Choroidal Line Scan Measurements in Swept-Source Optical Coherence Tomography as Surrogates for Volumetric Thickness Assessment

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• PURPOSE: To compare choroidal thickness of different areas on swept-source optical coherence tomography (SSOCT) line and cube scans for their interchangeable use.

• DESIGN: Validity analysis.

• METHODS: SSOCT line and cube scans were obtained from 21 patients with various choroidal thicknesses. Subfoveal center point choroidal thickness, mean central millimeter choroidal thickness, and mean 6-mm-area choroidal thicknesses were obtained from both eyes by 2 independent graders in a reading center setting. Cross-correlations were performed using Passing and Bablok regression models. A 95% confidence interval of slope that included 1 was considered to indicate no significant difference. Average choroidal thickness of center point, Early Treatment Diabetic Retinopathy Study grid subfields, and total grid area of 6 mm on both scans and the correlation between different areas served as main outcome measures.

• RESULTS: No significant difference between line scans/corresponding subfields of cube scans (outer nasal 0.92–1.11, inner nasal 0.88–1.06, central 0.94–1.11, inner temporal 0.95–1.12, outer temporal 0.93–1.17). No significant difference between subfoveal center point measurement/mean of choroidal thickness in the central millimeter of cube scans (0.89–1.08). Significant difference of subfoveal center point measurement or mean of central millimeter area of cube scans to entire 6-mm area of cube scans (1.01–1.53 and 1.03–1.38).

• CONCLUSIONS: Measurements on a single SSOCT horizontal line scan can represent the entire choroid but subfoveal center point measurements are only indicative for the central millimeter area. There is a consistent overestimation of choroidal thickness when trying to estimate overall choroidal thickness from any central measurement. (Am J Ophthalmol 2016;162:150–158. © 2016 by Elsevier Inc. All rights reserved.)

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CHOROIDAL THICKNESS WAS FIRST MEASURED in vivo by ultrasound more than 3 decades ago.[1] The measurements were inaccurate and small changes could not be detected. Optical coherence tomography (OCT) is the most frequently used imaging technique in ophthalmology today, and its continuous technical advances have allowed imaging not only of the retina but also of the choroid. With enhanced-depth imaging and long-wavelength OCT at 1050-nm, the choroid can now be assessed in vivo to its full extent and with high accuracy for the first time.

The choroid is a vascular layer with many functions in healthy and diseased eyes, including regulating temperature and intraocular pressure.[2,3] Its most important function is to supply the outer retina with oxygen and nutrients. The foveal avascular zone of the choroid is the primary source of nutrients.[4] Choroidal thickness is variable and many studies have shown factors that influence choroidal thickness. Age has the greatest influence—the older we get, the more the choroid thins.[5] Women have a thinner choroid than men, and axial length is also a known influence factor (the greater the axial length, the thinner the choroid).[6] Environmental factors that affect choroidal thickness, such as drinking coffee,[7] smoking,[8] and even drinking more than 1000 mL of water in less than 1 hour,[9] have been identified. Blood pressure,[10] eye pressure,[11] and hypercholesterolemia are other possible influences.[12] All these factors generate the need for an easy, manageable scanning and evaluation protocol for the choroid.

Many earlier studies measured subfoveal choroidal thickness at a single point in order to evaluate the degree of choroidal thinning as a sign for choroidal disease involvement. But, unlike the retina, which is known to have a different layer structure at the fovea, there is no evidence that subfoveal choroidal thickness is sufficient for drawing conclusions about the entire choroid. On the one hand, new OCT technologies allow us to image more than 1 B-scan at the foveal center and to evaluate more than 1 single subfoveal point. On the other hand, manual evaluation is time-consuming and automatic analyses need to be

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validated first. Therefore, there is a need for a scanning protocol that allows conclusions of the highest possible validity and covers a larger area of the choroid and that is also applicable for daily clinical use.

To date, the only marketed swept-source 1050-nm OCT device has a standard protocol of 256 × 256 scans. This protocol results in 65 536 scanning and evaluation points, which is too many to be feasible for manual evaluation and thus excludes clinical use. An automated analysis of the choroid where more evaluation points increase accuracy of an algorithm is currently not available in clinical practice. Therefore manual segmentation remains necessary.

Compared with the standard protocol of 256 × 256 scans, single B-scans are easy to obtain with a shorter acquisition and post-processing analysis time than for the cube scan. Manual segmentation of 1 or 2 single B-scans (horizontal and/or vertical) is not very time-consuming and is therefore feasible in clinical practice. Hence, many studies that analyzed choroidal thickness in the past used single-point measurements to draw conclusions for the entire choroid.[7,8,13,14] In our study we aimed to evaluate if a line scan can represent the entire cube scan area and the subareas for which they can serve as valid predictors.

METHODS

• **STUDY DESIGN, PARTICIPANTS AND OPTICAL COHERENCE TOMOGRAPHY EXAMINATION:** The presented study is a prospectively designed validity analysis study that was approved by the ethics committee of the Medical University of Vienna. OCT scans were all obtained from patients attending the uveitis outpatient clinic of the Department of Ophthalmology at the Medical University of Vienna. A high spread of different choroidal thicknesses could be expected in these patients. Images were taken according to a predefined imaging protocol to guarantee a standardized procedure. All participating patients gave informed consent prior to the study and the study adhered to the tenets of the Declaration of Helsinki and the standards of Good Scientific Practice of the Medical University of Vienna.

