean duration of diabetes of 22.8 ± 9.5 years, and mean hemoglobin A1c of 7.9 ± 1.1% ($n = 30$). Of these participants, 39.5% had type 1 diabetes and 44.8% were women. Forty-four eyes

Table 3. ICCs and 95% CIs for SDOCT Parameter Grading Among Scan Types

	ICC (95% CI)			
SDOCT Variable	Spectralis HR vs. Spectralis HS	Spectralis HR vs. Cirrus Cube	Spectralis HR vs. Cirrus HD 5-Line	Spectralis HR vs. AngioVue OP
DRIL extent (μm)	0.93 (0.88–0.96)	0.84 (0.75–0.91)	0.76 (0.63–0.86)	0.87 (0.79–0.93)
By blurriness	0.94 (0.90–0.96)	0.84 (0.74–0.90)	0.75 (0.61–0.85)	0.14 (0.01–0.71)
By cysts	0.94 (0.90–0.97)	0.91 (0.85–0.95)	0.87 (0.79–0.92)	0.88 (0.81–0.93)
By hyperreflective foci	0.67 (0.51–0.80)	0.75 (0.62–0.85)	0.65 (0.48–0.79)	0.44 (0.23–0.67)
Cyst area (μm^2)	0.92 (0.87–0.95)	0.92 (0.86–0.95)	0.95 (0.92–0.97)	0.95 (0.92–0.97)
COST visibility extent (μm)	0.90 (0.84–0.94)	0.75 (0.61–0.85)	0.59 (0.40–0.75)	0.85 (0.76–0.91)
SRF horizontal extent (μm)	0.87 (0.79–0.92)	0.87 (0.79–0.92)	0.94 (0.90–0.97)	NA*

*Only one AngioVue OP scan and no HR images had SRF present; therefore, agreement could not be assessed for this variable.

were classified as having current CI-DME, and nine were classified as recently resolved CI-DME. On Spectralis HR scans, the mean central subfield thickness was 342.9 ± 83.4 μm.

Scan Protocol Grading Agreement

ICCs and 95% CIs for SDOCT grading parameters were generated for the relationships between the extent of each variable for Spectralis HR versus Spectralis HS, Cirrus Cube, Cirrus HD 5-Line, and AngioVue OP scans (Table 3). ICCs comparing the grading of Spectralis HR and HS images were excellent for the assessment of overall DRIL horizontal extent (0.93; 95% CI, 0.88–0.96), DRIL caused by blur (0.94; 95% CI, 0.90–0.96), DRIL caused by cysts (0.94; 95% CI, 0.90–0.97), intraretinal cyst area (0.92; 95% CI, 0.87, 0.95), and COST visibility (0.90; 95% CI, 0.84–0.94). Agreement for SRF horizontal extent was also good (0.87; 95% CI, 0.79–0.92), but correlation for DRIL caused by hyperreflective foci (0.67; 95% CI, 0.51–0.80) was only moderate.

Agreement among variables graded on Cirrus Cube versus Spectralis HR scans was generally good, with ICCs ranging from 0.75 to 0.92. Overall agreement for DRIL extent was good (0.84; 95% CI, 0.75–0.91), as was subretinal fluid assessment (0.87; 95% CI, 0.79–0.92). Excellent agreement was found for intraretinal cyst area (0.92; 95% CI, 0.86–0.95) and DRIL caused by cysts (0.91; 95% CI, 0.85–0.95).

Variables graded on Cirrus HD 5-Line scans demonstrated lower correlations with Spectralis HR than either Spectralis HS or Cirrus Cube images for determination of overall DRIL extent (0.76; 95% CI, 0.63–0.86) and COST visibility (0.59; 95% CI, 0.40–0.75). However, Cirrus HD 5-Line scans showed excellent agreement with Spectralis HR images for intraretinal cyst area (0.95; 95% CI, 0.92–0.97) and SRF extent (0.94; 95% CI, 0.90–0.97).

