Calibration of Fundus Images Using Spectral Domain Optical Coherence Tomography

Brandon J. Lujan, MD; Fenghua Wang, MD; Giovanni Gregori, PhD; Philip J. Rosenfeld, MD, PhD; Robert W. Knighton, PhD; Carmen A. Puliafito, MD, MBA; Ronald P. Danis, MD; Larry D. Hubbard, MAT; Robert T. Chang, MD; Donald L. Budenz, MD, MPH; Michael I. Seider, BGS; O'Rese Knight, BS

BACKGROUND AND OBJECTIVE: Measurements performed on fundus images using current software are not accurate. Accurate measurements can be obtained only by calibrating a fundus camera using measurements between fixed retinal landmarks, such as the dimensions of the optic nerve, or by relying on a calibrated model eye provided by a reading center. However, calibrated spectral domain OCT (SD-OCT) could offer a convenient alternative method for the calibration of any fundus image.

PATIENTS AND METHODS: The ability to measure exact distances on SD-OCT fundus images was tested by measuring the distance between the center of the fovea and the optic nerve. Calibrated SD-OCT scans measuring 6 × 6 × 2 mm centered on the fovea and the optic nerve were analyzed in 50 healthy right eyes. The foveal center was identified using cross-sectional SD-OCT images, and the center of the optic nerve was identified manually. The SD-OCT scans were registered to each other, and the distances between the center of the optic nerve and fovea were calculated. The overlay of these SD-OCT fundus images on photographic fundus images was performed.

RESULTS: Any image of the fundus could be calibrated by overlaying the SD-OCT fundus image, and the measurements were consistent with previously defined calibration methods. The mean distance between the center of the fovea and the center of the optic nerve was 4.32 ± 0.32 mm. The line from the center of the optic nerve to the foveal center had a mean declination of 7.67 ± 3.88°. Mean horizontal displacement and vertical displacement were 4.27 ± 0.29 mm and 0.58 ± 0.29 mm, respectively.

CONCLUSIONS: The overlay of the SD-OCT fundus image provides a convenient method for calibrating any image of the fundus. This approach should provide a uniform standard when comparing images from different devices and from different reading centers.


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Address correspondence to Giovanni Gregori, PhD, McKnight Vision Research Center, Bascom Palmer Eye Institute, 1638 NW 10th Ave., Miami, FL 33136.
INTRODUCTION

A convenient, reliable, and standardized method for the accurate calibration of fundus images is not widely available. Currently, the software accompanying commercial fundus cameras “measures” distances on a fundus image by setting the amount of image magnification that an individual camera produces. However, in practice, inadvertent variation in magnification of the retinal image can occur. This is due in part to the variability of the relay lens magnification and due in part to the camera’s wide depth of focus, in which the incorrect position of an objective lens can be compensated for by the photographer using the focus knob. Inadvertent changes in the magnification of the image then occur, which directly result in inaccurate distance measurements using the software supplied by the digital camera manufacturers.

The problem of calibrating fundus images is not unique to digital photography but has been a problem since the introduction of fundus photography. The first widely recognized calibration technique based on Duke-Elder’s review was that the average optic disc was 1.5 mm in diameter. This later became the “standard disc diameter” and was used to generate a grading reticle in the Age-Related Eye Disease Study (AREDS), the Early Treatment of Diabetic Retinopathy Study (ETDRS), and the Macular Photocoagulation Study (MPS). This standard was then used to perform linear and area measurements on the fundus image. However, an extensive postmortem study of the nerve size as well as rigorous photographic studies of the optic nerve head later demonstrated that this was an underestimate of the average nerve diameter and that there was significant variability in the size of the optic disc.

Another approach to calibrate a fundus image uses the dimensions of other fundus features, most notably the distance between the optic nerve and the fovea. The Fundus Photograph Reading Center (FPRC) at the University of Wisconsin has found that this distance between the fovea and the center of the optic nerve is approximately 4.5 mm and that there was significant variability in the size of the optic disc.

Another approach used by reading centers is to calculate distances on fundus photographs based on images obtained from a sample eye containing a reticle of a known size. Once the reticle is imaged, a conversion factor is calculated between the known size of the reticle and its dimensions on the image. This way, any fundus image can be calibrated as long as the image is obtained using the same camera. However, each camera will have a different conversion factor, and these sample eyes are not readily available.

In this article, we report on the use of the calibrated spectral domain optical coherence tomography (SD-OCT) fundus image as a convenient universal technique for the calibration of any fundus image. We also repeat the measurements performed by the FPRC using the geometric center of the optic nerve and the foveal center. However, our approach uses the absolute anatomic foveal center defined cross-sectionally by SD-OCT.

