Polarization-Sensitive Optical Coherence Tomography and Conventional Retinal Imaging Strategies in Assessing Foveal Integrity in Geographic Atrophy

Ramzi G. Sayegh,1 Stefan Zotter,2 Philip K. Roberts,1 Maciej M. Kandula,3 Stefan Sacu,1 David P. Kreil,3 Bernhard Baumann,2 Michael Pircher,2 Christoph K. Hitzenberger,2 and Ursula Schmidt-Erfurth1

1Department of Ophthalmology, Medical University of Vienna, Vienna, Austria
2Center for Medical Physics and Biomedical Engineering, Medical University of Vienna, Vienna, Austria
3Chair of Bioinformatics Research Group, Department of Biotechnology, BOKU University Vienna, Austria

CORRESPONDENCE: Ursula Schmidt-Erfurth, Department of Ophthalmology, Medical University of Vienna, Wachinger Guertel 18-20, Vienna, Austria; Ursula.schmidt-erfurth@meduniwien.ac.at.

Submitted: July 1, 2014
Accepted: June 8, 2015

Citation: Sayegh RG, Zotter S, Roberts PK, et al. Polarization-sensitive optical coherence tomography and conventional retinal imaging strategies in assessing foveal integrity in geographic atrophy. Invest Ophthalmol Vis Sci. 2015;56:5246–5255. DOI: 10.1167/iovs.14-15114

PURPOSE. To compare current imaging methods with respect to their ability to detect the condition of the fovea in patients with geographic atrophy (GA).

METHODS. The retinas of 176 eyes with GA were imaged using two spectral-domain optical coherence tomography (SD-OCT) systems, Cirrus HD-OCT and Spectralis HRA+OCT, and fundus autofluorescence (FAF) and infrared imaging (IR) was used in the scanning laser ophthalmoscope (SLO) mode. Polarization-sensitive OCT (PS-OCT), which selectively visualizes the RPE in addition to SD-OCT features, was used to image 95 eyes. Geographic atrophy lesions were categorized as fovea spared, involved, or not quantifiable (grades 0, 1, and 2). Morphologic gradings were subsequently correlated with best-corrected visual acuity (BCVA) measurements to independently identify the corresponding functional condition of the fovea. Cohen’s κ statistics with a bootstrap method was applied to compare retinal imaging methods.

RESULTS. In PS-OCT, 84% of eyes with BCVA greater than or equal to 20/40 were detected, whereas in conventional retinal imaging the rate ranged from 27% in FAF to 45% in the SD-OCT segment. Cohen’s κ statistics revealed significant differences between the gradings of PS-OCT and conventional imaging with κ = 0.488 and a global Hotelling’s T² statistic of 17.9 with a P value of P = 0.003. Statistical tests revealed no statistically significant differences between the conventional retinal imaging modalities.

CONCLUSIONS. Polarization-sensitive OCT can better allow correct grading of the fovea in relation to BCVA and identify foveal sparing than other imaging modalities. The differences in imaging precision should be considered in diagnostic and therapeutic evaluations.

Keywords: AMD, geographic atrophy, retinal imaging, polarization-sensitive optical coherence tomography, fovea
Identification of the Foveal Condition in GA

The Spectralis HRA+OCT volume scans were acquired using the high speed mode (scan width: 768 A scans) with a standard of 49 B scans per volume set with a width and height of 20°×20°. A scans covered a depth of 1.9 mm and consisted of 496 voxels. Each B-scan was averaged using the automatic real-time mode of the Spectralis device with 30 frames per B scan. The resulting density was 768×49×496 voxels.

For this specific study, nonnormalized FAF data acquisition was used in a resolution of 768×768 pixels in the high speed mode and brightness and contrast were individually adjusted during data acquisition for optimal visualization of the FAF intensity distribution at the posterior pole and the foveal location. Fundus autofluorescence images were obtained by recording a 7-second video using a 30°×30° frame size in the FAF mode of the Spectralis HRA+OCT. One image comprising the mean FAF intensity was calculated out of 15 frames.

The Spectralis HRA+OCT cSLO device for IR imaging uses a wavelength of 820 nm. Infrared images were acquired with a frame size of 30°×30° and a resolution of 768×768 pixels. The technical properties of FAF, IR, and SD-OCT and procedures are described in detail elsewhere.27,57

No general comparison of the absolute dimensions of the scanned areas in the different OCT models was possible because the Cirrus HD-OCT device does not provide angular field-of-view information about the scan patterns applied and the Spectralis HRA+OCT device calculates the individual scaling based on the focus setting. Furthermore, the physical dimension of the area scanned by the Spectralis HRA+OCT device varies with the setting of the scanner focus.