Inclusion criteria were patients over 18 years of age, no pregnancy, and the presence of an acute or chronic stage of uveitis of any form. All patients were imaged once with a DRI-1, Atlantis Swept-Source OCT (Topcon, Tokyo, Japan) operating at a 1050-nm wavelength. Exclusion criteria were ocular opacity due to cataract, vitreous opacification or corneal opacities that might lead to poor image quality that prevents evaluation of the choroid, and poor visual acuity precluding fixation during the OCT examination.

OCT images were obtained from each patient after a full ophthalmologic examination including visual acuity testing, eye pressure measurement with Goldmann applanation tonometry, and fundus biomicroscopy in fully dilated pupils. The scanning protocol used was a 12 × 9-mm macular wide-field cube scan with 256 × 256 scanning points and a pseudo-averaging of 3 scans (averaging of each B-scan with 2 consecutive B-scans [previous and next B-scan]) and a 12-mm horizontal line scan at the foveal center point with a real averaging mode of 96 scans.

The main outcome measures were the average choroidal thickness of the center point, Early Treatment Diabetic Retinopathy Study (ETDRS) grid subfields and entire ETDRS grid area of 6 mm of the line and cube scans, and the correlation between different areas.

• **STANDARDIZED IMAGE EVALUATION:** All scans were exported, saved in the database of the Vienna Reading Center (VRC), and analyzed with custom VRC software by an experienced VRC grader. An ETDRS grid[15] was positioned at the foveal center point in line and cube scans. The B-scan position of the line scan was compared to the B-scan of the cube scans that contains the center point, and if the line scan did not hit the foveal center point the eye was excluded from the study. The software automatically showed the inner and outer choroidal border of the choroid using an automatic algorithm validated by the VRC. This was used as the starting point for choroidal delineation in the line scans. The 2 borders comprising the choroid were delineated with the highest possible accuracy. As a last step, choroidal thickness in the ETDRS "fields" outer nasal, inner nasal, center, inner temporal, and outer temporal was calculated. The annotated B-scan had a length of 12 mm (256 scanning points), of which 6 mm (128 scanning points) were used in the ETDRS grid. Therefore, each millimeter of the ETDRS grid comprised 21 or 22 (128/6) scanning points. This means for our automated calculations that after segmentation correction of the line scan, mean choroidal thickness was automatically calculated by the software from 32 scanning points in the outer nasal and outer temporal, 21 scanning points from the inner nasal and inner temporal, and 22 scanning points from the central millimeter choroidal thickness. In many cases no segmentation adjustment was necessary, as the segmentation performed very well. If it had to be adjusted, the segmentation correction of each line scan took only a few seconds; the images were very clear and the choroid could be well delineated, as the image was averaged from 96 B-scans of the same location. Line scans where a full delineation of the 6-mm area was not possible owing to poor image quality were excluded from the analysis.

The cube scan was analyzed by manual inspection of each result of the automatic choroidal delineation. If large errors (deviation of >10% of total choroidal thickness or deviation of more than 1 mm length on any B-scan) were present, the scans were excluded from the study. A deviation of >10% was chosen because this is about the reported 95% confidence interval of a choroidal thickness in a healthy population.[5] Smaller errors were manually

