

## **Supplemental Method 1. Definitions for healthy, glaucoma suspect, and primary open-angle glaucoma (POAG) eyes**

Healthy eyes were defined as: (1) Intraocular pressure (IOP)  $\leq$  21mmHg, without a history of elevated IOP; (2) normal-appearing optic discs with intact neuroretinal rims and retinal nerve fiber layer (RNFL); (3) normal visual field (VF) test, defined as pattern standard deviation (PSD) within the 95% confidence limits and glaucoma hemifield test (GHT) results within normal limits. Glaucoma suspect was defined as having elevated IOP ( $\geq$  22 mm Hg) or a suspicious-appearing optic disc without repeatable glaucomatous VF damage. POAG was defined as the presence of repeatable ( $\geq$ 2 consecutive tests) and reliable abnormal VF results (fixation losses and false negatives  $\leq$ 33% and false positives  $\leq$ 15%) using the 24-2 Swedish Interactive Thresholding Algorithm (SITA) with either a PSD outside the 95% normal limits or a GHT result outside the 99% normal limit.

## **Supplemental Method 2. Examinations performed in Diagnostic Innovations in Glaucoma Study (DIGS)**

All DIGS participants underwent the following examinations: (1) annual comprehensive ophthalmic examination in both eyes with best-corrected visual acuity (BCVA), dilated fundus examination, slit-lamp biomicroscopy, and stereoscopic optic disc photography; (2) semi-annual examination of VF, intraocular pressure measurement (Goldmann applanation tonometry), and optical coherence tomography (OCT)/OCT angiography imaging; (3) gonioscopy and ultrasound pachymetry at the first visit.

### **Supplemental Method 3. Exclusion criteria for poor-quality optical coherence tomography angiography (OCTA) image**

An OCTA image was considered of poor quality and excluded if any of the following was present: (1) low scan quality < 4; (2) image cropping or local weak signal; (3) residual motion artifacts visible as irregular vessel pattern on the en-face angiogram; (4) poor clarity; (5) off-centered fovea; (6) uncorrectable severe segmentation errors.

#### **Supplemental Method 4. Definitions for event-based and trend-based glaucomatous visual field (VF) progression**

Event-based analysis was performed using the Guided Progression Analysis (GPA) software from the Humphrey Field Analyzer, which identified “likely progression” and “possible progression” when  $\geq 3$  test points on VF showed changes exceeding variability limits expected based on two and three consecutive baseline VF measurements, respectively. Trend-based analysis uses linear regression analysis to estimate the rate of VF change, and defines VF progression when a significantly negative slope ( $p < 0.05$ ) was observed.

## **Supplemental Method 5. Detailed description of metrics demonstrating long-term variability**

Intraclass correlation coefficient (ICC) represents the variability of a parameter for a subject group based on the between-subject variance divided by total random effect and error variation, with a value  $> 0.7$  usually considered acceptable. Within-subject test-retest standard deviation (Sw) is the square root of the within-subject mean square for error in a mixed-effects model, representing the component of variance due to random error. Root mean squared error (RMSE) captures the precision of a parameter by calculating the differences between the actual measurements obtained and the values predicted by estimation. As compared to ICC, CV, and Sw, RMSE can better consider the glaucomatous and age-related change of clinical measurements in longer follow-up. Therefore, ICC, CV, and Sw are only calculated for a stable eye cohort with limited follow-up in this study, while RMSE was also calculated in the extended cohort with unlimited follow-up.

| <b>Supplemental Table 1. CV (%) of VF and OCT/OCTA parameters in the stable eye cohort</b>  |        |             |      |              |      |
|---|--------|-------------|------|--------------|------|
| <b>24-2 VF</b>  |        | <b>OCTA</b> |      | <b>OCT</b>   |      |
| <b>MD</b>   | -34.75 | <b>wiVD</b> | 3.31 | <b>wiGCC</b> | 0.83 |
| <b>PSD</b>  | 14.74  | <b>pfVD</b> | 3.38 | <b>pfGCC</b> | 0.76 |
| Abbreviations: CV = coefficient of variation; MD = mean deviation; OCT = optical coherence tomography; OCTA = optical coherence tomography angiography; pfGCC = parafoveal ganglion cell complex; pfVD = parafoveal vessel density; PSD = pattern standard deviation; VF = visual field; wiGCC = whole-image ganglion cell complex; wiVD = whole-image vessel density |        |             |      |              |      |