Polarization-Sensitive (PS)-OCT Imaging

A new wide-field, high-speed PS-OCT system developed by the Center for Medical Physics and Biomechanical Engineering, Medical University of Vienna was used in this study.58 Compared with earlier PS-OCT systems,32,33 it acquires a denser volume scan (up to 1024×250 A scans) over a larger scan field (up to 40°×40°). We used the highest density pattern with a scan field of 30°×30° for this study. The technical principles of this device have been described previously.32,53,59,60 The system enables measurement of four variables simultaneously: the intensity of the backscattered light (as in conventional SD-OCT imaging), the birefringence retardation, optic axis orientation, and the degree of polarization uniformity (DOPU). Retinal layers can then be classified in polarization preserving (e.g., photoreceptor layers), depolarizing (e.g., RPE cells) and birefringent layers (e.g., retinal nerve fiber layer). As only melanin-containing structures in the RPE distinctly depolarize backscattered light,51 PS-OCT is able to specifically identify the RPE layer under physiological and pathological conditions. Degree of polarization uniformity values will be close to 1 in polarization-preserving layers but lower in depolarizing (RPE) structures. Retinal structures are consistent with polarization-preserving and birefringent layers, while the RPE is displayed as a depolarizing layer. Areas of DOPU less than 0.75 were delineated to generate a precise RPE segmentation and displayed in red on top of intensity B scans, generating a point-to-point overlay of depolarizing tissue within the regular intensity-based SD-OCT image (Figs. 1–3). Thus, a complete axial dataset displaying distinct retinal and RPE layers was obtained.

The extent of areas with disturbed RPE is delineated by summing up the number of depolarizing pixels (DOPU < 0.75) along each A scan throughout the entire three-dimensional (3D) PS-OCT dataset. A 2D en face map visualizing the pattern of depolarizing material at the RPE level is formed (Figs. 1B, 2E1, 2E2). In addition to detection of areas with a complete absence of RPE, another map is obtained that allows detection of any thinning, thickening or distortion of RPE. This map is consistent with the en face maps obtained by FAF and IR imaging, as
**FIGURE 1.** Example of a patient with foveal sparing in polarization-sensitive retinal imaging. Example of a patient with BCVA of 20/22 Snellen equivalents imaged by PS-OCT. (A) The acquired en face intensity projection image during the PS-OCT volume scan acquisition. (B) En face map of depolarizing tissue thickness and visualizing the multifocal areas of atrophy and the foveal sparing in this patient. (C) The DOPU image used to identify depolarizing tissue in the position of the yellow line in image (A). (D) The intensity B-scan image in the position of the yellow line in image (A). (E) The same B scan as in (C) segmented by the GA software and showing the depolarizing tissue overlay (RPE) in red.

**FIGURE 2.** Examples of patients with fovea spared and involved by the GA process in conventional and polarization-sensitive retinal imaging. Images (A1–F1): Example of a patient with BCVA of 20/20 Snellen equivalent graded as grade 0 (fovea spared), by near IR (A1), SD-OCT (Spectralis HRA-OCT [B1]), FAF (C1), SD-OCT (Cirrus HD-OCT [D1]), and PS-OCT (E1, F1). Image (E1) represents the calculated en face map of depolarizing tissue based on PS-OCT B scans (F1). The fovea contour and neurosensory layers in the fovea are well defined in the PS-OCT and SD-OCT images (yellow arrows). The choroidal signal enhancement is detectable at the borders of the foveal depression (red arrows). The fovea is spared and encircled in yellow in the conventional en face images (A1, C1). In PS-OCT (F1), the depolarizing tissue is segmented in red by the GA software (white arrow indicates intact RPE in the foveal area), and the fovea contour and neurosensory layers are preserved. Images (A2–F2): Example of a patient with best corrected visual acuity of 20/160 Snellen equivalent graded as grade 1 (fovea involved) in all retinal imaging modalities. (A2) Infrared imaging, (C2) Fundus autofluorescence imaging, (B2, D2) SD-OCT, and (E2, F2) PS-OCT. The fovea contour and the neurosensory layers are altered in the PS-OCT and SD-OCT images (red arrow SD-OCT, green arrow PS-OCT). The fovea has a typical GA fluorescence pattern in the en face images (red circle).
Identification of Foveal Sparing

A systematic grading scale was established and SD-OCT and PS-OCT scans, FAF and IR images were graded (RS) according to a predetermined grading protocol in an anonymized and masked manner (i.e., in a random sequence for each eye).

