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Spectral Domain Optical Coherence Tomography Imaging of Drusen in Non-Exudative Age-Related Macular Degeneration

Giovanni Gregori, PhD, Fenghua Wang, MD, Philip J. Rosenfeld, MD, PhD, Zohar Yehoshua, MD, Ninel Z Gregori, MD, Brandon J. Lujan, MD, Carmen A. Puliafito, MD, MBA, and William J. Feuer, MS

Department of Ophthalmology, Bascom Palmer Eye Institute, University of Miami Miller School of Medicine, Miami, FL

Abstract

Purpose—To measure drusen area and volume in eyes with non-exudative age-related macular degeneration (AMD) using spectral domain optical coherence tomography imaging (SDOCT).

Design—Evaluation of diagnostic technology

Participants—One hundred three eyes from 74 patients with drusen

Methods—Patients with drusen secondary to non-exudative AMD were enrolled in this study. Five separate SDOCT scans, each consisting of 40000 uniformly spaced A-scans organized as 200 A-scans in each B-scan and 200 horizontal B-scans, were performed on each eye. Each scan covered a retinal area of 6×6 mm centered on the fovea. A novel algorithm was used to quantitatively assess drusen area and volume. Measurements from the entire scans, as well as in regions contained within 3 mm and 5 mm circles centered on the fovea, were analyzed. Test-retest standard deviations of drusen area and volume measurements were calculated for each eye.

Main Outcome Measure—Drusen area and volume

Results—The algorithm created drusen maps that permitted both qualitative and quantitative assessment of drusen area and volume. Both the qualitative appearance and the quantitative measurements of drusen area and volume were highly reproducible over the 5 different datasets. The intraclass correlation coefficient (ICC) was above 0.99 for both area and volume measurements on the entire dataset as well as the 3 mm and 5 mm circles. The correlation between lesion size and the test-retest standard deviations can be eliminated by performing a square-root transformation of the area measurements and a cube-root transformation of the volume measurements. These transformed data allowed for the inclusion of all drusen sizes in the calculation of an estimated single pooled test-retest standard deviation which will be useful for longitudinal studies of drusen natural history.

Corresponding author: Giovanni Gregori, PhD, Bascom Palmer Eye Institute, 900 NW 17th Street, Miami, FL 33136. Telephone: 305-482-4412, Fax: 305-326-6306, ggregori@med.miami.edu.

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Conclusions—A novel algorithm for the qualitative and quantitative assessment of drusen imaged using SDOCT was shown to be highly reproducible. The ability to assess drusen volume reliably represents a new quantitative parameter to measure in AMD and may be useful when assessing disease progression, particularly in trials for treatments of non-exudative AMD.

Keywords

Non-exudative age-related macular degeneration; spectral domain; optical coherence tomography; drusen; segmentation

Introduction

Macular drusen are a characteristic clinical feature of age-related macular degeneration (AMD). Drusen are one of the earliest signs of AMD and are characterized as hard or soft as well as small ($<63\ \mu\text{m}$), intermediate ($>63\ \mu\text{m}$ but $<125\ \mu\text{m}$) or large ($\geq 125\ \mu\text{m}$).¹ The size and number of drusen along with pigmentary changes in the macula constitute important findings that are used for staging of disease severity and predicting the likelihood of disease progression and vision loss.^{1–3} The presence of large drusen or confluent drusen as well as drusen types, such as soft and indistinct, have been recognized as risk factors for progression to advanced AMD which includes central geographic atrophy and choroidal neovascularization (CNV).

Historically, color fundus photographs have been used as the gold standard for reading centers to assess the clinical stage of non-exudative AMD.⁴ These high-quality stereoscopic fundus photographs were used to assess the extent of drusen and pigmentary abnormalities and to establish severity scales for AMD that are predictive of disease progression.^{5, 6} While color fundus photographs are useful for assessing the *en-face* appearance of the macula, these images do not provide direct information on the geometry of the retinal pigment epithelium (RPE) and cannot be used to measure quantitative properties such as drusen volume.

Optical coherence tomography (OCT) provides the opportunity to assess the effect of drusen on the geometry of the RPE *in vivo*. Time-domain OCT identified drusen as localized elevations and disruptions in the structure of the RPE and Bruch's membrane complex in non-exudative AMD.⁷ However, the relatively slow acquisition times of time-domain OCT resulted in considerable distortion of the actual geometry of the drusen/RPE/Bruch's membrane complex in each B-scan due to the presence of eye movements. Time domain OCT was limited further by the difficulty of accurately positioning a B-scan relative to retinal landmarks, the difficulty in scanning the same location reproducibly, and the impossibility of generating dense scanning patterns needed for volumetric analyses. Thus, time-domain OCT was unsuitable for quantitative measurements of drusen.