| <b>Supplemental Table 2. Main effect of age, CCT, and IOP on the variability of VF and OCT/OCTA parameters in the stable eye cohort</b>   |                               |                           |                |
|---|-------------------------------|---------------------------|----------------|
|   | <b>β Coefficient (95% CI)</b> | <b>R-squared (95% CI)</b> | <b>P-value</b> |
| <b>VF MD</b>  |                               |                           |                |
| Age   | 0.00 (-0.06, 0.07)            | 0.00 (0.00, 0.02)         | 0.934          |
| CCT   | -0.01 (-0.03, 0.01)           | 0.03 (0.01, 0.08)         | 0.436          |
| IOP   | -0.08 (-0.27, 0.12)           | 0.03 (0.00, 0.07)         | 0.440          |
| <b>VF PSD</b>   |                               |                           |                |
| Age   | 0.02 (-0.04, 0.09)            | 0.02 (0.00, 0.06)         | 0.604          |
| CCT   | 0.00 (-0.02, 0.02)            | 0.01 (0.00, 0.03)         | 0.777          |
| IOP   | 0.10 (-0.07, 0.28)            | 0.07 (0.03, 0.13)         | 0.261          |
| <b>wiVD</b>   |                               |                           |                |
| Age   | 0.13 (0.05, 0.21)             | 0.25 (0.17, 0.33)         | <b>0.002</b>   |
| CCT   | -0.03 (-0.06, -0.00)          | 0.14 (0.08, 0.22)         | <b>0.033</b>   |
| IOP   | -0.01 (-0.24, 0.23)           | 0.00 (0.00, 0.02)         | 0.937          |
| <b>pfVD</b>   |                               |                           |                |
| Age   | 0.13 (0.05, 0.21)             | 0.22 (0.15, 0.30)         | <b>0.002</b>   |
| CCT   | -0.03 (-0.06, -0.00)          | 0.12 (0.06, 0.20)         | <b>0.042</b>   |
| IOP   | -0.00 (-0.25, 0.24)           | 0.00 (0.00, 0.02)         | 0.980          |
| <b>wiGCC</b>  |                               |                           |                |
| Age   | 0.25 (0.03, 0.48)             | 0.61 (0.54, 0.66)         | <b>0.032</b>   |
| CCT   | -0.09 (-0.17, -0.02)          | 0.66 (0.60, 0.71)         | <b>0.020</b>   |
| IOP   | -0.11 (-0.77, 0.55)           | 0.03 (0.00, 0.08)         | 0.741          |
| <b>pfGCC</b>  |                               |                           |                |
| Age   | 0.28 (0.04, 0.53)             | 0.64 (0.59, 0.70)         | <b>0.028</b>   |
| CCT   | -0.10 (-0.18, -0.02)          | 0.69 (0.63, 0.73)         | <b>0.020</b>   |
| IOP   | -0.15 (-0.87, 0.56)           | 0.05 (0.01, 0.11)         | 0.673          |
| <p>*Values are shown in β coefficient (95% CI).<br/> **Statistically significant p value is shown in bold.<br/> Abbreviations: CCT = central corneal thickness; IOP = intraocular pressure; MD = mean deviation; OCT = optical coherence tomography; OCTA = optical coherence tomography angiography; pfGCC = parafoveal ganglion cell complex; pfVD = parafoveal vessel density; PSD = pattern standard deviation; VF = visual field; wiGCC = whole-image ganglion cell complex; wiVD = whole-image vessel density</p> |                               |                           |                |