The grading system was designed according to disease progression with grade 0 fovea spared, grade 1 fovea involved and grade 2 fovea not quantifiable. By SD-OCT, the fovea was graded as involved when the RPE in the central portion of the fovea was continuously absent, associated with an enhanced light transmission into the choroid, and/or the RPE band was absent compared with the normal RPE band. The fovea was graded as spared when the central portion of the foveal depression showed a regular morphology with normal inner and outer retinal layers and could be identified in five consecutive B scans in Cirrus HD-OCT and three B scans in Spectralis HRA+OCT and PS-OCT (Figs. 1, 2B1, 2D1, 2F1, 3A3–A5). The number of B scans analyzed were different because the OCT systems used acquired different scan densities. Polarization-sensitive OCT identified foveal sparing using the algorithm and color-coding described above. Foveal sparing was graded whenever a continuous depolarizing RPE band extended to the central foveal area. By FAF, the fovea was defined as involved when the gray-scale image in FAF had identical intensity values in the region of the supposed fovea as in the central region of the GA lesion. The images were analyzed simultaneously when the combination of FAF and IR images was used. When none of the criteria described above were met, the fovea was graded as fovea not gradable. Examples of typical gradings are given in Figure 3.

Correlation of BCVA and Morphologic Sparing or Involvement

After grading the morphology in the different imaging modalities, the results of the grading were related with functional values from BCVA testing. The diameter of the fovea was assumed to be 1.5 mm. Therefore, the radius of the physiological fovea is 0.75 mm or 2.65\( \times 0.8 \) (assuming a standard eye length of 24 mm). From the center of the focal BCVA distribution of the posterior pole (Fig. 4; see also fig. 4 in Ref. 43), a BCVA greater than 20/40 can be expected within a distance of 2.65\( \times 0.8 \) from the foveal center. Therefore, for our

Figure 3. Examples of patients demonstrating the grading system in conventional and PS-OCT imaging. Images (A1–A5) show five different eyes imaged by all the retinal imaging devices used in this study and are examples for grade 0 (fovea spared). (A1) Infrared image of a patient with BCVA of 20/20 Snellen equivalents. (A2) Fundus autofluorescence image of a patient with BCVA 20/22. (A3) Spectral-domain OCT B scan (Spectralis) of a patient with BCVA of 20/32. (A4) Spectral-domain OCT B scan (Cirrus HD-OCT) of a patient with BCVA of 20/32. (A5) Segmented PS-OCT B scan of a patient with BCVA 20/40. The images (B1–B5) represent five different eyes of patients where the fovea was graded as fovea involved (grade 1) in all retinal imaging devices. Respective BCVA results were (B1) IR image, BCVA = 20/80; (B2) FAF image, BCVA = 20/80; (B3) Spectralis SD-OCT, BCVA = 20/200; (B4) Cirrus SD-OCT, BCVA = 20/100; (B5) PS-OCT B scan, BCVA = 20/100. Images (C1–C5) represent five examples of eyes where the fovea was graded as not quantifiable (grade 2). Respective BCVA results corresponding to the images were (C1) IR image, BCVA = 20/50; (C2) FAF image, BCVA = 20/160; (C3) Spectralis SD-OCT, BCVA = 20/200; (C4) Cirrus SD-OCT, BCVA = 20/100; (C5) PS-OCT B scan, BCVA = 20/25.
study we arbitrarily concluded that a BCVA greater than 20/40 can be associated with a morphologic foveal sparing and a BCVA less than 20/40 with a fovea, which is affected by disease. This functional information was used in the comparative analysis of the retinal imaging modalities’ ability to be graded correctly according to the BCVA threshold.

Statistical Analysis

An ANOVA was used to analyze the relation between the BCVA functional values and the morphologic grading results from all the imaging systems (the BCVA results in letters were analyzed and then converted into Snellen VA for descriptive purposes). To compare the ability of the retinal imaging methods to reliably grade the fovea, we constructed a reference grading (“known truth”) based on the BCVA of each eye. We then computed a weighted and an unweighted Cohen’s κ statistic to obtain a κ statistic for each method compared with the reference grading. For a weighted κ, where weight was set to equal, we assumed that an unclear grading (grade 2) was equally better than a wrong grading as it was worse than a right grading. For an unweighted κ, any grading different from the reference grading, including an unclear grading, was considered equally bad. To identify significant differences between κ coefficients, κ statistics for different methods were obtained for the same cohort and were thus expected to be correlated. We tested the hypothesis that $\kappa_1 = \ldots = \kappa_n$, where $\kappa_i$ is the agreement between FAF and the reference BCVA and $\kappa_i$ for $i = 2 \ldots n$ are the agreements of the alternative methods with the BCVA reference. We tested the significance of differences relative to randomly expected variance using an established bootstrap method with 2001 iterations.