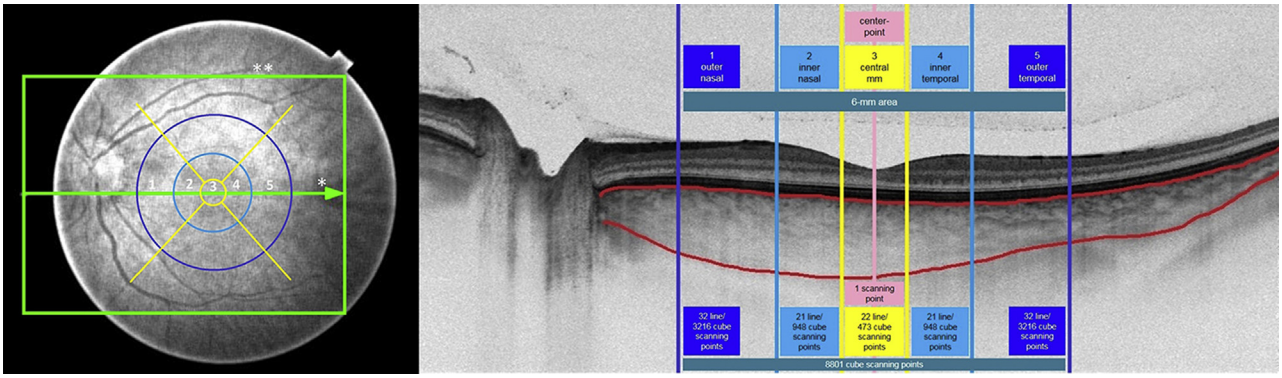

FIGURE 1. Examples to show line and cube scan choroidal thickness measurement and Early Treatment Diabetic Retinopathy Study (ETDRS) subfields. (Left) A representative fundus image showing the position of a 12-mm line scan (*) and a 12 × 9-mm cube scan (**) in relation to the fundus image and the ETDRS subfields (from left to right) outer nasal (1), inner nasal (2), central mm (3), inner temporal (4), outer temporal (5) of a left eye; the entire 6-mm area corresponds to the addition of fields 1+2+3+4+5. All line scan measurements and calculations derived from the single green line (*). All scanning points (A-scans) on the line in each subfield 1–5 were averaged into 1 subfield value. All scanning points (A-scans) on the several B-scans of the 256 × 256 cube scan (**) crossing each subfield 1–5 were averaged into 1 subfield value. The center point measurement was the central point measurement in subfield number 3. (Right) A representative B-scan showing the choroidal thickness measurement on a line scan. The choroid is delineated between the 2 red lines. The space between the red lines represents choroidal thickness. The illustrated B-scan corresponds to the green line scan (*) on the left image. The thickness between the 2 red lines at the center of the fovea on this scan corresponds to the central point measurement in subfield number 3 on the left image. Each of the subfields comprises a certain number of scanning points that were used for automated calculation of choroidal thickness values after manual adjustment of the segmentation lines at the choroidal borders.

corrected, a time-consuming procedure because of the large number of B-scans and the worse resolution compared to the line scan, as the cube scans are not averaged. Automatically calculated thickness values for each ETDRS subfield were also noted from the cube scan areas. The 12 × 9-mm cube scan comprised 256 × 256 (65 536) scanning points. Therefore, each subfield comprised the following scanning points (number of A-scans): 473 scanning points (central millimeter), 948 scanning points (inner nasal and temporal), and 3216 scanning points (outer nasal and temporal), which were used for the automated calculation of the choroidal thickness values by the software.

As a last step, the choroidal thickness value of a single-point subfoveal measurement at the center point was noted as a value from a single measurement point from the cube and line scans (manual measurement of orthogonal line measurement between delineated choroidal boarders of line scans or of scan through center point in cube scans; see Figure 1 for choroidal borders and position of center point measurement). The value of the "mean" choroidal thickness in the entire 6-mm area of the cube scan was calculated by using the known number of points in each subfield, as described in the paragraph above.

The same trained and experienced grader from the VRC analyzed the scans in random order. To guarantee high quality, all data were checked by a second expert grader and if discrepancies appeared the graders reached agreement by analyzing the scans again together.

Examples to show line and cube scan choroidal thickness calculations and ETDRS subfields on a representative fundus image showing the position of a 12-mm line scan and a 12 × 9-mm cube scan and the ETDRS subfields, as well as a representative B-scan showing the choroidal thickness calculation on a line scan, are given in Figure 1. Figure 1 also gives an overview of the number of scanning points in each subfield. All scanning points (A-scans) on the line in each ETDRS subfield were averaged into 1 line scan subfield value. All scanning points (A-scans) on the several B-scans of the cube scan crossing each ETDRS subfield were averaged into 1 cube scan subfield value. Thus, each of the subfields comprises a certain number of scanning points (see above-mentioned numbers) that were used for automated calculation of choroidal thickness values after manual adjustment of the segmentation lines at the choroidal borders. The center point measurement was the central point measurement in the central millimeter subfield and was only calculated from 1 manual measurement point.

• **STATISTICAL EVALUATION:** Passing and Bablok regression was used for all statistical comparisons. A 95% confidence interval of slope that included 1 was considered to indicate no significant difference in calculated intervals between the calculated values. Likewise, if the 95% confidence interval for the intercept did contain 0, this was taken as no significant constant shift between calculations. A test for linearity was performed before testing for these statistical differences. If the linearity testing was positive (no significant deviation from linearity) and there was no significant difference between areas, values from both areas could be used interchangeably. If the linearity testing was positive and there was a significant difference between

areas, a linear conversion formula could be found to use values from one area for the calculation of the values of the other area. If there is a significant deviation from linearity, there is no simple linear conversion formula (change of unit of calculated value and/or origin).

• **SCAN ANALYSIS:** As the primary objective, values from line and cube scan calculations of the corresponding outer nasal, inner nasal, central, inner temporal, and outer temporal ETDRS subfields were compared.

As the secondary objective, cross-comparisons of the values of single-point subfoveal measurements at the center point, mean values of all calculation points in the entire central millimeter area, and mean values of all calculation points in the entire 6-mm area of the cube scan were performed. The comparisons included:

A) the value of a single-point subfoveal measurement at the center point from cube scans vs the calculated mean value of all scanning points in the entire central millimeter area;
B) the value of a single-point subfoveal measurement at the center point from cube scans vs the calculated mean value of all scanning points in the entire 6-mm area; and
C) the calculated mean value of all scanning points in the entire central millimeter area vs the calculated mean value of all scanning points in the entire 6-mm area.

In addition, we evaluated if a conversion formula could be applied to any of the results where a significant difference was found for 2 areas but linearity testing was positive, meaning that they cannot represent entire areas but there is a regular error.

RESULTS

• **PATIENT POPULATION AND SCAN EXCLUSION:** Forty-two eyes were screened for the study. Visual acuity testing and slit-lamp examination including fundus biomicroscopy were performed prior to OCT scanning. Consequently, 1 eye with poor study preconditions (media opacities, poor visual acuity precluding fixation) was excluded without OCT measurements. Forty-one eyes of 21 patients remained for OCT scanning. Scans of 3 eyes of 3 patients had to be excluded owing to poor image quality and/or poor automated segmentation quality in the cube scan, but these patients' second eyes remained in the study. No scans had to be excluded owing to a wrong B-scan location (not scanned at foveal center point), impossible line scan annotation, or lack of agreement between graders. Thus, choroidal thickness values from scans of 38 eyes of 21 patients remained for statistical analysis.