The recent introduction of spectral domain OCT (SDOCT), also known as Fourier domain or high speed OCT, resolved many of the limitations experienced with time domain technology. SDOCT is able to acquire high-speed, high-resolution, high-density three dimensional (3-D) images covering the central macula. As a result, SDOCT datasets can capture the real retinal geometry and are less affected by eye movements. Furthermore, it is possible to generate an OCT fundus image (OFI) that represents an *en face* summary view of all the B-scans from the dataset. The OFIs can be used to register the SDOCT datasets to the fundus photos and to calibrate color fundus images so that exact correlations can be achieved between the retinal cross-sectional geometry seen on the OCT B-scans and the retinal landmark seen on *en-face* imaging.^{8–10}

SDOCT can generate very high quality B-scans that show new details of the drusen structure and morphology.¹¹ The high speed of SDOCT also permits the acquisition of raster scans with a large number of lower density B-scans. Segmentation algorithms have been developed to extract quantitative information from these three dimensional (3-D) SDOCT datasets. For example, the commercially available Cirrus HD-OCT (Carl Zeiss Meditec Inc, Dublin, CA), includes software that generates 3-D maps of the internal limiting membrane and the RPE. Segmentation of the RPE provides information on the RPE geometry and therefore a unique perspective of drusen. If the actual RPE geometry can be compared to the geometry of a virtual RPE free of deformations, which we call here the RPE floor, then a difference map could be generated and quantitative assessment of drusen could be performed.

The idea of using the difference between the actual RPE segmentation and some kind of normal RPE interpolation to produce measurements of RPE deformation from SDOCT datasets was presented soon after SDOCT technology was developed. However, for such a strategy to have any clinical usefulness, it needs to be implemented in a robust and reproducible manner, imposing considerable demands on the performance of a fully automated algorithm (Invest Ophthalmol Vis Sci 2008; 49: E-4234 and E-5394). Szkulmowski et al¹² published an algorithm capable to producing maps of RPE deformation, but their approach was not robust in that all of their examples showed some type of artifact. In addition, their semi-automated algorithm required significant operator interaction and was relatively slow. Yi et al¹³ published a single example of a drusen map using a strategy similar to the one presented in this current report, but their algorithms were never validated and seem unlikely to yield correct results on a wide variety of patients or scan conditions. For instance, they appear to use a straightforward second order polynomial fit of the RPE boundary to estimate the RPE floor, an approach that cannot in general produce a good result.

This report describes the performance of a fully automated algorithm that implements the strategy described above to measure drusen area and drusen volume. Our proprietary algorithm, developed by the first author and licensed to Carl Zeiss Meditec, consists of two main parts: a segmentation algorithm of the actual RPE, which is the one already available on the Cirrus HD-OCT, and an algorithm to determine the virtual RPE which is free of any deformations and referred to as the RPE floor. The full algorithm will be included in future versions of the Cirrus HD-OCT software. This report describes the first test of such an algorithm to determine if it is possible to generate fully automated, reproducible, quantitative, SDOCT measurements of drusen area and volume in patients with non-exudative AMD.

Methods

This prospective study was approved by the institutional review board of the University of Miami Miller School of Medicine and was compliant with the Health Insurance Portability and Accountability Act of 1996. Patients with a clinical diagnosis of non-exudative AMD were recruited from the retina service at the Bascom Palmer Eye Institute. All patients signed a research consent form after a detailed explanation of the study.

The clinical diagnosis of non-exudative AMD was confirmed by the Bascom Palmer Eye Institute retina faculty. Digital photography, fluorescein angiography, and OCT (Stratus OCT and/or Cirrus HD-OCT, Carl Zeiss Meditec Inc, Dublin, California), were obtained to document the absence of CNV prior to recruiting patients for the study. Patients with other retinal pathologies including diabetic retinopathy, hypertensive retinopathy, and central

serous chorioretinopathy were excluded. Eyes with geographic atrophy were also excluded from this study.