RESULTS

Patient Characteristics and Balance Between Groups

One hundred seventy-six eyes from 96 patients (60 women, mean age 78 years) were included and imaged using a Cirrus

<table>
<thead>
<tr>
<th>Grading</th>
<th>Number of Eyes (%)</th>
<th>Mean BCVA</th>
<th>BCVA SE</th>
<th>Lower Bound</th>
<th>Upper Bound</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cirrus</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 0</td>
<td>60 (34)</td>
<td>20/37</td>
<td>20/500</td>
<td>20/44</td>
<td>20/32</td>
</tr>
<tr>
<td>Grade 1</td>
<td>96 (55)</td>
<td>20/67</td>
<td>20/1000</td>
<td>20/80</td>
<td>20/59</td>
</tr>
<tr>
<td>Grade 2</td>
<td>20 (11)</td>
<td>20/48</td>
<td>20/333</td>
<td>20/69</td>
<td>20/37</td>
</tr>
<tr>
<td>Total</td>
<td>176 (100)</td>
<td>20/51</td>
<td>20/1000</td>
<td>20/57</td>
<td>20/47</td>
</tr>
<tr>
<td>Spectralis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 0</td>
<td>56 (31.8)</td>
<td>20/36</td>
<td>20/500</td>
<td>20/43</td>
<td>20/32</td>
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<td>20/1000</td>
<td>20/74</td>
<td>20/54</td>
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<td>20/67</td>
<td>20/250</td>
<td>20/15/4</td>
<td>20/45</td>
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<td>Total</td>
<td>176 (100)</td>
<td>20/51</td>
<td>20/1000</td>
<td>20/57</td>
<td>20/47</td>
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<td>Grade 0</td>
<td>51 (54)</td>
<td>20/37</td>
<td>20/667</td>
<td>20/44</td>
<td>20/32</td>
</tr>
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<td>Grade 1</td>
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<td>20/91</td>
<td>20/125</td>
<td>20/7/4</td>
<td></td>
</tr>
<tr>
<td>Grade 2</td>
<td>1 (1)</td>
<td>20/25</td>
<td>-</td>
<td>-</td>
<td>-</td>
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<tr>
<td>Total</td>
<td>95 (100)</td>
<td>20/50</td>
<td>20/667</td>
<td>20/44</td>
<td>20/32</td>
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<tr>
<td>FAF</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Grade 0</td>
<td>38 (22)</td>
<td>20/36</td>
<td>20/400</td>
<td>20/44</td>
<td>20/31</td>
</tr>
<tr>
<td>Grade 1</td>
<td>101 (57)</td>
<td>20/67</td>
<td>20/1000</td>
<td>20/80</td>
<td>20/57</td>
</tr>
<tr>
<td>Grade 2</td>
<td>37 (21)</td>
<td>20/42</td>
<td>20/400</td>
<td>20/53</td>
<td>20/34</td>
</tr>
<tr>
<td>Total</td>
<td>176 (100)</td>
<td>20/51</td>
<td>20/1000</td>
<td>20/57</td>
<td>20/47</td>
</tr>
<tr>
<td>IR</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 0</td>
<td>40 (28)</td>
<td>20/37</td>
<td>20/500</td>
<td>20/43</td>
<td>20/32</td>
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<tr>
<td>Grade 1</td>
<td>83 (47)</td>
<td>20/80</td>
<td>20/667</td>
<td>20/1000</td>
<td>20/65</td>
</tr>
<tr>
<td>Grade 2</td>
<td>44 (25)</td>
<td>20/42</td>
<td>20/500</td>
<td>20/50</td>
<td>20/35</td>
</tr>
<tr>
<td>Total</td>
<td>176 (100)</td>
<td>20/51</td>
<td>20/1000</td>
<td>20/57</td>
<td>20/47</td>
</tr>
<tr>
<td>FAF+IR</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 0</td>
<td>40 (25)</td>
<td>20/36</td>
<td>20/500</td>
<td>20/43</td>
<td>20/32</td>
</tr>
<tr>
<td>Grade 1</td>
<td>78 (44)</td>
<td>20/83</td>
<td>20/1000</td>
<td>20/105</td>
<td>20/71</td>
</tr>
<tr>
<td>Grade 2</td>
<td>54 (31)</td>
<td>20/42</td>
<td>20/500</td>
<td>20/50</td>
<td>20/36</td>
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<tr>
<td>Total</td>
<td>176 (100)</td>
<td>20/51</td>
<td>20/1000</td>
<td>20/57</td>
<td>20/47</td>
</tr>
</tbody>
</table>

