Additive Diagnostic Role of Imaging in Glaucoma: Optical Coherence Tomography and Retinal Nerve Fiber Layer Photography

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PURPOSE. To investigate the additive diagnostic role of spectral-domain optical coherence tomography (SD-OCT) and red-free retinal nerve fiber layer photography (RNFLP) in making clinical glaucoma diagnosis.

METHODS. Four diagnostic combination sets, including the most recent image from each measurement of 196 glaucoma eyes (including the 44 preperimetric glaucoma eyes) and 101 healthy eyes, were prepared: (1) stereo disc photography and Humphrey visual field (SH), (2) SH and SD-OCT (SHO), (3) SH and RNFLP (SHR), and (4) SHR and SD-OCT (SHRO). Each randomly sorted set was serially presented at 1-month intervals to five glaucoma specialists who were asked to evaluate them in a subjective and independent manner. The specialists’ glaucoma-diagnostic performances based on the sets were then compared.

RESULTS. For each specialist, adding SD-OCT to SH or SHR increased the glaucoma-diagnostic sensitivity but not to a level of statistical significance. For one specialist, adding RNFLP to SH significantly increased the sensitivity. Each specialist showed a high level of specificity regardless of the diagnostic set. The overall sensitivity of all specialists’ assessments was significantly increased by adding RNFLP or the combination of SD-OCT and RNFLP to SH (P < 0.001); however, adding SD-OCT to SH or SHR did not significantly increase the sensitivity. A similar relationship was noted also for the preperimetric glaucoma subgroup.

CONCLUSIONS. In contrast to RNFLP, SD-OCT did not significantly enhance the diagnostic accuracy of detecting glaucoma or even of preperimetric glaucoma. Our results suggest that, at least for glaucoma specialists, the additive diagnostic role of OCT is limited.

Keywords: additive diagnostic role, spectral-domain optical coherence tomography, retinal nerve fiber layer photography, glaucoma diagnosis, glaucoma specialist

The key components of glaucoma diagnosis are evaluation of structural damage represented by the change of the optic nerve head (ONH) or retinal nerve fiber layer (RNFL) and evaluation of functional damage by visual field test.1 Due to the lack of a single definitive glaucoma-diagnostic measure, the cornerstone of glaucoma diagnosis remains the clinician’s overall assessment of integrated findings from clinical evaluation of the ONH, RNFL, and visual field.

Over the past few years, spectral-domain optical coherence tomography (SD-OCT) has emerged from the numerous structural imaging approaches as a modality offering an outstanding glaucoma-diagnostic ability.2–6 Optical coherence tomography enables quantitative evaluation of ONH and peripapillary RNFL thickness with high reproducibility and repeatability, for excellent diagnostic performance.7,8 Previous studies on the glaucoma-diagnostic performance of OCT mostly have evaluated the effectiveness of the device itself, using thickness parameters and its internal diagnostic classification. However, in clinical practice, identification of glaucoma does not depend on any single computerized imaging device. Rather, the clinician’s judgment as based on a combination of findings from optic disc, RNFL, and visual field evaluations is integral to any reasoned diagnosis. Therefore, there is a need to evaluate the impact of SD-OCT on the diagnostic accuracy of the clinician’s assessment when combined with the established glaucoma-diagnostic tools.

With respect to retinal diseases, SD-OCT has provided guidelines for a vitreomacular disease classification system,9 and has influenced clinical decisions affecting the diagnosis and management of chronic diseases, such as AMD10,11 and macular edema.12,13 However, as far as we know, there is no study regarding OCT’s additive influence on clinical glaucoma-diagnostic decisions. Therefore, in the present study, we investigated the additive diagnostic role of SD-OCT for...
glaucoma specialists in diagnosing glaucoma when used in conjunction with conventional structural (optic disc and RNFL) and functional (visual field) measurements. Additionally, the effect of additive red-free RNFL photography (RNFLP) and of different combination sets on the glaucoma specialists’ diagnoses of patients within a glaucoma group and a preperimetric glaucoma subgroup were examined.