A Cirrus HD-OCT instrument was used for this study. Each eye was imaged 5 separate times in a single session using a raster scan protocol (200×200). This protocol resulted in the acquisition of a SDOCT dataset consisting of 40000 uniformly spaced A-scans organized as 200 A-scans in each B-scan and as 200 horizontal B-scans in each raster array. Each scan covered a retinal area of 6×6 mm centered on the fovea. The operator assessed the quality of the scan during its acquisition and, whenever possible, an effort was made to delete datasets with poor signal strength or with significant motion artifacts. The patient was repositioned during the scanning session as necessary, but there was no specific requirement to reset the patient or the instrument after acquiring each of the five separate datasets.

The raw OCT datasets were exported to a personal computer for analysis. A proprietary algorithm developed by the first author and commercially available on the Cirrus HD-OCT instrument was used to segment the RPE. A separate algorithm, also developed by the first author, was used to automatically determine the RPE floor, a virtual RPE free of any deformations (Figs 1, 2; Fig 2 available at <http://aaajournal.org>). As a result of this analysis, a drusen thickness map was generated by tracking the distance between the real RPE and the interpolated RPE floor at each of the 40000 measurement data points. In order to reduce spurious noise, the algorithm was designed to ignore RPE deformations with height below a given threshold. This threshold was set to 10 pixels (19.5 μ m).

Every image was reviewed post-acquisition by one of the authors in order to mark the foveal center. The position of the fovea was determined manually by scanning through the OCT dataset to find the spot where the geometry of the inner retinal layers best matched the known anatomical configuration in the fovea. The relative location of the foveal center in the OCT dataset was then reported in x and y coordinates based on pixel position within the 200 × 200 array of A-scans.

Quantitative measurements of drusen area and drusen volume were obtained for the full dataset as well as for the retinal region within circles centered on the fovea with diameters of 3 mm and 5 mm. The test-retest standard deviations (SD) of each set of measurements were calculated for each eye. In order to understand the correlation between the lesion size and the test-retest standard deviations, the data were also analyzed after transforming it according to its scaling properties. Therefore, the test-retest standard deviations for the square root of the drusen area measurements and the cube root of the drusen volume measurements were computed.

The intraclass correlation coefficient of reproducibility is used as a summary statistic.¹⁴ All statistical calculations were carried out with the software SPSS V16.0 (SPSS Inc. Chicago, IL, USA).

Results

One hundred three eyes from 74 patients were enrolled in this study. A total of 103 sets of OCT images repeated five times were obtained and analyzed. The sample included 29 men and 45 women with a mean age of 73.9 years (range 38-95, SD 10.7).

A review of the acquired datasets lead to the exclusion of two images because of exceedingly poor image quality due to large motion artifacts, leaving two eyes with only four repeated scans. The drusen area and drusen volume were automatically computed from each image over three different regions: the full 6×6 mm square covered by the scan (full scan; FS), a circular region with a diameter of 5 mm centered at the fovea (C5), and a

circular region with a diameter of 3 mm centered at the fovea (C3). In 8 of the 513 OCT images entered in the study, the actual fovea location was found to be more than 0.5 mm away from the geometric center of the scanned OCT dataset. Therefore, the C5 measurements could not be obtained from these images and they had to be excluded from this particular analysis. Since two sets of measurements were left with fewer than 4 eligible repeated scans, these sets were dropped from the C5 analysis altogether. For the C5 analysis, this left a total of 6 measurement sets (out of 101) with 4 repeated datasets instead of 5.

Examples of the segmentation algorithm are shown in Figures 1 and 2 (Fig 2, available at <http://aaojournal.org>). In these figures, the 6×6 mm scan area is superimposed on a color fundus photograph of a macula containing drusen. Two representative B-scans are identified with the boundaries of the actual RPE segmentation and the interpolated RPE floor highlighted on these B-scans in red and yellow, respectively (Figs 1B and 2B). The surface renderings in three dimensional space of the RPE segmentation and the RPE floor are also shown along with the retinal thickness map. The retinal thickness map clearly shows retinal thinning overlying some of the drusen. The quantitative difference maps (Figures 1F and 2E) depict the difference between the actual RPE segmentation and the interpolated RPE floor, revealing the configuration, area, and height of the drusen.