Grading results for all axial (Cirrus HD-OCT, Spectralis SD-OCT, PS-OCT) and en face (IR, FAF, FAF+IR) imaging modalities reflecting foveal involvement/integrity based on morphologic features in absolute and relative numbers. The corresponding BCVA values are indicated in mean BCVA and BCVA range and correlate significantly ($P < 0.0001$) with the gradings for each imaging modality. Grade 0, fovea spared; grade 1, fovea involved; grade 2, fovea not quantifiable.
Identification of the Foveal Condition in GA

TABLE 2.

Comparison of Gradings and BCVA in Conventional Retinal Imaging Systems (176 Eyes) and PS-OCT (95 Eyes)

<table>
<thead>
<tr>
<th>OCT Modalities and Comparison</th>
<th>FAF Grade 0</th>
<th>FAF Grade 1</th>
<th>FAF Grade 2</th>
<th>IR Grade 0</th>
<th>IR Grade 1</th>
<th>IR Grade 2</th>
<th>FAF+IR Grade 0</th>
<th>FAF+IR Grade 1</th>
<th>FAF+IR Grade 2</th>
</tr>
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<tbody>
<tr>
<td><strong>Mean BCVA Eyes (%)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cirrus grade 0</td>
<td>17 (10)</td>
<td>20/30</td>
<td>20/53</td>
<td>15 (10)</td>
<td>20/30</td>
<td>20/53</td>
<td>18 (10)</td>
<td>20/30</td>
<td>20/50</td>
</tr>
<tr>
<td>Cirrus grade 1</td>
<td>16 (9)</td>
<td>20/30</td>
<td>20/47</td>
<td>18 (10)</td>
<td>20/30</td>
<td>20/48</td>
<td>15 (10)</td>
<td>20/30</td>
<td>20/45</td>
</tr>
<tr>
<td>Spectralis grade 1</td>
<td>20 (11)</td>
<td>20/44</td>
<td>20/51</td>
<td>15 (10)</td>
<td>20/30</td>
<td>20/48</td>
<td>22 (11)</td>
<td>20/30</td>
<td>20/45</td>
</tr>
<tr>
<td>Spectralis grade 2</td>
<td>2 (1)</td>
<td>20/45</td>
<td>20/285</td>
<td>2 (1)</td>
<td>20/45</td>
<td>20/167</td>
<td>2 (1)</td>
<td>20/45</td>
<td>20/285</td>
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<tr>
<td>PS-OCT grade 2</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
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</tr>
</tbody>
</table>

Morphologic gradings for all axial OCT imaging modalities and corresponding en face IR/FAF features. The largest inconsistencies were found between FAF gradings and PS-OCT/BCVA values.

The bootstrap test yielded a global Hotelling's $T^2$ statistic of 2.04 with a $P$ value of 0.73 in a weighted approach and of 1.17 with a $P$ value of 0.88 in an unweighted approach for the comparison of conventional retinal imaging modalities with each other.

Analysis of Foveal Grading in All Imaging Modalities and Relation to BCVA

All grading results and comparisons between the imaging modalities and comparisons offer the grading results with the threshold of BCVA greater than or equal to 20/40 or BCVA less than 20/40 are listed in Tables 1 through 4 and Figure 5. Furthermore, the ANOVA relating the gradings in the different imaging systems to the corresponding BCVA values showed that the differences between the groups (grades 0, 1, and 2) were highly significant with $P$ less than 0.001 for all systems.

Cohen's $k$ Statistics for the Comparison of Conventional Retinal Imaging

We considered the three possible grading results from the 176 eyes imaged by all retinal imaging systems except for PS-OCT and compared them with our reference BCVA threshold (BCVA $\geq$ 20/40 and BCVA < 20/40). We did this using a weighted and unweighted approach (see Methods section for details) of Cohen's $k$ statistics. The weighted $k$ ranged between $k = 0.255$ with $P$ less than 0.01 for Spectralis-OCT and $k = 0.564$ with $P$ less than 0.01 for the combination of FAF and IR imaging for all the conventional retinal imaging methods. In an unweighted $k$ statistic, $k$ ranged between $k = 0.229$ with $P$ less than 0.01 for Cirrus HD-OCT and $k = 0.295$ with $P$ less than 0.01 for FAF.