## METHODS

This study is based on a review of medical records for the eyes of consecutive open-angle glaucoma patients and healthy individuals examined at the Glaucoma and General Ophthalmology Clinic of Seoul National University Hospital between 2010 and 2012. The study adhered to the Declaration of Helsinki and was approved by the Institutional Review Board of Seoul National University Hospital.

### Subjects

All subjects underwent complete ophthalmic examinations, including visual acuity measurement, IOP measurement by Goldmann applanation tonometry, refractive error measurement, slit-lamp biomicroscopy, gonioscopy, and dilated fundus and stereoscopic optic disc examination. After maximum pupil dilation, the subjects were imaged by stereo disc photography (SDP), RNFLP (Vx-10; Kowa Optomed, Inc., Tokyo, Japan), and SD-OCT (Cirrus-HD; Carl Zeiss Meditec, Inc., Dublin, CA, USA). They also underwent standard automated perimetry (SAP) with Swedish interactive threshold algorithm and the 30-2 standard program (Humphrey Field Analyzer II; Carl Zeiss Meditec, Inc.).

The inclusion criteria were as follows: best-corrected visual acuity of 20/40 or better, spherical refraction within ±3 diopters, cylinder correction within ±3.0 D, open anterior chamber angle on gonioscopic and slit-lamp examination, as well as reliable SDP, RNFLP, SD-OCT, and SAP. Only a high-quality photograph with a well-focused and evenly illuminated image was used; the detailed criteria for reliable SD-OCT and visual field are provided below.

Subjects were excluded if they had any history of diseases that might cause nonglaucomatous optic neuropathy or RNFL damage, diseases that can affect the peripapillary area where SD-OCT measurements are obtained, diseases other than glaucoma that can affect the visual field, or intraocular surgery other than simple cataract extraction. In cases in which both eyes were eligible, one eye was chosen randomly for inclusion.

### Determination of Diagnosis

For the diagnostic determination, two experienced glaucoma specialists (KHP and KEK) evaluated each subject’s examination (SDP, RNFLP, OCT, and SAP) and medical records independently, and classified eyes as either “healthy individual” or “glaucoma.” Disagreements were adjudicated by a third observer (DMK).

Glaucomatous eyes were classified as perimetric glaucoma or preperimetric glaucoma according to the presence of glaucomatous visual field defect on SAP. Eyes were classified as perimetric glaucoma if they had a glaucomatous optic disc appearance (i.e., increased cup-to-disc ratio, neuroretinal rim thinning, notching, and/or RNFL defect) and glaucomatous visual field defect. Glaucomatous visual field defect was defined as presence of a cluster of three or more non–edge points with P less than 5% probability of being normal, one with P less than 1% on pattern deviation plot; pattern standard deviation with P less than 5%; or glaucoma hemifield test outside the normal limits, as confirmed on two consecutive tests within a month. Only reliable visual fields with fixation loss of 15% or less, false-positive error rates of 15% or less, and false-negative error rates of 15% or less were included. Meanwhile, preperimetric glaucoma was defined as a glaucomatous optic disc appearance with/without RNFL defect and a normal SAP result, where progression was confirmed by SDP or RNFLP performed at least 1 year before inclusion. Eyes with preperimetric glaucoma had documented evidence of progressive glaucomatous change in the optic disc (e.g., focal or diffuse thinning of the neuroretinal rim, increased notching, or enlargement of the RNFL defects), which was also reviewed by two specialists (KHP and KEK).

The healthy individuals included in the present study were from the general population that visited the general ophthalmology clinic for regular health check-ups or refractive errors. They all had an IOP below 22 mm Hg without IOP-lowering medication, no history of elevated IOP, a normal appearance of optic disc and RNFL, and a normal visual field. Normal appearance of optic disc was defined as the absence of glaucomatous optic neuropathy and pallor or swelling of the optic disc. Normal visual field was defined as a mean deviation (MD) and pattern standard deviation with P more than 5% probability of being normal; absence of any cluster of three points or more with P less than 5% on pattern deviation plot; and glaucoma hemifield test within normal limits.

### Spectral-Domain OCT Measurements

All the SD-OCT images were obtained by a single, well-trained technician using Cirrus OCT (software version 6.0), as described previously. Only good-quality scans with well-focused images, no overt misalignment, no overt decentration of the measurement circle location around the optic disc, and a signal strength of 8 or greater (10 maximum) were included in the analyses.