Out of 21 patients, 15 patients suffered from posterior uveitis or panuveitis (toxoplasmosis, syphilis, serpiginous-like choroiditis, punctate inner choroidopathy, idiopathic chorioretinitis, or retinal vasculitis; Behçet or birdshot chorioretinitis; Vogt-Koyanagi-Harada disease), 1 patient had an idiopathic intermediate uveitis, 1 patient had scleritis, and 4 patients suffered from HLA-B27-associated anterior uveitis. The mean age of the study group of 21 patients was 42.1 years and the ratio of men to women was 10:11 (48% men). The mean age of the study group of 38 eyes (age of patients with 2 included eyes counted double) was 42.5 years and the ratio of male to female eyes was 17:21 (45% male eyes). Mean choroidal central millimeter thickness in line scans was 306 μm ± 94 μm and the mean choroidal thickness value of single-point subfoveal measurements at the center point in line scans was 312 μm ± 108 μm, with a range between 112 and 719 μm; mean choroidal central millimeter thickness in cube scans was 302 μm ± 87 μm and the mean choroidal thickness value of single-point subfoveal measurements at the center point in cube scans was 307 μm ± 96 μm with a range between 112 and 536 μm.

• **LINEARITY TESTING:** There was no significant deviation from linearity for any of the areas tested, meaning that either all areas would either be representative for the other area or a conversion formula could be found for this particular case.

• **PRIMARY OBJECTIVE:** Line Scan Versus Cube Scan Measurements

For the primary objective, if line scan measurements can represent the thickness in corresponding ETDRS subfields of a cube scan, there would be no significant difference between the corresponding subfields (outer nasal 0.92–1.11, inner nasal 0.88–1.06, central 0.94–1.11, inner temporal 0.95–1.12, outer temporal 0.93–1.17). Regression equations of each subfield are given in Figures 2 and 3.

In Table 1 exemplary calculations for 200 μm, 300 μm, and 400 μm of choroidal thickness in each area could be found to estimate what the deviation in line scan thickness from cube scan thickness in corresponding areas was. For example, if the line scan had measured 300 μm mean central millimeter choroidal thickness, the thickness would be 296 μm in the cube scan, which is a deviation of −1.3% and is not statistically significant. All values of significance are shown in Table 1. These calculations show that horizontal line scan measurements are indicative for corresponding horizontal cube scan areas without conversion.

• **SECONDARY OBJECTIVES: CROSS-COMPARISONS OF DIFFERENT AREAS:** For the secondary objective, if:

A) the value of a single-point subfoveal measurement at the center point from cube scans can represent the entire central millimeter area of a cube scan, there would be no significant difference between calculated values (0.89–1.08), meaning values of single-point subfoveal measurements at the center point are

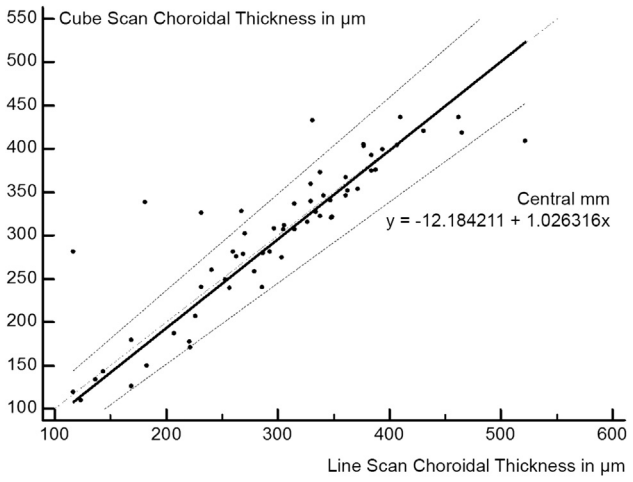

FIGURE 2. Regression equation for choroidal thickness in central millimeter Early Treatment Diabetic Retinopathy Study (ETDRS) subfield. The regression equation of choroidal thickness in the central millimeter ETDRS subfield can be used for the conversion calculation between a choroidal thickness value measured on an optical coherence tomography (OCT) line scan in order to get the estimated value from an OCT cube scan. The equation shows that a conversion is not necessary, as line scan measurements can represent the thickness in the corresponding ETDRS subfield of a cube scan. There was no significant difference between the corresponding subfields in Passing and Bablok regression analysis, where a 95% confidence interval of slope that includes 1 is considered to indicate no significant difference in measured intervals between the measurements and/or calculations: central mm 0.94–1.11. All values are in µm; the Passing and Bablok correlation equation is printed as a bold line and its 95% confidence intervals are printed as coarse dotted lines; the identity line, meaning the line where both methods would deliver the same results, is printed as a dotted line.

indicative for the entire central millimeter area on a cube scan without conversion;

B) the value of a single-point subfoveal measurement at the center point from cube scans can represent the entire 6-mm area of a cube scan, there would be a significant difference between calculated values (1.01–1.53), meaning values of single-point subfoveal measurements at the center point are not indicative for the entire 6-mm area on a cube scan without conversion; and

C) the mean of calculation points in the central millimeter area of a cube scan can represent the entire 6-mm area of a cube scan, there would be a significant difference between calculated values (1.03–1.38), meaning mean central millimeter choroidal thickness on a cube scan is not indicative for the entire 6-mm area on a cube scan without conversion.