Agreement variables between Spectralis HR and AngioVue OP images demonstrated good correlation for overall DRIL horizontal extent (0.87; 95% CI, 0.79–0.93) and DRIL caused by cysts (0.88; 95% CI, 0.81–0.93) but low to moderate agreement for DRIL caused by blur (0.14; 95% CI, 0.01–0.71) or hyperreflective foci (0.44; 95% CI, 0.23–0.67). Agreement was excellent for intraretinal cyst area (0.95; 95% CI, 0.92–0.97) and good for COST visibility (0.85; 95% CI, 0.76–0.91).

Absolute and Normalized Differences Among Grading of Scan Protocols

Because thresholds of DRIL extent and other SDOCT variables have been previously evaluated relative to current and future VA,[7] we evaluated absolute differences in variables that were graded between the scan modalities evaluated in this study (Table 4). Absolute differences between HR and OP scans acquired for group B cannot be directly compared to results from group A because the two cohorts differed in average extent of each variable. Within group A, however, the absolute difference in overall DRIL extent between Spectralis HR and HS scans was lower than the absolute differences in DRIL between HR scans and the Cirrus HD 5-Line or Cube (Fig. 3). Spectralis HR and HS scans also exhibited the lowest differences for DRIL caused by blur, cysts, and hyperreflective foci. The HR and HS scans showed the smallest differences in grading of cyst area and COST visibility but did not significantly differ in estimation of subretinal fluid extent.

Table 4. Absolute Differences for Each SDOCT Modality from Spectralis HR

	Mean ± SD			
SDOCT Variable	Spectralis HR vs. Spectralis HS	Spectralis HR vs. Cirrus Cube	Spectralis HR vs. Cirrus HD 5-Line	Spectralis HR vs. AngioVue OP
DRIL extent (µm)	60.0 ± 55.0	98.2 ± 88.6	130.8 ± 112.1	51.1 ± 71.6
By blurriness	38.2 ± 38.6	66.0 ± 80.1	66.9 ± 90.1	3.7 ± 9.1
By cysts	43.9 ± 41.5	57.8 ± 47.1	67.8 ± 67.2	39.1 ± 75.3
By hyperreflective foci	36.5 ± 36.8	27.9 ± 34.6	35.1 ± 41.5	17.5 ± 14.5
Cyst area (µm^2)	4013.9 ± 6766.3	4936.8 ± 6368.5	5132.2 ± 5139.0	2701.6 ± 4075.1
COST visibility extent (µm)	86.7 ± 103.6	124.2 ± 128.9	183.2 ± 147.6	138.4 ± 132.3
SRF horizontal extent (µm)	20.8 ± 88.8	18.9 ± 88.4	15.6 ± 49.4	1.9 ± 10.1