PATIENTS AND METHODS

We initially evaluated the right eyes of 56 healthy patients (27 men) with a mean age 47.1 ± 16.7 years (range, 20-73 years). Approval to perform these evaluations was obtained from the Institutional Review Board at the University of Miami Miller School of Medicine, and informed consent was obtained from each patient before all examinations. Each patient was refracted and had best-corrected Snellen visual acuities ≥ 20/30. The range of the spherical equivalent of refractive error was -10.375 diopters (D) to +3 D, with a mean of -0.52 ± 2.50 D and a median of zero D. To establish clinical normalcy, each patient underwent slit-lamp examination, gonioscopy, and dilated fundus examination. Furthermore, each patient had intraocular pressure, central corneal thickness, and axial length measurements that were within the established normal ranges. Finally, Humphrey visual field examinations were performed, and all patients had a reliable test result without any pathologic scotomas. Patients with tilted optic nerves, signs of myopic degeneration, or a history of ocular disease were excluded from the study.

A single Cirrus high-definition (HD)-OCT unit (Carl Zeiss Meditec, Inc., Dublin, CA) was used to acquire all SD-OCT images from both eyes of each patient. This machine uses a superluminescent diode laser centered at a wavelength of 840 nm, which generates an axial resolution of approximately 5 μm. The Cirrus HD-
OCT is calibrated to scan a square $6 \times 6$ mm region of the posterior pole by using a model eye. The model eye has a curved back surface, and at 840 nm has a focal length of 17.23 mm and a refractive error of 1.35 D. We performed two sets of scans for each eye, one centered on the fovea by patient fixation and one centered on the optic nerve using an internal fixation target. The scan protocol for both the macula and optic nerve was a $200 \times 200$ raster scan (the first number refers to the number of A-scans in each horizontal B-scan, whereas the second number is the total number of horizontal B-scans) and was acquired in approximately 1.5 seconds. Multiple scans of each type were performed to reduce the likelihood of motion artifact. If an entire set of one type of image from the right eye had poor signal strength or demonstrated a motion artifact, that patient was excluded. In this article, this technology will be referred to generically as SD-OCT.

All macular cross-sectional SD-OCT B-scans were reviewed by a retinal specialist (BJL) to ensure that there was no pathology affecting the fovea and to confirm that there was an anatomically normal foveal depression. Three patients were excluded from the study because of pathology on the macular B-scans that was not revealed clinically or by fundus photography. Specifically, one patient showed retinal pigment epithelium changes under the fovea, and two had abnormalities of the vitreoretinal interface.

The horizontal and vertical B-scans that contained the center of the fovea were then identified. This determination was based on the lowest point of the foveal depression in both horizontal and vertical planes. The location of these B-scans within the SD-OCT dataset could then be visualized en face by generating an SD-OCT fundus image. This technique, which was described previously, integrates the signal intensity along each A-scan and then displays the intensity relative to other A-scans. The horizontal and vertical B-scans that included the foveal center were identified by lines on the SD-OCT fundus image such that their intersection was the foveal center.

The center of the optic nerve was identified on the SD-OCT fundus image of the optic nerve by manually centering the cross-hairs of a standard disc diameter as defined by the ETDRS. In overlaying this circle over the optic nerve, the amount of optic disc substance in each of the four quadrants defined by a horizontal and vertical cross-hair was visually equalized. The researchers were careful to use the neuroretinal rim as the outer boundary and not peripapillary atrophy, scleral crescents, or other anatomic irregularities. This method has been shown by the FPRC to be a reliable way to identify the center of the optic nerve (R.P. Danis, personal communication, 2008).

The macular and optic nerve SD-OCT fundus images with their respective centers identified were then manually registered to each other. This was accomplished by an alignment of the optic nerve SD-OCT fundus image with the macular SD-OCT fundus image based on an overlap of the retinal vasculature. Thus, a composite SD-OCT fundus image was generated that contained both the confirmed foveal center and the manually identified center of the optic disc. This alignment required a rotation in eight cases. There were three eyes that could not be registered adequately because of lack of overlapping features, and these were excluded from the study. Therefore, we proceeded to analyze distances on the remaining 50 eyes (25 men).

Once the composite SD-OCT fundus image was formed, the horizontal and vertical displacement between the center of the optic nerve and the center of the fovea could be directly measured in pixels. The horizontal displacement was the horizontal distance from the center of the optic nerve to a vertical line that intersected the center of the fovea. Likewise, the vertical displacement was the vertical distance between the center of the fovea and its intersection with the horizontal displacement line. The distance between the foveal center and the center of the optic disc was then calculated from these displacements. This distance will be referred to as the fovea-nerve distance. All distance measurements were then converted to millimeters using the known calibration of the image. The angle between the horizontal displacement line and the fovea-nerve distance line will be referred to as the angle of declination.

**RESULTS**

The foveal center could be identified by horizontal and vertical B-scans in all 50 macular SD-OCT scans. The exact en face location of the intersection of B-scans passing through the foveal center was identified on the SD-OCT fundus image using the Cirrus HD-OCT 2.0 software (Fig. 1). The center of the optic nerve could be determined on the
SD-OCT fundus image using the standard disc diameter circle in each eye. The fovea-nerve distance, the angle of declination, and the horizontal and vertical displacements between the fovea and the center of the optic nerve were successfully obtained in all cases (Fig. 2), and the results are summarized in the Table.