An optic disc cube was obtained from a three-dimensional data set composed of 200 A scans from each of 200 B scans covering a 6-mm² area centered on the optic disc. After generating an RNFL thickness map from the cube data set, the software automatically determines the center of the disc and then positions a 3.46-mm diameter calculation circle for RNFL thickness measurement. Using these data, SD-OCT provides thickness parameters including average, 12 clock-hour sectors, and four quadrant sectors. An internal analysis algorithm measures ONH parameters, such as the rim area, the cup-to-disc area ratio, and the vertical cup-to-disc diameter ratio.

For the four quadrants and 12 clock-hour sector map of RNFL analysis, the yellow (outside the 95% normal limit) or red (outside the 99% normal limit) color code based on a comparison with an internal normative database is provided. Spectral-domain OCT also provides RNFL thickness deviation maps that apply the yellow and red colors of age-matched normative data to superpixels in which average thickness falls within the less than 5% and less than 1% normal-distribution percentiles, respectively.

### Preparation and Evaluation of Combination Sets of Diagnostic Measurements

For each subject, four combination sets of diagnostic measurements using SDP, RNFLP, Humphrey visual field, and SD-OCT were prepared: (1) SDP and Humphrey visual field (SH), (2) SH and SD-OCT (SHO), (3) SH and RNFLP (SHR), (4) SHR and SD-OCT (SHRO). For SD-OCT image, the currently available Cirrus HD-OCT ONH and RNFL analysis printout showing RNFL thickness measurements and diagnostic classifications was provided, which included average RNFL thickness, ONH parameter analyses, a temporal-superior-nasal-inferior-temporal...
RNFL thickness plot, an RNFL deviation map, and quadrant and clock-hour maps. Combination sets were created by adding RNFLP, SD-OCT, or both to the SH set, because detection of structural change in the disc and of visual field defect are fundamental to the diagnosis of glaucoma. Each set was composed of the single most recent reliable image from each device. In addition, each set had the same image from each diagnostic device: SH, SHO, SHR, and SHRO sets had the same SDP images and Humphrey visual fields; SHO and SHRO sets had the same OCT images; and SHR and SHRO sets had the same RNFLP images. For all sets, the images were saved as JPEG files and each patient’s images were put into one folder. In each set, the folders containing subjects’ examinations were randomly sorted independently of diagnosis or of glaucoma severity. Five fellowship-trained glaucoma specialists (SHK, JWK, MHS, JHS, MK) from five different academic medical centers evaluated each combination set of examinations independently, and each was masked to all clinical information as well as the number of healthy individuals and glaucoma patients. The specialists were instructed to diagnose each subject as either “glaucoma” or “healthy individual,” based on their clinical experiences without specified diagnostic criteria for each examination. They evaluated the combination sets at 1-month intervals in the same SH, SHO, SHR, SHRO order without receiving any information on any of the previous evaluation results.

### Statistical Analysis

The baseline characteristics of the study subjects were compared by one-way ANOVA for continuous variables and by χ² test for categorical variables. The interobserver agreement among the glaucoma specialists in discriminating the glaucoma and preperimetric glaucoma subgroup from healthy individuals was assessed by Kappa (κ) statistics. The strength of agreement was categorized according to the method of Landis and Koch:16 0 = poor, 0 to 0.20 = slight, 0.21 to 0.40 = fair, 0.41 to 0.60 = moderate, 0.61 to 0.80 = substantial, and 0.81 to 1.00 = almost perfect. The specificity and sensitivity of each specialist’s assessment using each diagnostic set were calculated, and the McNemar test was used to compare them for the diagnosis of glaucoma or preperimetric glaucoma subgroup. Along with the diagnostic performances of individual specialists, their collective performance was assessed using the generalized estimating equation (GEE) and the concept of “group diagnosis.” The GEE,17 a method for estimating the generalized linear model parameters with a possible unknown correlation between outcomes, was used to compare the sensitivity of the five glaucoma specialists’ overall assessments based on the four diagnostic sets.