Regression equations of these 3 scenarios are shown in Figure 4. In Table 2 exemplary calculations for 200 µm, 300 µm, and 400 µm of choroidal thickness in each area can be found to estimate what the deviation between each comparison area would be—for example, if:

A) the central millimeter calculated value was 300 µm of choroidal thickness, taking into consideration all scanning points of the cube scan (473 scanning points) in the central millimeter, and the calculated central millimeter choroidal thickness from 1 center point measurement from cube scans (1 measurement point) was 304 µm, there was a statically nonsignificant deviation of +1.3%,

B) the 6-mm-area calculated value was 300 µm of choroidal thickness, taking into consideration all scanning points of the cube scan (8801 scanning points) in the 5 ETDRS subfields (outer nasal/temporal, inner nasal/temporal, and central millimeter), and the calculated 6-mm choroidal thickness from the mean of central millimeter scanning points (473 scanning points) was 335 µm, there was a statistically significant deviation of +11.7%, and

C) the 6-mm-area calculated value was 300 µm of choroidal thickness, taking into consideration all scanning points of the cube scan (8801 scanning points) in the 5 ETDRS subfields (outer nasal/temporal, inner nasal/temporal, and central millimeter), and the calculated 6-mm choroidal thickness from 1 center point measurement from cube scans (1 measurement point) was 330 µm, there was a statistically significant deviation of +10.0%.

All deviation values in percent are shown in Table 2.

These results also show that there is a consistent overestimation of choroidal thickness when trying to estimate the 6-mm-area thickness from any central measurement or calculation in a cube scan. None of the equations shows a statistically significant deviation from linearity. Therefore, the regression equations can be used for conversion.

DISCUSSION

THE STUDY PRESENTED SHOWS THAT HORIZONTAL LINE scans are representative for corresponding cube scan EDTRS subfields and that the values measured do not need to be converted in order to draw conclusions on the choroid in the corresponding cube scan areas. Furthermore, the value of a single-point subfoveal measurement at the center point in a cube scan can represent the choroid in the entire central millimeter of the cube scan and the values measured do not need to be converted in order to draw conclusions on the choroid in the entire central millimeter. However, the study also shows that neither single subfoveal choroidal center point measurements on a cube scan nor mean central millimeter calculations on a cube scan can represent the entire 6-mm area of the choroid around the fovea of the cube scan. Nevertheless, a linear conversion