Then, we assessed significant deviations by means of a bootstrap procedure for comparing correlated $k$ coefficients for all conventional retinal imaging methods. We obtained a global Hotelling's $T^2$ statistic of 5.73 with $P = 0.017$.

Cohen's $k$ Statistics for the Comparison of Conventional Retinal Imaging and PS-OCT

We used a weighted approach of Cohen's $k$ statistics for the 95 eyes imaged by all retinal imaging systems including PS-OCT for comparing the conventional retinal imaging modalities with PS-OCT. $k$ ranged between $k = 0.221$ for Cirrus HD-OCT with $P$ less than 0.01 and $k = 0.493$ with $P$ less than 0.01 for PS-OCT. The bootstrap test yielded a global Hotelling's $T^2$ statistic of 5.73 with $P = 0.017$.

We also used an unweighted approach with which $k$ ranged between $k = 0.187$ for Cirrus HD-OCT with $P$ less than 0.01 and $k = 0.488$ with $P$ less than 0.01 for PS-OCT. The bootstrap test then yielded a global Hotelling's $T^2$ statistic of 17.9 with a $P$ value of $P = 0.003$. 
DISCUSSION

Identifying the foveal status could be relevant for the visual prognosis of patients during disease progression as well as in the evaluation of therapeutic efficacy in upcoming clinical trials. Therefore, the aim of this study was to analyze if PS-OCT imaging is superior to conventional imaging and if conventional retinal imaging modalities differ in their assessments of the condition of the fovea, particularly foveal sparing. Best-corrected visual acuity was used as an external factor in our analysis to differentiate between foveal sparing and foveal involvement. We compared the functional threshold of BCVA greater than or equal to or less than 20/40 with the grading results of the fovea anatomically denoted as fovea spared (grade 0), fovea involved (grade 1), or fovea not quantifiable (grade 2) and found statistically significant differences between BCVA and the grading groups with all imaging methods, with \( P < 0.0001 \) (ANOVA).

The statistical analyses presented in Table 1 show that the BCVA results of the gradings in the 95% confidence interval of every system consistently adhered to the BCVA thresholds. For example, BCVA in grade 0 ranged from 20/44 to 20/31 Snellen for all imaging systems.

A comparison of SD-OCT (Spectralis only) with FAF and a combination of near IR plus FAF imaging found a BCVA ranging from 0.30 to 0.12 logarithm of minimal angle resolution in eyes with foveal sparing.\(^1\) This result accords with our results of a BCVA of 20/40 or higher for grade 0, if the fovea is to be graded as spared.

The mean BCVA in all retinal imaging methods for grade 1 in our study was between 20/125 and 20/74. Therefore, we can conclude that our grading 1 for an involved fovea was reliable.

The mean BCVA in en face imaging for grade 2 was between 20/53 and 20/34. A possible explanation is that the fovea in this group of eyes graded with grade 2 was in the process of ongoing destruction and therefore assessing if the fovea was spared or involved was difficult. The BCVA for grade 2 had a wider range for the OCT systems (i.e., between 20/154 in Spectralis and 20/37 in Cirrus imaging and in one case in PS-OCT; BCVA = 20/25). The explanation for the wider range in the OCT systems could be that residual RPE-like hyper-reflective structures observed in OCT scans are functional or that they are not functional and are over interpreted.

We found no statistically significant differences between the conventional retinal imaging modalities with the conservative and robust Cohen’s \( \kappa \) statistical measure. However, although not statistically significant, the SD-OCT segment did show more positive results in discerning foveal sparing in the descriptive statistics. When comparing the modalities the drawbacks of the FAF and IR systems should also be considered. Making decisions upon foveal involvement is challenging with FAF imaging as the macular pigment in the neurosensory foveal retina blocks the blue excitation light.\(^9,11,27,48\) In both FAF and IR en face imaging distinguishing the exact position of the foveal center in the absence of a structural foveal depression is harder than with SD-OCT.

Although we found no statistically significant differences between the conventional retinal imaging modalities, when analyzing our grading results in combination with BCVA, the subgroup of eyes scanned with PS-OCT showed statistically significant differences in grading the fovea relative to BCVA compared with conventional retinal imaging.