| <b>Supplemental Table 3. Main effect of age, CCT, and IOP on the variability of VF and OCT/OCTA parameters in the extended cohort including all eyes</b>  |                               |                           |                  |
|---|-------------------------------|---------------------------|------------------|
|   | <b>β Coefficient (95% CI)</b> | <b>R-squared (95% CI)</b> | <b>P-value</b>   |
| <b>VF MD</b>  |                               |                           |                  |
| Age   | -0.01 (-0.07, 0.06)           | 0.00 (0.00, 0.01)         | 0.825            |
| CCT   | -0.00 (-0.02, 0.01)           | 0.01 (0.00, 0.02)         | 0.625            |
| IOP   | -0.33 (-0.48, -0.17)          | 0.35 (0.31, 0.39)         | <b>&lt;0.001</b> |
| <b>VF PSD</b>   |                               |                           |                  |
| Age   | 0.01 (-0.03, 0.06)            | 0.01 (0.00, 0.02)         | 0.622            |
| CCT   | 0.01 (-0.01, 0.02)            | 0.04 (0.02, 0.07)         | 0.282            |
| IOP   | 0.29 (0.18, 0.41)             | 0.44 (0.40, 0.48)         | <b>&lt;0.001</b> |
| <b>wiVD</b>   |                               |                           |                  |
| Age   | 0.12 (0.07, 0.18)             | 0.14 (0.10, 0.18)         | <b>&lt;0.001</b> |
| CCT   | -0.01 (-0.03, 0.01)           | 0.01 (0.00, 0.03)         | 0.222            |
| IOP   | -0.14 (-0.27, -0.00)          | 0.02 (0.01, 0.04)         | <b>0.048</b>     |
| <b>pfVD</b>   |                               |                           |                  |
| Age   | 0.13 (0.07, 0.19)             | 0.14 (0.11, 0.18)         | <b>&lt;0.001</b> |
| CCT   | -0.01 (-0.03, 0.01)           | 0.01 (0.00, 0.03)         | 0.260            |
| IOP   | -0.17 (-0.31, -0.03)          | 0.03 (0.02, 0.06)         | <b>0.022</b>     |
| <b>wiGCC</b>  |                               |                           |                  |
| Age   | 0.14 (-0.04, 0.32)            | 0.14 (0.11, 0.18)         | 0.126            |
| CCT   | -0.03 (-0.08, 0.02)           | 0.07 (0.04, 0.10)         | 0.306            |
| IOP   | -0.36 (-0.77, 0.05)           | 0.12 (0.09, 0.16)         | 0.086            |
| <b>pfGCC</b>  |                               |                           |                  |
| Age   | 0.17 (-0.03, 0.36)            | 0.18 (0.14, 0.22)         | 0.093            |
| CCT   | -0.03 (-0.09, 0.02)           | 0.09 (0.06, 0.12)         | 0.269            |
| IOP   | -0.44 (-0.88, 0.01)           | 0.16 (0.12, 0.19)         | 0.057            |
| *Values are shown in β coefficient (95% CI).  |                               |                           |                  |
| **Statistically significant p value is shown in bold.   |                               |                           |                  |
| Abbreviations: CCT = central corneal thickness; IOP = intraocular pressure; MD = mean deviation; OCT = optical coherence tomography; OCTA = optical coherence tomography angiography; pfGCC = parafoveal ganglion cell complex; pfVD = parafoveal vessel density; PSD = pattern standard deviation; VF = visual field; wiGCC = whole-image ganglion cell complex; wiVD = whole-image vessel density |                               |                           |                  |



**Supplemental Table 4. Long-term TRV of sectoral OCT and OCTA parameters**

| <b>OCT</b>         |                               | <b>OCTA</b>        |               |
|--------------------|-------------------------------|--------------------|---------------|
| <b>wiGCC</b>       | <b>TRV(<math>\mu</math>m)</b> | <b>wiVD</b>        | <b>TRV(%)</b> |
| Superior hemifield | 2.38                          | Superior hemifield | 4.22          |
| Inferior hemifield | 2.27                          | Inferior hemifield | 4.43          |
| <b>pfGCC</b>       |                               | <b>pfVD</b>        |               |
| Temporal sector    | 2.04                          | Temporal sector    | 4.49          |
| Superior sector    | 2.71                          | Superior sector    | 5.25          |
| Nasal sector       | 2.61                          | Nasal sector       | 4.97          |
| Inferior sector    | 2.75                          | Inferior sector    | 5.65          |

Abbreviations: OCT = optical coherence tomography; OCTA = optical coherence tomography angiography; pfGCC =parafoveal ganglion cell complex; pfVD = parafoveal vessel density; TRV = test-retest variability; wiGCC = whole-image ganglion cell complex; wiVD = whole-image vessel density