Additionally, the sensitivity and specificity of the “group diagnosis” for each combination set were evaluated, and the exact binomial distribution method was used to calculate their 95% confidence interval. The group diagnosis was determined as if by “majority vote”: if, for example, three specialists diagnosed a subject as “glaucoma” and two as “healthy individual,” the group diagnosis was considered to be “glaucoma.” All of the statistical analyses were performed with Statistical Package for the Social Sciences version 21.0 for Windows (SPSS, Inc., Chicago, IL, USA) and R version 3.0.2 (http://www.R-project.org). R Foundation for Statistical Computing, Vienna, Austria) with GEE and irr packages. Statistical significance was defined as a P value less than 0.05. Bonferroni adjustment was applied for multiple comparisons of the sensitivity and specificity of specialists’ assessments.

### Results

On initial assessment, 210 open-angle glaucoma patients and 120 healthy individuals were included consecutively. The following 33 eyes of 33 subjects were excluded: 6 with unreliable SDP, 10 with unreliable RNFLP, 11 with inadequate OCT images, and 6 with unreliable SAP. This left a final sample of 196 eyes of 196 open-angle glaucoma patients and 101 eyes of 101 healthy individuals.

The baseline characteristics of the study population are summarized in Table 1. No significant differences between the perimetric or preperimetric glaucoma patient subgroup and the healthy individuals were found for age, sex, spherical equivalent, or IOP.

### Interobserver Agreement Among Glaucoma Specialists

The interobserver agreement among the five glaucoma specialists in discriminating glaucoma from healthy individuals, represented as κ for each diagnostic combination set, ranged from 0.928 for SH to 0.970 for SHRO (Table 2). Meanwhile, the agreement in discriminating the preperimetric glaucoma subgroup from healthy individuals ranged from 0.831 for SH to 0.970 for SHRO (Table 2).

Cases in which specialist consensus was lacking were mostly from the preperimetric glaucoma subgroup: 14 (31.8%) of 44 cases with SH, nine (20.5%) cases with SHO, six (13.6%) cases with SHR, and five (11.4%) cases with SHRO. Agreement in 15 preperimetric glaucoma cases changed as a result of adding OCT to SH: 10 cases from disagreement to agreement, and five cases from agreement to disagreement. Moreover, there were several cases in the healthy group for which the
specialists’ diagnoses were discordant: five (5.0%) of 101 cases by SH, two (2.0%) cases by SHO, three (3.0%) cases by SHR, and four (4.0%) cases by SHRO. Agreement in seven cases changed as the result of adding OCT to SH: five cases from disagreement to agreement, and two cases from agreement to disagreement.

Sensitivity and Specificity of Combination Sets for Each Glaucoma Specialist’s Diagnosis of Glaucoma and Preperimetric Glaucoma

Each glaucoma specialist showed a different level of glaucoma-diagnostic accuracy (sensitivity and specificity) using four combination sets (Table 3), but common findings were noted. First, adding OCT to SH or SHR increased the sensitivity but not to a level of statistical significance. Adding RNFLP to SH increased the sensitivity. However, after Bonferroni correction, it remained significant for only one specialist. Second, there was a trend of increasing sensitivity with an increasing number of diagnostic measurements, though a significant increment was found only in the comparison of SH and SHR for one specialist. The diagnostic sensitivity started from approximately 93% using SH, and reached almost 100% using all of the examinations. Third, specificity was not affected by adding any diagnostic measurements to SH.

The sensitivities were generally lower in detecting preperimetric glaucoma subgroup than in detecting glaucoma, but with all of the available diagnostic measurements, they gradually attained a level of over 90%. The specificities were almost the same regardless of the diagnostic measurement sets. In the diagnosis of preperimetric glaucoma, the increasing trend of sensitivity with the addition of diagnostic measurements was similar to that in the diagnosis of glaucoma, but with larger differences between the sets (Table 4). There was no significant increase in the sensitivity by adding SD-OCT to SH or SHR. Adding RNFLP to SH significantly increased the sensitivity in the case of only one specialist.