The descriptive grading results showed PS-OCT correlated better than en face imaging with BCVA (e.g., from Table 2, in 22 eyes PS-OCT grade 0/FAF grade 1, mean BCVA of 20/37; or in 12 eyes, PS-OCT grade 0/IR grade 1, mean BCVA of 20/38). Fundus autofluorescence has the advantage over PS-OCT of being able to predict lesion progression toward hyperfluorescence at the edges of the lesion.\(^18,22,49,50\) However, PS-OCT provides more detailed information about the condition of the RPE layer in terms of thinning, thickening, detachment, and

Identification of the Foveal Condition in GA

Table 3. Comparison of All OCT Grading Results and BCVA Values

<table>
<thead>
<tr>
<th></th>
<th>Spectralis Grade 0</th>
<th>Spectralis Grade 1</th>
<th>Spectralis Grade 2</th>
<th>PS-OCT Grade 0</th>
<th>PS-OCT Grade 1</th>
<th>PS-OCT Grade 2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Eyes (%)</td>
<td>Mean BCVA</td>
<td>Eyes (%)</td>
<td>Mean BCVA</td>
<td>Eyes (%)</td>
<td>Mean BCVA</td>
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<tr>
<td>Cirrus grade 0</td>
<td>46 (26)</td>
<td>20/36</td>
<td>11 (6)</td>
<td>20/34</td>
<td>3 (2)</td>
<td>20/118</td>
</tr>
<tr>
<td>Cirrus grade 1</td>
<td>3 (2)</td>
<td>20/35</td>
<td>91 (52)</td>
<td>20/67</td>
<td>2 (1)</td>
<td>20/133</td>
</tr>
<tr>
<td>Cirrus grade 2</td>
<td>7 (4)</td>
<td>20/36</td>
<td>6 (3)</td>
<td>20/71</td>
<td>7 (4)</td>
<td>20/30</td>
</tr>
<tr>
<td>Spectralis grade 0</td>
<td>40 (22)</td>
<td>20/36</td>
<td>8 (8)</td>
<td>20/71</td>
<td>7 (4)</td>
<td>20/30</td>
</tr>
<tr>
<td>Spectralis grade 1</td>
<td>5 (5)</td>
<td>20/40</td>
<td>29 (31)</td>
<td>20/91</td>
<td>0 -</td>
<td>-</td>
</tr>
<tr>
<td>Spectralis grade 2</td>
<td>6 (6)</td>
<td>20/41</td>
<td>6 (6)</td>
<td>20/100</td>
<td>0 -</td>
<td>-</td>
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</tbody>
</table>

Comparison of morphologic grading and corresponding BCVA results for all axial imaging modalities. Grading results and corresponding BCVA values are more consistent in PS-OCT than in Cirrus HD-OCT or the Spectralis SD-OCT system. Spectralis results are the most confident of the conventional OCT systems.

Table 4. Grading and BCVA Results in Conventional Retinal Imaging Systems (176 Eyes) and in PS-OCT (95 Eyes) in Eyes Where BCVA Was Over and Under 20/40 Snellen Equivalents