The fovea-nerve distance and the horizontal displacement followed a Gaussian distribution and showed less variability compared with its mean (the coefficient of variability) than the vertical displacement or the angle of declination. The lower and upper quartiles of the fovea-nerve distance were 4.12 and 4.52 mm respectively, whereas 94% of our sample had a fovea-nerve distance between 3.91 and 4.90 mm. Similarly, the lower and upper quartiles of the horizontal displacement were 4.07 and 4.48 mm, and 94% of our sample had values between 3.83 and 4.77 mm. The horizontal displacement had the smallest coefficient of variability of any of the parameters analyzed.

The measurements of the angle of declination and the vertical displacement had coefficients of variability that were significantly larger than the other two parameters. The lower and upper quartiles of the angle of declination were 4.83° and 10.27° respectively, and 94% of measurements were between 0.38° and 13.75°. The lower and upper quartiles of the vertical displacement were 0.38 and 0.73 mm, and 94% of vertical displacements were between 0.03 and 1.08 mm. One of the eyes had a negative vertical displacement, meaning that the imaged foveal center was located above the optic nerve.

There was no correlation between the fovea-nerve distance and the age of the patient ($r = 0.11$) and a moderate correlation between the refractive error ($r = 0.47$) and the axial length ($r = -0.42$) was found.

**DISCUSSION**

One advantage of SD-OCT technology is the ability to generate an SD-OCT fundus image directly from the $6 \times 6$ mm calibrated scan. Precise distance measurements can therefore be performed directly using this image. The ability to overlay the SD-OCT

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<td>Vertical displacement</td>
<td>0.58</td>
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**Figure 1.** Horizontal (H) and vertical (V) B-scans through the foveal center. The SD-OCT fundus image with the position of these B-scans through the foveal center is identified.

**Figure 2.** Composite SD-OCT fundus image of the fovea centered scan and the optic nerve centered scan showing the various measurements performed. H, horizontal displacement; V, vertical displacement. The fovea-nerve distance can be computed from these horizontal and vertical displacements. $\alpha$, angle of declination between the horizontal displacement line and the fovea-nerve distance line.
fundus image on any other image of the fundus using shared landmarks permits the calibration of digital fundus photographs, fluorescein angiograms, and fundus autofluorescence images obtained from any system (Fig. 3). Moreover, these measurements will be more accurate for an individual compared with presumed calibrations obtained from population-based measurements.

One of the major strengths of this calibration study was the ability to locate the foveal center directly from cross-sectional SD-OCT data and not from a fundus photograph where this may be ambiguous. The distribution of macular pigment and the geometry of retinal vessels may be proxies for the foveal center, but the accuracy of these assumptions has not been proven. Furthermore, the presence of pathology can significantly limit the ability to recognize even these indirect clues regarding the location of the foveal center. Because we used multiplanar cross-sectional data in our study, the identification of the foveal center was more anatomically accurate than in any previously reported work.

Although we can obtain very precise fundus distance measurements using SD-OCT, we found from the data analyzed in this study that the fovea-nerve distance varies little within this population of healthy individuals. These results were in close agreement with other published results.\(^6,18\) Furthermore, the coefficients of variability for the vertical dimension and for the angle of declination were similar to those in a study that used a scanning laser ophthalmoscope to functionally assess a patient’s preferred retinal locus as a proxy for the fovea.\(^19\)

As expected, the refractive error in a patient has a role in the amount of magnification of the SD-OCT fundus image.\(^13\) Despite this, the mean fovea-nerve distance varied by only 7.3% over a range of refractive errors in our study. The refractive error is generally stable in a given eye, and this permits comparisons over time.

The parameters in this study with the greatest coefficient of variability were the vertical displacement and, consequently, the angle of declination. This is due either to biological variability or to angular rotation of the eye. To register images from 16% of the eyes in our study, the SD-OCT fundus image of the optic nerve needed to be rotated relative to the SD-OCT fundus image of the macula. This confirms that rotation of the eye occurs during some SD-OCT scans and suggests that rotation is a component of the variability.

Our data demonstrate that the fovea-nerve distance and the horizontal displacement between the fovea and the optic nerve do not vary significantly among patients. Furthermore, the range of both the horizontal and vertical displacements was less than

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Figure 3. Composite SD-OCT fundus image registered to a digital fundus photograph. Registration was performed by maximizing blood vessel overlap.

Figure 4. Reticle constructed from the mean dimensions determined by this study overlying the optic nerve head on the scanning laser ophthalmoscope generated by the Cirrus HD-OCT. Use of the reticle could allow the foveal center to be obtained without operator judgment, even in the presence of severe macular pathology.
1.05 mm in 94% of the eyes in this study in each dimension. Given these biometric data, we envision the creation of a simple reticle (Fig. 4) that would use the optic nerve as a landmark to acquire data centered on the fovea without the subjective judgment of the SD-OCT operator. This reticle would be useful when there is significant macular pathology and no other means exist to identify the foveal center.

In summary, we have developed a simple and direct approach for calibrating any fundus image using an SD-OCT fundus image. Based on the measurements obtained in this study, we have also developed a simple reticle that can be used to maximize the likelihood that an SD-OCT scan will be centered on the fovea whenever macular pathology precludes accurate identification of the foveal center.

REFERENCES