Comparison of Overall Sensitivity of Combination Sets for Diagnosis of Glaucoma and Preperimetric Glaucoma

The overall sensitivities of the five glaucoma specialists’ assessments using the four combination sets of diagnostic measurements were compared by GEE (Table 5). Significant increase in the sensitivity was gained by adding RNFLP (P < 0.001) or the combination of SD-OCT and RNFLP (P < 0.001) to SH. SHR, relative to SH, improved the glaucoma-diagnostic accuracy by a factor of approximately four. On the other hand, no significant differences were found in the following comparisons after Bonferroni correction: SH versus SHO (P = 0.035), SHR versus SHRO (P = 0.054), SHR versus SHO (P = 0.126). Nonetheless, the odds ratio increased when diagnostic measurements were added to SH, regardless of the type of measurement: additive OCT to SH or SHR was approximately 2-fold more likely to enhance the glaucoma-diagnostic accuracy. In detecting the preperimetric glaucoma subgroup, similar results were found for the overall sensitivity of all of the glaucoma specialists’ assessments among the diagnostic sets (Table 5). Although an approximately 2-fold increase in diagnostic accuracy was observed when adding OCT to either SH (P = 0.073) or SHR (P = 0.111), this difference was not significant. By contrast, adding RNFLP (P = 0.001) or the combination of SD-OCT and RNFLP (P < 0.001) to SH
TABLE 4. Comparison of Diagnostic Performance (Sensitivity and Specificity) of Each Glaucoma Specialist Using Four Combination Sets of Diagnostic Measurements to Discriminate Preperimetric Glaucoma Subgroup From Healthy Controls

<table>
<thead>
<tr>
<th>Glaucoma Specialist</th>
<th>SH vs. SHO</th>
<th>SH vs. SHR</th>
<th>SHO vs. SHR</th>
<th>SHR vs. SHRO</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Sensitivity (%)</td>
<td>Specificity (%)</td>
<td>Odds Ratio</td>
<td>Sensitivity (%)</td>
</tr>
<tr>
<td>1</td>
<td>72.5 vs. 81.4 (0.424)</td>
<td>72.5 vs. 86.0 (0.047)</td>
<td>81.4 vs. 86.0 (0.344)</td>
<td>86.0 vs. 93.0 (0.250)</td>
</tr>
<tr>
<td>2</td>
<td>77.3 vs. 88.4 (0.388)</td>
<td>77.3 vs. 93.0 (0.039)</td>
<td>88.4 vs. 93.0 (0.375)</td>
<td>93.0 vs. 97.7 (0.500)</td>
</tr>
<tr>
<td>3</td>
<td>81.8 vs. 95.3 (0.109)</td>
<td>81.8 vs. 97.7 (0.039)</td>
<td>95.3 vs. 97.7 (1.000)</td>
<td>97.7 vs. 97.7 (1.000)</td>
</tr>
<tr>
<td>4</td>
<td>72.5 vs. 81.4 (0.267)</td>
<td><strong>72.5 vs. 93.0 (0.006)</strong></td>
<td>81.4 vs. 93.0 (0.125)</td>
<td>93.0 vs. 95.3 (1.000)</td>
</tr>
<tr>
<td>5</td>
<td>76.5 vs. 86.0 (0.074)</td>
<td>76.5 vs. 93.0 (0.039)</td>
<td>86.0 vs. 93.0 (0.125)</td>
<td>93.0 vs. 95.3 (1.000)</td>
</tr>
</tbody>
</table>

The data in parentheses are the P values according to the McNemar test. The level of significance was set as 0.013 (0.05 divided by 4) after Bonferroni correction and significant values are in bold.

significantly enhanced the diagnostic performance of the specialists’ evaluations, approximately 5- and 9-fold, respectively.

The Figure plots the sensitivity and specificity of the group diagnosis for each combination set. These results were similar to those of each and collective specialists’ performance. A trend of increasing glaucoma- and preperimetric-glaucoma-diagnostic sensitivity with the number of diagnostic measurements was noted. Additionally, higher sensitivities were noted for glaucoma than for preperimetric glaucoma diagnosis.