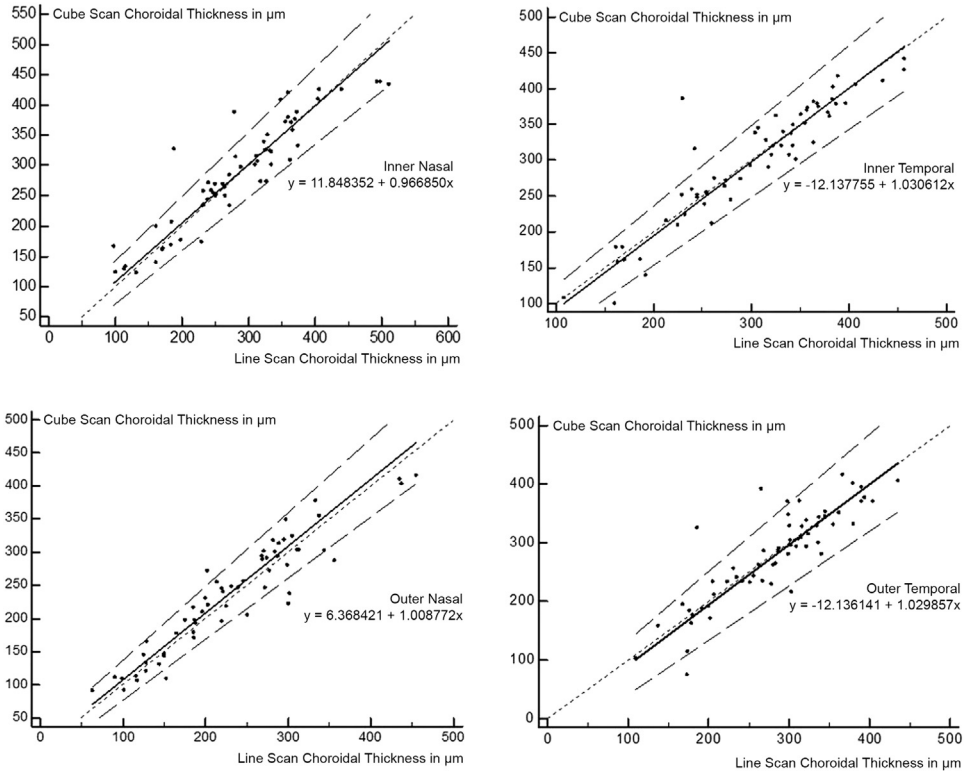

FIGURE 3. Regression equations for choroidal thickness in corresponding nasal and temporal Early Treatment Diabetic Retinopathy Study (ETDRS) subfields. The regression equation of choroidal thickness in the ETDRS subfield outer and inner nasal and temporal subfields can be used for the conversion calculation between choroidal thickness values measured on an optical coherence tomography (OCT) line scan in order to get the estimated values from an OCT cube scan. The equation shows that a conversion is not necessary, as line scan measurements can represent the thickness in corresponding ETDRS subfields of a cube scan. There was no significant difference between the corresponding subfields in Passing and Bablok regression analysis, where a 95% confidence interval of slope that includes 1 is considered to indicate no significant difference in measured intervals between the measurements and/or calculations: (Top left) inner nasal 0.88–1.06, (Top right) inner temporal 0.95–1.12, (Bottom left) outer nasal 0.92–1.11, (Bottom right) outer temporal 0.93–1.17. All values are in µm, the Passing and Bablok correlation equation is printed as a bold line, and its 95% confidence intervals are printed as coarse dotted lines; the identity line, meaning the line where both methods would deliver the same results, is printed as a dotted line.

TABLE 1. Choroidal Thickness Deviation in Line Scan Measurements Calculated From Cube Scans in Corresponding Areas[a]

	Cube Scan Thickness (µm) and its Percentage Deviation From Line Scan Thickness									
Line Scan Thickness (µm)	Outer Nasal		Inner Nasal		Central Millimeter		Inner Temporal		Outer Temporal	
200	208	+4%	205	+2.5%	193	−3.5%	194	−3%	194	−3%
300	309	+3%	302	+0.7%	296	−1.3%	297	−1%	297	−1%
400	410	+2.5%	399	−0.3%	398	−0.5%	400	±0%	400	±0%

[a]Cube scan thickness was calculated with regression equations from Figures 2 and 3 for different line scan thickness values from 200 to 400 µm.

can be found to adjust for overestimation, and if the correct adjustment is made it is also possible to draw conclusions on the central 6-mm choroid from single-point measurements.

We found a constant overestimation of the mean choroidal thickness of the entire 6-mm area when only the central choroidal thickness was used for the calculation. This finding can be explained by the earlier literature. The choroid is very variable in thickness, with the thickest point subfoveally and thinning nasally and temporally.[16,17] For example, the choroid measurements between the foveal center point and 2.5 mm distance from the fovea in the nasal and temporal direction showed a mean subfoveal thickness of 272 µm, thinning temporally to 218 µm and nasally to 157 µm in healthy eyes.[17] A choroidal thickening