Figure 3 (available at <http://aaojournal.org>) demonstrates the method used to identify the foveal center. The entire dataset is searched for the foveal center based on the configuration of the internal limiting membrane and the outer nuclear layer. Once identified, the foveal center is represented by an X and Y location. The X location is the A-scan number along the horizontal B-scan crossing the foveal center and the Y location is the B-scan number in the entire dataset that contains the foveal center. This manually detected foveal center is then used as the center for the circles in the C3 and C5 analyses. Figure 4A depicts a color fundus photograph with a superimposed registered OCT fundus image containing the 3 mm and 5 mm circles centered on the foveal center. Figure 4B shows the same image as 4A in the absence of the OCT fundus image to demonstrate the position of the circles on the color fundus photograph.

Both the qualitative appearance of the drusen maps and the quantitative parameters (area and volume) were shown to be highly reproducible over the 5 different datasets. Figure 5 (available at <http://aaojournal.org>) shows a typical example that illustrates our results. Although there is some variability, both in the placement of the scan, and in the identification of the foveal center, the differences in the measured drusen area and volume are small, particularly within the 3mm circle. The mean and the standard deviations of the drusen volume and area were computed for the full dataset, the 5mm circle, and the 3mm circle (Figs 6 and 7, available at <http://aaojournal.org>). The standard deviations are plotted versus the mean values for each of the different regions analyzed. The standard deviation graphs show that both area and volume are reproducible in that the standard deviations are small in comparison to the means over the entire range of measurements. The qualitative behavior of the two parameters is very similar: larger lesions are associated with somewhat larger test-retest standard deviations. The correlation between lesion size and test-retest standard deviations was statistically significant (Area C3: $r=0.58$, $p<0.001$, $n=103$; Volume C3: $r=0.82$, $p<0.001$, $n=103$). As shown in Figures 6 and 7 (available at <http://aaojournal.org>), the distribution of standard deviations for the full OCT dataset (Figures 6A, 7A) is wider than the distribution observed when measurements are obtained from the circular regions centered at the fovea (5mm and 3mm diameter circles). Figures 6 and 7 show that the linear fit estimates are very close in all three situations, which demonstrates the basic stability of our method. However, the residual error around the linear fit becomes progressively smaller (r^2 values are progressively larger) as we go from the full dataset to the 3mm circle. This effect is consistent with the summary statistics for the

distributions of SD and the coefficient of variation (COV) over the different retinal regions (Table 1, available at <http://aaojournal.org>). The circles centered on the fovea provide a useful strategy to improve the reproducibility of the measurements compared with the measurements obtained from the entire dataset. The relatively larger standard deviations observed in the measurements taken on the full datasets is attributable in large part to variability in the scan placement.

The correlation between the test-retest standard deviations and lesion size is related to the scaling property of the measurements and is not unexpected. When the data are transformed according to their dimensional characteristics (a square-root transformation of the area measurements and a cube root transformation of the volume measurements, as described in the methods section) prior to the calculation of test-retest standard deviations, the correlations between lesion size and test-retest standard deviations are eliminated (Area C3: $r=0.13$, $p=0.19$, $n=103$; Volume C3: $r=.005$, $p=0.96$, $n=103$). Figure 8 (available at <http://aaojournal.org>) shows the standard deviation of the cubic root of the drusen volumes plotted versus the mean volumes, and Figure 9 (available at <http://aaojournal.org>) shows the standard deviation of the square roots of the drusen areas plotted versus the mean areas. These graphs show that the standard deviations are uniformly distributed across the full measurement range.

Reproducibility, as assessed with the intraclass correlation coefficient, was excellent on both the original measurement scale and on the transformed scale (all ICCs above 0.99, Tables 1 and 2; Table 1 available at <http://aaojournal.org>). Use of the square root and cube root transformed data allow for the inclusion of all drusen sizes in the calculation of an estimated single pooled test-retest standard deviation reported in Table 2. This estimate is important if this measurement technique is to be used for longitudinal studies examining the natural history of drusen area and volume. For example, the pooled SD for drusen volume (C3) was 0.009 mm. Therefore, a detectable change for the cube root of the C3 drusen volume can be defined as $\sqrt{2} \times 1.96 \times 0.009 = 0.025$ mm.¹⁵ For a given eye, any change in the cube root of the C3 drusen volume smaller than 0.025 mm would be within the 95% confidence interval and therefore not statistically significant. This confidence interval for the transformed data can be expressed in terms of the original volume measurements. For example, a change in the C3 drusen volume of a given eye would only be statistically significant if the new measured drusen volume were smaller than $[(\text{baseline volume})^{1/3} - 0.025]^3$ or larger than $[(\text{baseline volume})^{1/3} + 0.025]^3$.