DISCUSSION

Over the past few years, SD-OCT has become one of the most popular and widely used imaging devices in clinical glaucoma diagnostics. Most of previous studies have shown OCT results to be in very good agreement with conventional diagnostic modalities, which include evaluation of the optic disc (and/or RNFL) and visual field. However, current clinical diagnosis of glaucoma is still based on such conventional diagnostic tests, with OCT as an adjunct. Surprisingly, though, OCT’s additive value to glaucoma diagnostics in the clinical setting has not, at least to our knowledge, been fully investigated. This study was performed, therefore, to evaluate the potential of OCT as an additive measurement modality for improvement of the glaucoma-diagnostic accuracy. Our results showed that OCT did not significantly increase the diagnostic yield in detecting glaucoma or even preperimetric glaucoma (for which conventional diagnostic methods are limited). Hence, the present study implies that the current performance of OCT may have not yet surpassed the current practice entailing clinicians’ evaluation of conventional measurement data, emphasizing the importance of clinical interpretation and integration of optic disc, RNFL, and visual field.

Along with OCT, we examined the additive glaucoma-diagnostic role of another imaging modality, RNFLP. In our results, RNFLP showed a significant additive value in diagnosing both glaucoma and preperimetric glaucoma. In the preperimetric glaucoma subgroup, 15 (29.5%) and 9 (20.5%) of 44 cases misdiagnosed by SH and SHO, respectively, were correctly diagnosed by SHR. Moreover, there were five (11.4%) cases in which RNFL defect shown on RNFLP was not detected by OCT. Qualitative examination of RNFLP enables direct visual confirmation of the whole RNFL defect’s shape and pattern and, at the same time, of the associated glaucomatous disc change. This crucial advantage of RNFLP probably accounts for the high diagnostic performance of specialists. Optical coherence tomography–derived RNFL measurement, by contrast, is limited to the peripapillary area and cannot provide detailed visualization of concurrent corresponding disc change. However, the disadvantages of RNFLP evaluation, namely its subjectivity, the technical difficulty incurred in obtaining high-quality images, and its limited effectiveness for Caucasians, place limitations on its generalized application.

In the current study, diagnosis based on clinical structural evaluation and the visual field seemed adequate. These are in line with the finding of Deleon-Ortega et al.19 and Vessani et al.19 that the glaucoma-detection performance of the best parameter from each imaging device could not exceed that of

TABLE 5. Comparison of Overall Sensitivity of Five Glaucoma Specialists Using Four Combination Sets of Diagnostic Measurements to Discriminate Glaucoma or Preperimetric Glaucoma Subgroup From Healthy Controls

<table>
<thead>
<tr>
<th>Diagnostic Combination Sets</th>
<th>Detecting Glaucoma</th>
<th>Detecting Preperimetric Glaucoma</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Odds Ratio</td>
<td>P</td>
</tr>
<tr>
<td>SH vs. SHO</td>
<td>2.072 (1.054–4.074)</td>
<td>0.035</td>
</tr>
<tr>
<td>SH vs. SHR</td>
<td>3.938 (1.879–8.254)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SH vs. SHRO</td>
<td>8.632 (2.988–24.939)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SHO vs. SHR</td>
<td>1.901 (0.834–4.330)</td>
<td>0.126</td>
</tr>
<tr>
<td>SHO vs. SHRO</td>
<td>4.166 (1.662–10.443)</td>
<td>0.002</td>
</tr>
<tr>
<td>SHR vs. SHRO</td>
<td>2.192 (0.986–4.872)</td>
<td>0.054</td>
</tr>
</tbody>
</table>

The GEE was used to estimate the odds ratio (95% confidence interval) and P values. The level of significance was set at 0.008 (0.05 divided by 6) after Bonferroni correction, and significant values are shown in bold.
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an expert’s assessment of masked SDP. The interobserver diagnostic agreements among the specialists also were excellent, regardless of the glaucoma subtype. The agreement for the preperimetric glaucoma and healthy groups was changed by adding diagnostic measurements (OCT, RNFLP) to SH, although the difference was small. However, the level of training should not be overlooked. Vessani et al.19 reported that SDP evaluation by glaucoma experts showed performance better than or equal to the best parameter for each imaging technique, but that evaluation by general ophthalmologists did not. The major disadvantage of evaluation by SDP or RNFLP is its high dependence on the skill level of observers.18,20 Alternatively, OCT makes the quantitative and objective RNFL evaluation possible by offering various key thickness measurements. As our results are from experienced glaucoma specialists, the additive diagnostic ability of OCT should be interpreted with caution. For a more complete picture of the additive diagnostic role of SD-OCT for general ophthalmologists, further study is needed.