<table>
<thead>
<tr>
<th></th>
<th>BCVA &gt; 20/40</th>
<th>Mean BCVA</th>
<th>BCVA &lt; 20/40</th>
<th>Mean BCVA</th>
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<tr>
<td></td>
<td>Eyes (%)</td>
<td>Mean BCVA</td>
<td>Eyes (%)</td>
<td>Mean BCVA</td>
</tr>
<tr>
<td>Cirrus grade 0</td>
<td>34 (47)</td>
<td>20/26</td>
<td>26 (25)</td>
<td>20/87</td>
</tr>
<tr>
<td>Cirrus grade 1</td>
<td>37 (46)</td>
<td>20/36</td>
<td>69 (66)</td>
<td>20/118</td>
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<tr>
<td>Cirrus grade 2</td>
<td>11 (15)</td>
<td>20/32</td>
<td>9 (9)</td>
<td>20/125</td>
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<tr>
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<td>22 (21)</td>
<td>20/80</td>
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<tr>
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<td>20/31</td>
<td>74 (71)</td>
<td>20/118</td>
</tr>
<tr>
<td>Spectralis grade 2</td>
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<td>20/31</td>
<td>8 (8)</td>
<td>20/154</td>
</tr>
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<td>PS-OCT grade 0</td>
<td>32 (84)</td>
<td>20/29</td>
<td>19 (33)</td>
<td>20/74</td>
</tr>
<tr>
<td>PS-OCT grade 1</td>
<td>5 (13)</td>
<td>20/33</td>
<td>38 (67)</td>
<td>20/125</td>
</tr>
<tr>
<td>PS-OCT grade 2</td>
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<td>20/25</td>
<td>0 -</td>
<td>-</td>
</tr>
<tr>
<td>FAF grade 0</td>
<td>27 (38)</td>
<td>20/29</td>
<td>11 (11)</td>
<td>20/100</td>
</tr>
<tr>
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<td>78 (75)</td>
<td>20/105</td>
</tr>
<tr>
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<td>20/29</td>
<td>15 (14)</td>
<td>20/118</td>
</tr>
<tr>
<td>IR grade 0</td>
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<td>20/29</td>
<td>17 (16)</td>
<td>20/80</td>
</tr>
<tr>
<td>IR grade 1</td>
<td>15 (21)</td>
<td>20/29</td>
<td>68 (65)</td>
<td>20/125</td>
</tr>
<tr>
<td>IR grade 2</td>
<td>25 (35)</td>
<td>20/30</td>
<td>19 (18)</td>
<td>20/95</td>
</tr>
<tr>
<td>FAF+IR grade 0</td>
<td>30 (42)</td>
<td>20/28</td>
<td>14 (14)</td>
<td>20/87</td>
</tr>
<tr>
<td>FAF+IR grade 1</td>
<td>13 (18)</td>
<td>20/33</td>
<td>65 (63)</td>
<td>20/125</td>
</tr>
<tr>
<td>FAF+IR grade 2</td>
<td>29 (40)</td>
<td>20/28</td>
<td>25 (24)</td>
<td>20/91</td>
</tr>
</tbody>
</table>

In PS-OCT, 38 eyes > BCVA 20/40 SE and 57 eyes < BCVA 20/40 SE.

In conventional retinal imaging, 72 eyes > BCVA 20/40 SE and 104 < BCVA 20/40 SE.
porosity at the GA rim. This information is more useful for advanced analysis of GA pathophysiology than the hyperfluorescent feature surrounding the GA lesion in FAF alone without any corresponding morphologic details. Moreover, 3D RPE mapping by PS-OCT segmentation is an automatic function and may lead to a GA classification based on distinct morphologic features in the near future.

Polarization-sensitive OCT detected 84% of eyes with BCVA greater than or equal to 20/40, whereas SD-OCT only detected 47% (Table 4). Furthermore, 15 eyes were graded 1 with PS-OCT and either 0 or 2 with Cirrus HD-OCT with a mean BCVA of 20/77 and 20/154, respectively. In 14 eyes, the grading differed between PS-OCT grade 1 and Spectralis HRA+OCT either grade 0 or 2 with mean BCVA 20/71 and 20/100 (Table 3). The explanation for the different gradings could be that in SD-OCT pathologic residual structures in the RPE no longer contribute to visual function. Cirrus HD-OCT and Spectralis HRA+OCT unlike PS-OCT have no tissue-specific differentiation function and could therefore mislabel and overinterpret hyperreflective unspecific residual structures as viable.

It is noteworthy, however, that PS-OCT can be used in an en face mode in addition to axial OCT scanning based on the PS-OCT algorithm described earlier.33–35,41 Hence, PS-OCT integrates the advantages of axial and en face imaging in a single approach but for now it is more time consuming and unavailable commercially.

The limitations of our study are mostly related to the subjective grading of each imaging method by the grader and the BCVA threshold chosen. Although other thresholds have been tried and the results were no different, comparing retinal imaging methods using an external factor other than BCVA in GA, for example, fixation stability in microperimetry, could have led to other results.

In conclusion, our study shows that PS-OCT, an advanced OCT technology, can reliably assess the fovea and delineate the area of atrophy, while simultaneously discerning neurodegenerative processes in the retina. Polarization-sensitive OCT may provide new insights into the pathophysiology of atrophic AMD. Our results should encourage investigators to include PS-OCT in future clinical trials seeking to develop agents and strategies to preserve the RPE and the neurosensory retina in the sensitive fovea.

Acknowledgments

The authors thank Christoph Mitsch, MD, for his technical advice. Disclosure: R.G. Sayegh, None; S. Zotter, Canon, Inc. Tokyo (F); P.K. Roberts, Canon, Inc. Tokyo (F); M.M. Kandula, None; S. Sacu, None; D.P. Kreil, None; B. Baumann, Canon, Inc. Tokyo
References


