Supplementary materials

Short-term parafoveal cone loss despite preserved ellipsoid zone in rod cone dystrophy

Danial Roshandel, MD, Rachael C. Heath Jeffery, MChD, Jason Charng, BOptom, PhD, Danuta M. Sampson, PhD, Samuel McLenachan, PhD, David A. Mackey, MD, FRANZCO, Fred K. Chen, MBBS (Hons), PhD, FRANZCO

Table S1. Intra-session coefficient of repeatability of inter-cone distance in the control and patient groups.

Table S2. Individual baseline and follow-up inter-cone distance in the patient group.

Figure S1. Printout of the AODetect software showing examples of cone marking, segmentation, and mosaic parameters.

Figure S2. Patient enrolment flow chart.

Figure S3. Ultra-widefield autofluorescence imaging of the right eyes of the eight patients.

Figure S4. Examples of the images excluded from the statistical analysis due to inadequate quality.

Figure S5. Bland-Altman plot showing inter-session test-retest difference against mean cone density and inter-cone distance.
Table S1. Mean, standard deviation (SD) and range of inter-cone distance (ICD) and intra-session coefficient of repeatability (CoR) in control and patient groups in angular and metric units.

|                     | Control (n = 10) | Patient (n = 8) |
|---------------------|------------------|-----------------|
|                     | Baseline         | 6-month         |
| Mean ICD* arcmin (µm) |                  |                 |
| Mean                | 1.47 (7.16)      | 1.67 (8.01)     | 1.80 (8.64) |
| SD                  | 0.06 (0.47)      | 0.24 (1.49)     | 0.32 (1.93) |
| Min                 | 1.38 (6.53)      | 1.39 (6.62)     | 1.44 (6.93) |
| Max                 | 1.53 (7.80)      | 1.94 (10.62)    | 2.27 (11.66) |
| Test-retest difference* arcmin (µm) |                  |                 |
| Mean                | -0.01 (-0.06)    | -0.05 (-0.25)   | -0.08 (-0.37) |
| SD                  | 0.04 (0.18)      | 0.15 (0.70)     | 0.31 (1.53) |
| Min                 | -0.07 (-0.33)    | -0.38 (-1.83)   | -0.78 (-3.76) |
| Max                 | 0.04 (0.19)      | 0.06 (0.29)     | 0.27 (1.53) |
| CoR arcmin (µm)     |                  |                 |
| ±0.01 (±0.05)       | ±0.05 (±0.24)    | ±0.10 (±0.51)   |

* Measurement using the two tiles with the lowest ICD.

arcmin = minutes of arc; ICD = inter-cone distance; CI = confidence interval; CoR = coefficient of repeatability; SD = standard deviation.
Table S2. Individual baseline and follow-up inter-cone distance (ICD) in the patient group.

| ID | Baseline ICD (µm) | 6 months ICD (µm) | Change | Relative change (%) |
|----|-------------------|-------------------|--------|---------------------|
| 1  | 1.37 (6.73)       | 1.44 (7.07)       | 0.07 (0.34) | 5.1 (5.1)           |
| 2  | 1.52 (6.82)       | 1.58 (7.13)       | 0.06 (0.31) | 3.9 (4.5)           |
| 3  | 1.87 (8.14)       | 1.87 (8.13)       | 0.00 (-0.01)| 0.0 (-0.1)          |
| 4  | 1.66 (8.04)       | 1.88 (9.11)       | 0.22 (1.07) | 13.2 (13.3)         |
| 5  | 1.87 (10.55)      | 1.93 (10.98)      | 0.06 (0.43) | 3.2 (4.1)           |
| 6  | 1.88 (8.96)       | 2.07 (9.86)       | 0.19 (0.90) | 10.1 (10.0)         |
| 7  | 1.36 (6.50)       | 1.45 (6.92)       | 0.09 (0.42) | 6.6 (6.5)           |
| 8  | 1.46 (6.56)       | 1.49 (6.68)       | 0.03 (0.12) | 2.1 (1.8)           |

|    | Mean ICD (µm)    | Mean Relative change (%) |
|----|-----------------|--------------------------|
|    | 1.62 (7.79)     | 5.5 (5.6)                |
| SD | 0.23 (1.43)     | 4.4 (4.3)                |

* Lowest ICD among the 4 overlapping tiles.

† Statistically significant compared with baseline (paired samples t-test P<0.05).

arcmin = minutes of arc; ICD = cone density; SD = standard deviation.
**Figure S1.** Printout of the AODetect software version 3.0 (A) showing results of the analyses performed on the region of interest (ROI) on 4 overlapping tiles covering the ROI (marked as Tile 1-4). Cones were marked either automatically (red) or manually (green) (B) and segmentation was performed by the software (C). Cone mosaic parameters (including cone density) in the 4 tiles are reported in angular (D) and metric (E) units. Panels B-E show the enlarged view and results of the Tile 1 in panel A.
Figure S2. Patient enrolment flow chart.

220 inherited retinal diseases

67 other retinal dystrophies*

153 rod cone dystrophy

122 one or more exclusion criteria
- Pseudophakia
- Significant cataract
- Severe CMO/ERM
- Low vision/poor fixation
- Advanced atrophy

17 no follow-up AO imaging

6 follow-up interval > 6 m

8 enrolled in final analysis

*Including cone dystrophy, cone rod dystrophy, X-linked female carrier, choroideremia, syndromic RP, pericentral RP, pigmented paravenous chorioretinal atrophy, sectoral RP, unilateral RP.
**Figure S3.** Ultra-widefield autofluorescence imaging in the right eye of 8 patients with rod cone dystrophy (RCD). A macular hyper-autofluorescent ring was observed in all patients, except patient 1 (A) and patient 4 (D).
**Figure S4.** Tiles with inadequate image quality at the location of the region of interest (ROI) compared to a tile with good image quality at the same ROI. Yellow boxes represent the sampling window.
**Figure S5.** Bland-Altman plot shows no relationship between the inter-session test-retest difference and mean values for both cone density (CD; A) and inter-cone distance (ICD; B).