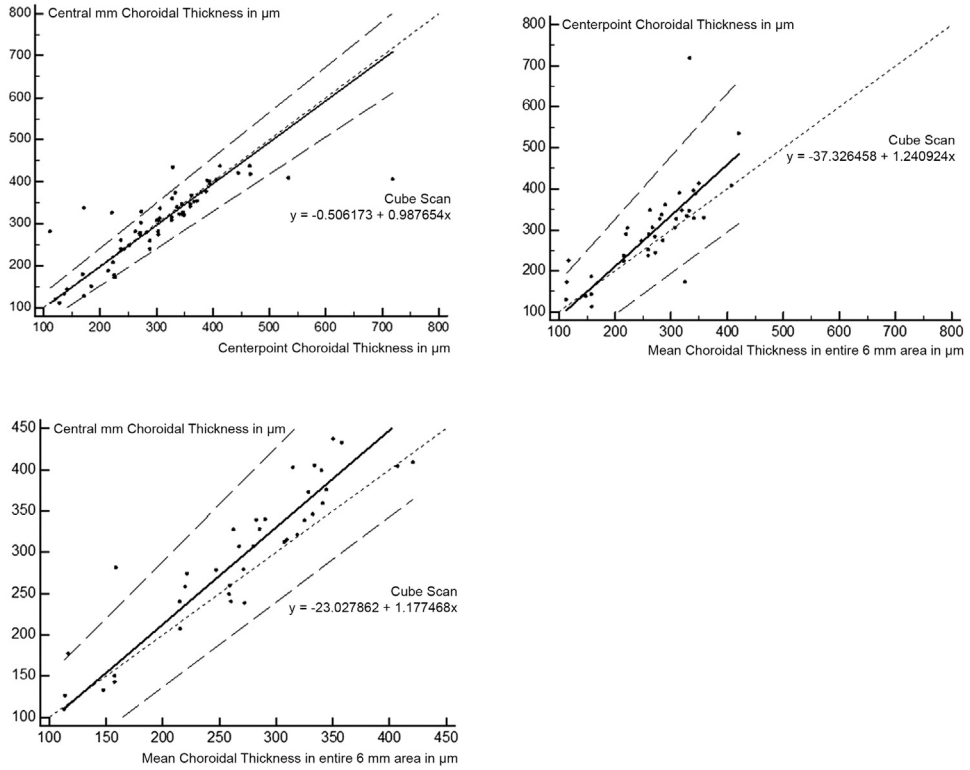

FIGURE 4. Regression equations for choroidal thickness for comparison of different areas. The regression equation of choroidal thickness between (Top left) the values of a single-point subfoveal measurement at the center point and the central millimeter Early Treatment Diabetic Retinopathy Study (ETDRS) subfield, between (Top right) the values of a single-point subfoveal measurement at the center point and the total 6-mm area of an ETDRS grid, and between (Bottom left) the central millimeter ETDRS subfield and the total 6-mm area of an ETDRS grid can be used for the conversion calculation between choroidal thickness values measured on an optical coherence tomography (OCT) cube scan in order to get the estimated values on the same cube scan for larger areas. The equation shows that a conversion is not necessary in the first comparison (Top left), as the value of a single-point subfoveal measurement at the center point can represent the entire central millimeter area of a cube scan. There was no significant difference between measurement values in Passing and Bablok regression analysis, where a 95% confidence interval of slope that includes 1 is considered to indicate no significant difference in measured intervals between the measurements and/or calculations: (Top left) 0.89–1.08. The equations show, furthermore, that a conversion is necessary, as the point or central millimeter measurements/calculations cannot represent the thickness in the 6-mm area. There was a significant difference between the corresponding areas in Passing and Bablok regression analysis, as the 95% confidence interval of slope does not include 1: (Top right) the value of a single-point subfoveal measurement at the center point vs mean of scanning point values in 6-mm area 1.01–1.53, (Bottom left) mean of scanning point values in central millimeter vs mean of scanning point values in 6-mm area 1.03–1.38. All values are in µm; the Passing and Bablok correlation equation is printed as a bold line and its 95% confidence intervals are printed as coarse dotted lines; the identity line, meaning the line where both methods would deliver the same results, is printed as a dotted line.

in the center of the choroid does not necessarily mean a thickening of the entire choroid. Earlier studies that measured not only 1 subfoveal point but more points in different areas showed that choroidal thickness is not always altered to the same extent in all areas. In highly myopic eyes, choroidal thinning to 101 µm ± 57 µm was found at the foveal center point and to 82 µm ± 35 µm nasally, but a thickening to 125 µm ± 60 µm was found temporally.[18] Findings were similar in another study. In patients with geographic atrophy, the subfoveal choroidal thickness was thinned to 158 µm ± 24 µm in patients compared with a healthy control group with a subfoveal choroidal thickness of 268 µm ± 19 µm. This thinning was not found nasally and temporally, where choroidal thickness was found to be 164 µm ± 21 µm temporally (+3.8%) and 142 µm ± 22 µm nasally (−10.1%), whereas the control group had thinning to 244 µm ± 17 µm temporally (−9.0%) and 220 µm ± 21 µm nasally (−17.9%).[19] These findings indicate that looking at an entire B-scan instead of one value of a single-point subfoveal measurement at the center point is necessary in diseased choroid and that choroidal changes are different in different diseases.

Earlier studies have already indicated that simply measuring subfoveal choroidal thickness is not enough for drawing conclusions on the entire choroid, and alternative scanning protocols have been suggested. One suggestion was to use 6

TABLE 2. Deviation of Choroidal Thickness Measurements in Different Scan Subfields Calculated From Smaller Cube Scan Subfields[a]

A			B			C		
Original Measurement in Central Millimeter	Estimated Value From Center Point Measurement	Deviation (%)	Original Measurement in 6-mm Area	Estimated Value From Center Point Measurement	Deviation (%)	Original Measurement in 6-mm Area	Estimated Value From Central Millimeter Measurement	Deviation (%)
200	203	+1.5	200	211	+5.5	200	212	+6
300	304	+1.3	300	335	+11.67	300	330	+10
400	406	+1.5	400	459	+14.75	400	448	+12

Choroidal thickness measurements are in μm.

[a]Choroidal thickness and its percentage deviation in different subfields, calculated with regression equations from Figure 4 for different calculated values for the example of 200, 300, and 400 μm. For example, the real value for column B, 6-mm area of 200, 300, or 400 μm in the columns with *"Original measurements"* originates from the mean of the scanning points used from the cube scan in the 6-mm area (8801 scanning points), whereas the calculated measurements in the columns with "*Estimated value from center point measurement*" originate from the center point measurement of the cube scan (1 measurement point) and the calculated regression equation. In this example the calculated regression equation overestimates the thickness in the 6-mm area, as the single center point measurement only uses the thickest choroidal measurement and does not take into consideration that the choroid thins in nasal and temporal areas.

radial line scans for generating choroidal thickness and volume maps.[20] This imaging protocol is an alternative but is still 6 times more work than using a single line scan, and probably no further information can be retrieved with this protocol. Another alternative protocol would be a horizontal and a vertical line scan, but this was not investigated in the present study. Researchers who suggested reducing the B-scan density of volume scans for evaluation of choroidal thickness over the posterior pole tested between 97 and 16 line scans with a spacing of 30–480 μm. They concluded that 16 scans with an inter-B-scan spacing of 480 μm are enough to estimate the choroidal thickness in the ETDRS subfields. They did not exclude the possibility that even fewer line scans, such as 1 single scan as we propose, could be enough.[21]

We decided to evaluate horizontal line scans only in our study and did not image patients with vertical line scans for the best applicability in daily clinical use. We believe it is possible to draw conclusions on the inferior and superior choroidal areas from subfoveal choroidal measurements. Ikuno and associates have measured choroidal thickness in 86 eyes at 5 locations of the choroid (center point, nasally, temporally, inferiorly, and superiorly). They concluded that choroidal thickness is decreasing nasally and temporally but is identical in inferior, central, and superior areas.[22] Therefore the evaluation of horizontal line scans only allows conclusions on the entire choroid, and no adjustment with any conversion formula has to be performed. This hypothesis would, of course, have to be confirmed on each particular disease, especially in diseases that are associated with a distinct pattern of retinal vascular changes over the posterior pole that might be the same in the choroidal vascular bed (eg, branch retinal vein occlusion).