The drusen area measurements are clearly correlated with the drusen volume measurements (Fig 10A, available at <http://aaojournal.org>). For small drusen, this relationship appears to be linear; however, this relationship changes as the drusen area increases. A linear regression analysis results in $R^2=0.73$ (C3). Once again, the underlying relationship between the area and volume measurements is clarified by transforming the data. An improved correlation is observed when the cube root of the drusen volume is plotted versus the square root of the drusen area (Fig 10B, available at <http://aaojournal.org>; $R^2=0.94$, C3).

Discussion

Automated quantitative measurements of drusen can be reproducibly obtained using software specifically developed for the Cirrus HD-OCT system. Both area and volume measurements of drusen were obtained from the maculae of patients with non-exudative AMD. While color fundus photography provides a two dimensional view of all drusen, SDOCT provides a 3-D representation of drusen and their effects on the geometry of the RPE and retina. While this strategy provides a novel perspective of drusen, it remains to be shown whether the ability to detect and quantify drusen objectively will be useful in the

routine care of patients. However, this strategy will certainly be useful in assessing the natural history of non-exudative AMD and as a potential endpoint in testing the efficacy of new treatments for non-exudative AMD.

The approach used in this report to obtain drusen measurements is essentially independent of the scan geometry, but the particular properties of the scan pattern used to acquire the OCT dataset will have an effect on the measurements. For a clinically meaningful assessment of drusen, one needs a scan pattern that uniformly and densely covers the largest possible retinal area without introducing appreciable distortions in the retinal geometry. The 200×200 dataset used in this study is a good compromise between these requirements. This scan pattern covers a square measuring 6×6 mm on the retina in about 1.5 seconds with A-scans uniformly spaced 30 μm apart in both the x (horizontal) and y-directions (vertical) directions. This scan pattern is fast enough to be able to produce datasets unaffected by appreciable eye motion artifacts in the typical patient. It should be noted that motion along the z-axis, while typically present, is not a problem for the algorithm used in this report. The sampling grid is also dense enough to resolve drusen with fairly small area and volume. Another important factor in determining a lower bound for the size of measureable drusen is the threshold for discriminating between a significant deviation from the interpolated RPE floor and the noise that accompanies any measurement technique. The value of this threshold clearly affects the performance of the algorithm in that higher values will improve reproducibility at the expense of ignoring smaller drusen while smaller values might identify more drusen but also introduce more noise. We found that a cut-off of 10 pixels (19.5 μm) was a reasonable choice as the minimal detectable difference between the RPE and the interpolated RPE floor. This choice is consistent with the spacing of the scanning pattern used in this study in which each data point was separated by 30 μm.

The ability to compare drusen measurements from different OCT datasets obtained from the same eye depends upon the operator of the SDOCT system. This is because the operator must center the scan on the foveal center. Even a skilled operator and a compliant subject do not always produce OCT datasets centered at or very close to the foveal center. This will typically result in variations in the location of repeated scans of any given eye. Consequently, if the entire dataset is used to measure drusen, then the results may not be reproducible. It should be noted that even with this limitation, the reproducibility of the entire datasets in this study was excellent. One strategy to overcome this potential limitation would be to use a SDOCT system with a built in laser eye-tracking system like that used in other SDOCT instruments. However, these laser tracking systems have limitations of their own. To acquire multiple, large, dense OCT datasets like the ones used in this study on a given day, long acquisition times would be necessary, and due to the imaging time constraints imposed by these laser tracking systems, it would almost be impossible to acquire all the data needed to perform a detailed drusen analysis, especially if the subject had poor visual acuity.

In our SDOCT system, we reduced the variance in drusen measurements from multiple OCT datasets by identifying the foveal center on the OCT fundus image and comparing measurements from regions contained within circles centered on the fovea. The foveal center was selected in every OCT dataset by a manual search of the B-scans, looking for the pixel position which best matched the known anatomical markers of the foveal center (i.e., absence of the inner retina and the presence of the outer nuclear layer and the photoreceptors). The shape of this foveal center is a recognizable feature in our patients with non-exudative AMD. While the fovea center identified using this method has some variability, it is clear from our results using the circles that the measurements show less variability than the measurements obtained from the full datasets (Table 1, available at <http://aaojournal.org>). At this time, the software on the commercially available Cirrus HD-

OCT instrument offers an automatic algorithm to locate the fovea position. This software was not used because we wanted to reduce the possible introduction of artifacts in this step. In theory, another strategy to reduce the variances reported in this paper even further would be to register all the patient's OCT fundus images from different OCT datasets with each other and then identify the foveal center only once in the combined registered dataset. Due to the excellent agreement in our current study, we would expect any improvement in the variances to be fairly small. It would be easy to combine our algorithm with an automated fovea localization algorithm and/or a registration algorithm to achieve fully automated drusen measurements. The reproducibility of the final results would of course be affected by the performance of these other separate algorithms.