Our results do not indicate that OCT is not useful for glaucoma detection. Rather, it might not be the final diagnostic tool. Still, careful interpretation is needed, as our study design might have resulted in an underestimation of its additive diagnostic value. In the clinical setting, the practice can be interrupted by any of many possible distractions and/or performed under time constraints. Objective measurements and summarized results on OCT, then, would be very helpful. In any case, it is clear that OCT, in the following ways, can serve as a useful adjunct modality for supplementing subjective structural evaluation with objective data: its diagnostic classification facilitates the discrimination of glaucomatous changes from natural age-related processes,5,5 it can minimize diagnostic performance variability between physicians, and it allows for objective evaluation of patients’ follow-up status. Also, by enabling serial measurement and comparison of ONH and RNFL parameters, OCT facilitates detection of their progressive change.21,22 Moreover, the rapid development of OCT technology has served to improve our understanding of glaucoma-pathophysiological factors, such as decreased inner retinal thickness in the macula,23,24 structural change in the lamina cribrosa,25,26 and reduced optic disc perfusion.27

Diagnosing preperimetric glaucoma with only SDP and the Humphrey visual field was probably the most challenging part for all specialists, as SDP was the only evidence underpinning the diagnosis. In the preperimetric glaucoma subgroup, OCT was helpful, particularly in cases in which subtle changes were not distinguishable on photographs, by demonstrating the actual value of RNFL thickness. By adding OCT, two (4.5%) and four (9.1%) cases misdiagnosed using SH and SHR, respectively, were correctly diagnosed. Nonetheless, OCT did not significantly contribute to the preperimetric glaucoma-detection sensitivity, either. This fact is probably related to the diagnostic accuracy of OCT being influenced by the extent of glaucomatous damage.28,29 Optical coherence tomography also carries a high probability of underdiagnosis, especially in preperimetric or early glaucoma,30 regardless of its excellent overall diagnostic ability.

Our study has several limitations. First, the gold standard diagnoses made by two glaucoma specialists (KHP and KEK) and a third adjudicator (DMK) might not be perfect. However, to minimize the possibility of misdiagnosis, they were provided access to all of the available relevant information. Second, the included subjects were all Korean, whose retinal nerve fibers were clearly distinctive enough for detection of glaucomatous change from RNFLP. This could have contributed to the improved sensitivity achieved by the addition of RNFLP. Third, as the observer-participants were qualified experts, we allowed them to evaluate the OCT report based on their respective clinical experience. The differences in their own OCT-interpretation preferences made for a lack of diagnostic consistency; still, the inclusion of five glaucoma experts in this study actually lowered the chance of bias. Fourth, the ganglion cell–inner plexiform layer thickness parameters were not included in the Cirrus OCT printout. However, given that previous studies have reported a similar diagnostic ability between ganglion cell–inner plexiform layer and RNFL,25,24,31 we considered the ONH and RNFL thickness parameters to be sufficient for diagnosis. Last, the specialists were instructed to evaluate the combination sets at 1-month intervals, as masked to the previous evaluation results. However, 1 month might not have been long enough to eliminate the memory effect, which fact could have influenced the data obtained.

In conclusion, the two imaging modalities showed different additive diagnostic roles, at least for glaucoma specialists. Our study demonstrated that SD-OCT, in contrast to RNFLP, could not significantly improve the diagnostic ability of assessments made by glaucoma specialists. Although OCT is still recognized as the dominant imaging modality for the assessment of...
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Glaucoma, our results draw attention to the fundamental importance of glaucoma specialists’ clinical expertise in detecting glaucomatous change and making diagnoses. Further studies conducted with clinicians other than glaucoma specialists and under different conditions are warranted to determine the additional role of OCT for nonglaucoma experts.

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