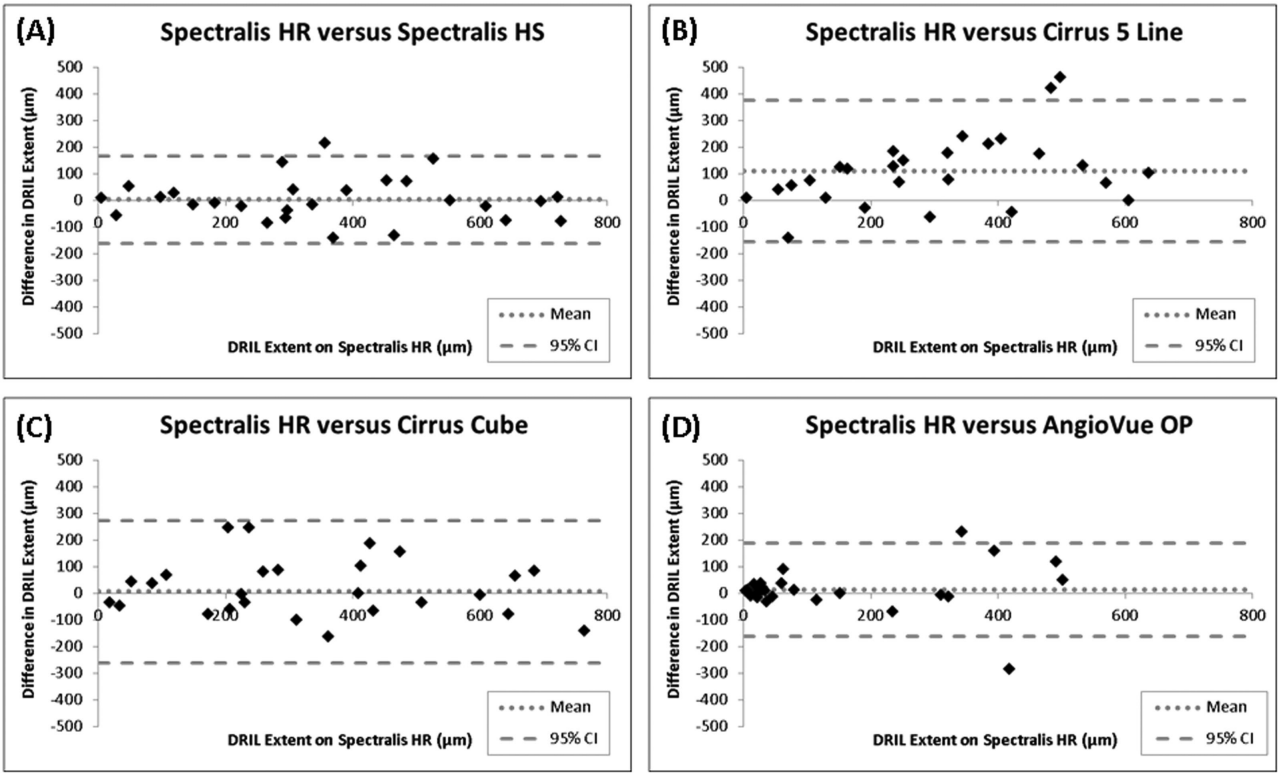

Figure 3. Bland–Altman plots for differences among DRIL extent values for Spectralis HR versus (**A**) Spectralis HS, (**B**) Cirrus HD 5-Line, (**C**) Cirrus Cube, and (**D**) AngioVue OP. The *dotted line* represents the mean difference, and the *dashed lines* correspond to the 95% CIs.

When we normalized the difference in overall DRIL extent for each pairwise comparison in groups A and B to the mean horizontal extent of DRIL on the Spectralis HR images for each group, mean differences of 16.14%, 27.01%, 34.99%, and 33.45% were found for Spectralis HS, Cirrus Cube, Cirrus HD 5-Line, and AngioVue OP scans, respectively. Pairwise comparisons of the normalized differences found significantly smaller mean differences between Spectralis HR/HS scans versus Spectralis HR and all other scan modalities (Spectralis HR/HS vs. Spectralis HR/Cirrus Cube, $P = 0.02$; Spectralis HR/HS vs. Spectralis HR/Cirrus HD 5-Line, $P = 0.0005$; Spectralis HR/HS vs. Spectralis HR/AngioVue OP, $P < 0.0001$). There were no statistically significant differences among comparison results for Spectralis HR/Cirrus Cube, Spectralis HR/Cirrus HD 5-Line, or Spectralis HR/AngioVue OP.

Discussion

In this study, we investigated the reproducibility of grading for a variety of SDOCT parameters across four different SDOCT modalities as compared to gold-standard Spectralis HR scans, the most used protocol for retinal morphology and function in DME studies. The highest correlations and least variability for DRIL, intraretinal cyst, COST visibility, and SRF extent assessments were present when comparing Spectralis HR and HS scans. However, good to excellent correlations for OCT variables were also observed when comparing Spectralis HR and Cirrus Cube or AngioVue OP scans. Correlations between Spectralis HR and Cirrus HD 5-Line scan gradings were lower for overall DRIL extent and COST visibility than for the other scan comparisons.

To the best of our knowledge, this study represents the first systematic exploration of DRIL and other SDOCT variable grading across various machines and scan protocols. These data improve the ability to interpret and compare results from studies that evaluate these parameters on SDOCT images from different scan protocols and machines. In addition, these results may prove useful in planning future studies by providing more precise estimates of the variability to be expected across these different modalities. Understanding the variability in estimation of DRIL extent may also improve our ability to set clinically meaningful thresholds as related to visual acuity outcomes.