A strength of our study is the broad range of choroidal thicknesses we included from a patient group with many different choroidal changes in order to draw conclusions on thickened and thinned choroid. Uveitis is known from histology to be a disease with high variability in choroidal thickness. Patients have, in general, a thickened choroid with disease in an active state and a thinned choroid with disease in a chronic state. Even though mean subfoveal choroidal thickness from cube scans (from line scans) was 307 μm ± 96 μm (312 μm ± 108 μm), which is about the known reported choroidal thickness for healthy choroid, the variability can be confirmed from the data in this study, with a range of choroidal thicknesses between 112 and 719 μm at the foveal center point. This supports the validity of our conclusions for choroids of different thicknesses. Unfortunately our statistical analysis did not take into account that there might be a correlation of choroidal thicknesses when having 2 eyes from the same person in the data set.

Our study shows that horizontal line scans are representative for the corresponding cube scan subfields. The advantages of line scans compared with cube scans are shorter scanning time, shorter evaluation time, less blinking and other artifacts, and a patient- and examiner-friendly setting. In a study of Mansouri et al the number of artifacts in different scanning protocols has been investigated; only 149 out of 162 cube scans could be retained for analysis (others had no averaging success and were not analyzed). Fourteen more scans had to be excluded because of blinking artifacts and/or motion artifacts. This means that 27 of 162 cube scans (16.7%) had to be excluded before they could be evaluated. In comparison, 162 out of 162 line scans could be retained for analysis and no scan had to be excluded because of blinking or motion artifacts.[23]

In conclusion, our study provides evidence supporting the use of measurements from horizontal line scans as surrogates for drawing conclusions on posterior pole choroidal thickness instead of performing time-consuming volumetric thickness assessments.

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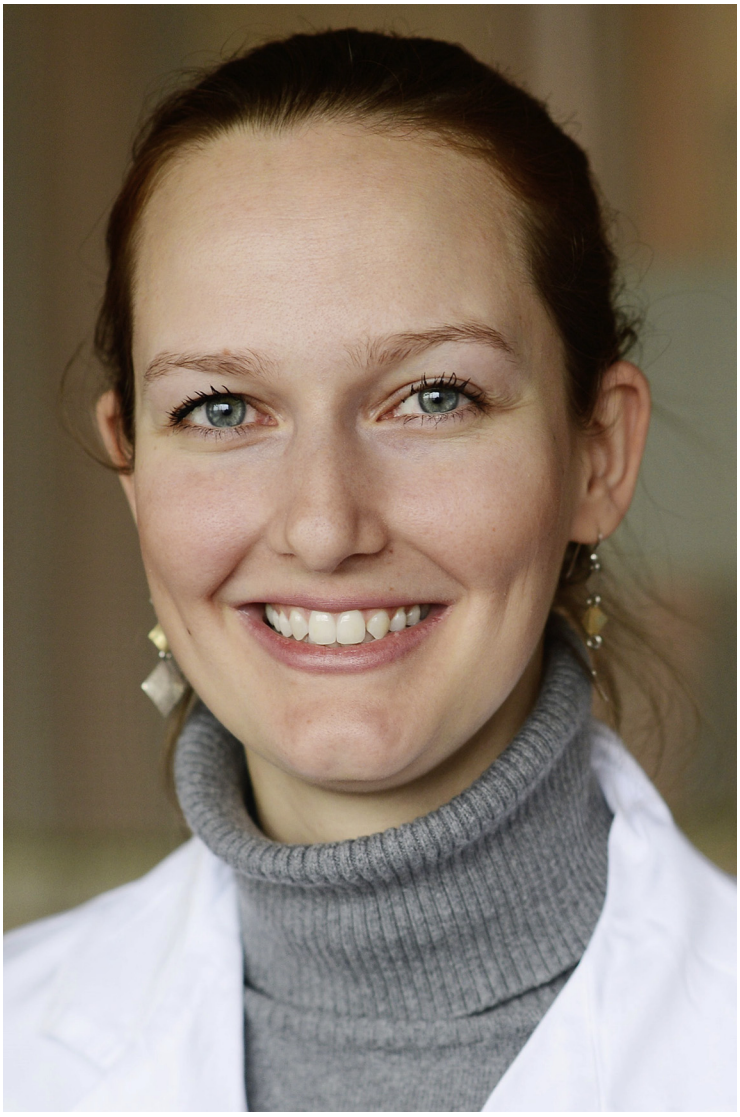

Biosketch

Bianca S. Gerendas coordinates the young international, interdisciplinary OPTIMA group (Ophthalmic Image Analysis) with the aim of individualized treatment for retinal diseases based on automated image analysis and population-based models from large-scale multimodal imaging data. Her primary research interests are retinal imaging/image analysis and translational ophthalmic research with a focus on diabetic retinopathy. She is a supervisor at the Vienna Reading Center and a resident at the Department of Ophthalmology, Medical University of Vienna, Austria.