When comparing the drusen configurations observed on a color fundus image with the drusen maps obtained using SDOCT, it is important to realize that some drusen are not detected from the OCT datasets using our technique and do not appear on the drusen map (Figs 1, 2; Fig 2 available at <http://aojournal.org>). It should be kept in mind that drusen maps from OCT datasets are representations of areas with significant disruption in the RPE geometry. However, not all drusen seen on color fundus images substantially affect the RPE geometry. Very shallow drusen may be missed because of the threshold used by the algorithm or because of limitations in the sensitivity of the RPE segmentation. Problems with the segmentation of the RPE can also be a source of error.¹⁶⁻¹⁹ Occasionally, it is possible to observe drusen with a weakly reflective RPE that are missed by the RPE segmentation, which follows the boundary of Bruch's membrane instead. While these considerations can certainly have an effect on the absolute accuracy of the measurements, the behavior of the algorithms remains, on the whole, quite consistent across different OCT datasets of the same retina. Therefore, the drusen measurements are reproducible and appear to be of clinical relevance. It remains to be determined whether the drusen identified using SDOCT provide any additional information than the drusen identified using color fundus images.

The algorithm does frequently fail in the presence of large areas of geographic atrophy (GA). The absence of RPE and photoreceptors in the area of GA and the corresponding loss of reflectivity in the OCT images can cause significant artifacts in the RPE segmentation where the computed boundary will occasionally dip into the choroidal region. In order to avoid this potential problem, eyes with extensive GA were excluded from the study sample. Current refinements of the drusen detection algorithm have greatly improved upon this problem and the new algorithm is currently being tested in eyes with both drusen and significant areas of GA.

Although drusen measurements made with SDOCT appear to correlate well with fundus photography,²⁰ it is important to understand that there need not be an exact one-to-one correspondence between drusen on fundus photography and the RPE deformations shown using SDOCT images. These two imaging strategies are fundamentally different. Fundus photography identifies abnormalities in macular pigmentation. Some pigmentary changes may very well not be associated with a disruption in the normal RPE geometry, or at least not sufficiently to be evident in the OCT images or identified by the software. Conversely, it is not necessarily true that all deformations in the RPE geometry seen on OCT images must be associated with obvious pigmentary changes shown on the color fundus photographs. For these reasons, color fundus photos and SD-OCT images offer complementary information and both may have an important role in assessing drusen. A careful analysis of the relationship between the drusen identified by both color fundus imaging and the SDOCT algorithm is clearly of interest and is currently ongoing.

We propose that drusen measurements obtained using SDOCT may be a uniquely useful clinical tool for assessing the natural history of drusen and disease progression. Other features of non-exudative AMD such as the extent of pigmentation observed on color fundus photos as well as the features of abnormal autofluorescence will continue to be useful in assessing disease severity and the likelihood of progression; however, these fundus features are qualitative in nature and open to the vagaries of interpretation. We propose that the change in drusen volume could be useful and should be investigated as a novel quantitative, reproducible clinical trial endpoint when investigating disease progression and treatments for non-exudative AMD.

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Figure 1.

Imaging small to medium drusen with spectral domain optical coherence tomography (SDOCT).

A. A color fundus photo is shown with the superimposed location of the SDOCT dataset indicated by the blue square. This location can be determined with the help of the OCT fundus image.

B. Two B-scans are shown from the SDOCT that correspond to the white lines on the fundus photo. The segmentation of the retinal pigment epithelium (RPE) is shown in red and the drusen floor is shown in yellow.

C. Surface rendering of the RPE segmentation.

D. Retinal thickness map.

E. Surface rendering of the virtual RPE free of any deformations and referred to as the RPE floor.

F. Drusen thickness map.

Figure 2.

Imaging large drusen with spectral domain optical coherence tomography (SDOCT).