Spectralis HR scans were used as the comparison standard in this study because the majority of previous studies exploring the relationship between retinal morphology and function in DME have been performed using this scan protocol. HR scans offer higher resolution views of the retinal architecture than HS scans, with scan rates of 768, 1024, and 1536 A-scans per B-scan versus 384, 512, and 768 A-scans per B-scan, respectively.[19,24,25] However, the HS mode presents an advantage in minimizing motion artifact through swift image acquisition, and it has been utilized in many recent multicenter clinical studies for retinal evaluation.[1–3] This study demonstrates that HS scans offer high reproducibility compared to HR scans for grading DRIL and other variables.

Cirrus scanning modalities have different specifications from Spectralis HR, with the Cirrus HD 5-Line Raster mode acquiring 4096 A-scans and the Cube mode 512 A-scans per B-scan. A study on eyes with neovascular age-related macular degeneration comparing the two Cirrus modalities has demonstrated that 5-Line Raster scans had high sensitivity (98.4%) for detecting fluid.[26] Although Cirrus Cube scans have lower resolution than 5-Line Raster scans, they demonstrated better reproducibility compared to Spectralis HR scans in this study, perhaps because of denser scan spacing. Cirrus Cube B-scans are spaced 47 µm apart, in contrast to Cirrus HD 5-Line Raster B-scans, which are spaced 250 µm apart. Consequently, Cirrus HD 5-Line Raster scans were not as precisely registered to the Spectralis HR images, which are spaced 120 µm apart. Thus, differences in grading may have been due to real differences in findings on B-scans centered on different locations. Although Cirrus HD 5-Line Raster scans generally demonstrated the lowest correlations with Spectralis HR, reproducibility of overall DRIL extent was still good ($r = 0.76$), and grading of cyst boundary area and SRF horizontal extent showed excellent reproducibility.

We also assessed DRIL extent between Spectralis HR scans and those obtained from AngioVue OP. OP B-scans as derived from the OCT angiography mode are 10 µm apart versus the HR scans that are 120 µm apart. We achieved precise registering of the OP to HR scans by substacking the 12th, 24th, and 36th B-scans superior and inferior to the foveal OP scans. However, the speed of OP scans is 70,000 A-scans per second compared to 40,000 A-scans per second for the HR mode. The results demonstrated a good to excellent reproducibility for DRIL horizontal extent, DRIL caused by cysts, intraretinal cyst area, and COST visibility but lower reproducibility for DRIL caused by either hyperreflective foci or blur. These differences for DRIL caused by hyperreflectivity and blur may have been due to the higher OP scan speed that may result in lower image definition.

Strengths of this study include the fact that all imaging technicians followed standard procedures and were all trained for clinical study protocol SDOCT imaging on Spectralis, Cirrus, and AngioVue devices. In addition, masked grading was performed on all study images by a centralized reading center with high intergrader reproducibility for DRIL extent. Limitations of this study include the assessment of only three types of commercially available SDOCT devices. Moreover, DRIL presence was not equally distributed between groups A and B. Group B had less severe DRIL extent compared to group A. Nonetheless, the correlation of overall DRIL extent was good between OP and HR scans, and normalized absolute differences suggest similar grading results between OP and Cirrus Cube or 5-Line scans. Finally, patient factors that can result in decreased image quality, such as

incomplete pupillary dilation or corneal desiccation, were not evaluated,[27–29] but these were expected to be similar for serial scans obtained for each patient. The order in which the scans were taken was changed between the patients to minimize the effects of reduced tear film or patient fatigue.

This study directly compared the reproducibility of grading for morphologic features such as DRIL extent, cyst area, COST visibility, and SRF extent in eyes with CI-DME across three different SDOCT instruments using five different imaging protocols. Although the highest reproducibility was seen for Spectralis HS versus Spectralis HR scans, comparison with Cirrus Cube, Cirrus HD 5-Line Raster, and AngioVue OP images also resulted in moderate to excellent agreement with Spectralis HR image findings. These data may be useful in planning and interpreting future studies that incorporate these specific protocols. These findings demonstrate that grading of DRIL and parameters such as intraretinal cyst area, COST, and SRF can be reproducible across multiple SDOCT devices and scan protocols, allowing clinicians and researchers flexibility in DME assessment for clinical care and research.

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