A. A color fundus photo is shown with the superimposed location of the SDOCT dataset indicated by the blue square. This location can be determined with the help of the OCT fundus image.

B. Two B-scans are shown from the SDOCT that correspond to the white lines on the fundus photo. The segmentation of the retinal pigment epithelium (RPE) is shown in red and the drusen floor is shown in yellow.

C. Surface rendering of the RPE segmentation.

D. Retinal thickness map

E. Drusen thickness map.

Figure 3.

Identification of the foveal center from within the spectral domain optical coherence tomography (SDOCT) dataset.

From within the SDOCT dataset, the location of a particular B-scan (right) and the location of the A-scan corresponding to the foveal center were identified. The A-scan containing the fovea is marked by a white line. This choice determines crosshairs intersecting at the fovea on the OCT fundus image (left). The black horizontal line corresponds to the location of the B-scan on the right. The white vertical line indicates the position of the particular A-scan also marked in white on the right.

Figure 4.

Registration of the spectral domain optical coherence tomography (SDOCT) scan on a color fundus image using the OCT fundus image.

A. The SDOCT dataset can be registered to a color fundus photo of the same eye by overlapping the OCT fundus image on the color fundus image. The fovea location is marked by a green cross on the OCT fundus image, while the white lines show circles centered on the foveal center with 3 and 5 mm diameters, respectively.

B. Using the registration in part A, the foveal location and the position of the circles can be superimposed on the fundus photo.

Figure 5.

Reproducibility of drusen maps obtained from spectral domain optical coherence tomography (SDOCT) datasets.

Five drusen maps are shown from five different SDOCT datasets of the same eye. The location of the 3mm circle centered at the fovea is shown in white. Drusen area and volume within the 3mm circle are shown under each drusen map.

Figure 6.

Relationship between the standard deviations of the measurements and the mean drusen volume measurements:

A. Full datasets. B. 5mm circles. C. 3mm circles.

Figure 7.
Relationship between the standard deviation of the measurements and the mean drusen area measurements:
A. Full datasets. B. 5mm circles. C. 3mm circles.

Figure 8.

Relationship between the standard deviation of the measurements and the mean for the cube root of drusen volume:

A. Full datasets. B. 5mm circles. C. 3mm circles.

Figure 9.
Relationship between the standard deviation of the measurements and the mean for the square root of drusen area:
A. Full datasets. B. 5mm circles. C. 3mm circles.

Figure 10.

Relationship between drusen area and drusen volume:

A. Drusen area plotted against volume measurements for the 3mm circle.

B. Square root of drusen area plotted against the cube root of drusen volume for the 3mm circle.

Table 1

Reproducibility of drusen area and drusen volume measurements.

	Mean Standard Deviation	Median Standard Deviation	Mean Coefficient of Variation	Median Coefficient of Variation	Intraclass Correlation Coefficient
Drusen Area (Entire Scan)	0.108	0.063	9.2%	5.0%	0.991
Drusen Area (5mm Circle)	0.079	0.048	7.5%	4.4%	0.994
Drusen Area (3mm Circle)	0.055	0.040	7.5%	4.8%	0.995
Drusen Volume (Entire Scan)	0.0065	0.0027	11.2%	5.6%	0.993
Drusen Volume (5mm Circle)	0.0041	0.0024	8.3%	5.0%	0.998
Drusen Volume (3mm Circle)	0.0032	0.0020	8.0%	5.8%	0.998

Table 2

Reproducibility of transformed drusen area and drusen volume measurements.

	Pooled Standard Deviation	Mean Standard Deviation	Median Standard Deviation	Mean Coefficient of Variation	Median Coefficient of Variation	Intraclass Correlation Coefficient
Square Root of Drusen Area (Entire Scan)	0.058	0.042	0.027	4.6%	2.5%	0.991
Square Root of Drusen Area (5mm Circle)	0.041	0.032	0.025	3.8%	2.2%	0.995
Square Root of Drusen Area (3mm Circle)	0.034	0.027	0.023	3.8%	2.4%	0.995
Cube Root of Drusen Volume (Entire Scan)	0.019	0.011	0.006	3.6%	1.9%	0.988
Cube Root of Drusen Volume (5mm Circle)	0.010	0.008	0.006	2.8%	1.7%	0.997
Cube Root of Drusen Volume (3mm Circle)	0.009	0.007	0.006	2.7%	1.9%	0.997