A novel method for the analysis of a Dissociated Optic Nerve Fibre Layer appearance

Antonio Rivera Real (1)
(Final Year Medical Student, a.rivera-real@newcastle.ac.uk),
Professor David HW Steel (1)(2) .
(1) Newcastle University, Faculty of Medical Sciences, Newcastle upon Tyne, NE1 7RU
(2) Sunderland Eye Infirmary, Sunderland, SR2 9HP

NHS South Tyneside and Sunderland NHS Foundation Trust

Background

- Peeling of the Internal Limiting Membrane (ILM) in Macular Hole (MH) surgery significantly improves visual outcomes by aiding hole closure. However, the procedure is known to have consequential effects on inner retinal anatomy including the appearance of a **Dissociated Optic Nerve Fibre Layer** (DONFL) within the surgical peel area [1]

Aim

- To develop a **novel method** for the measurement of DONFL

Method

- Images and measurements were taken from a database of 65 patients enrolled in the PRECISE study; a pilot randomised masked interventional study in the North of England.
- Baseline patient demographics included: age; sex; duration of MH; minimum linear diameter of MH.
- Posterior pole scans were performed three and six months post-MH surgery, 3D view transverse en-face images were produced that were then selected onto the ILM layer [**Figure 1**]. These were uploaded to ImageJ [2]. The six-month ILM surgical peel outline was traced to measure its area, perimeter and diameter. A circle of diameter 1000µm with the centre at the fovea was cleared to represent the natural depression of the fovea [**Figure 2**].
- The area within this circle and outside the ILM surgical peel was cleared and the automatic thresholding algorithm 'MaxEntropy' was then applied to remaining area [**Figure 3**]. The ImageJ plug-in 'MorphoLibJ' performed spatial organisation and mathematically removed defects of a small size in a non-biased and robust manner [**Figure 4**] [3]. The analyse particles function was used to obtain objective and quantifiable measurements of: DONFL count; total DONFL area; percentage of DONFL area within ILM peel outline; mean DONFL defect area and diameter.

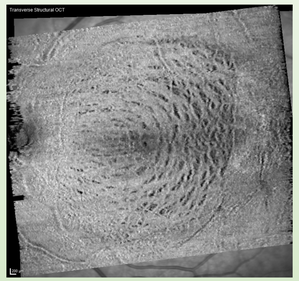


Figure 1: Posterior Pole OCT scan of study eye SUN010

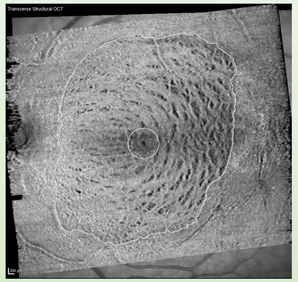


Figure 2: Surgical ILM peel and foveal outline of study eye SUN010

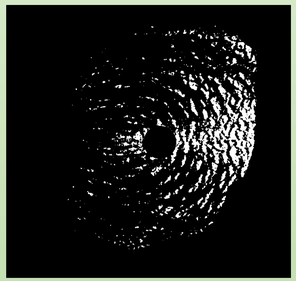


Figure 3: MaxEntropy of study eye SUN010

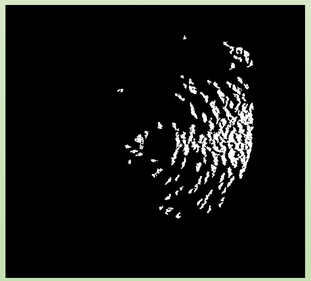


Figure 4: Morphological Reconstruction of study eye SUN010

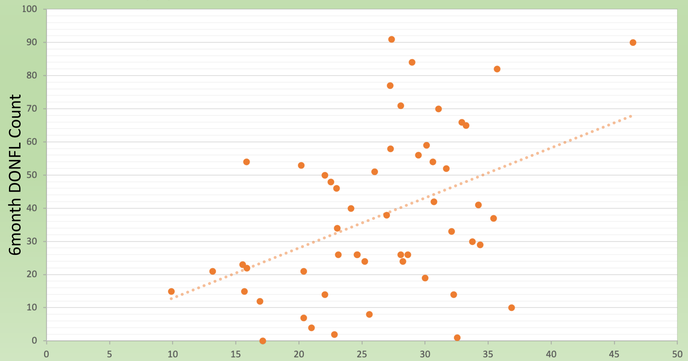


Figure 5: Scatter graph of every patients 6month ILM Peel Area (mm^2)

Results

- Mean six-month ILM peel area was 26.311mm^2 and diameter at 5.397-6.563mm. Standard disk area was calculated to be 10.034 with standard disk diameter at 2.998-3.646.
- **Median number of DONFL lesions** at three months was **30 defects** (22, 1-102) compared to a mean of **36.2 defects** at six months (23.8, 0-91); t(36)=0.662, p=0.512.
- Mean total DONFL area was 5.168mm^2 and 5.263mm^2 at three and six months respectively; t(36)=0.124, p=0.902 **[Figure 6].**
- The **median percentage coverage of DONFL defects within the ILM peel area** at three months was **19.70% and 20.35%** at six months; Z=-0.143, p=0.891.
- There was no significant difference in the mean DONFL area or diameter for individual defects at three and six months.
- A pearson correlation coefficient found a strong relationship between the number of DONFL defects and six-month ILM peel area (r=0.433, **p=0.001)[Figure 5]** and **diameter** (r=0.427, **p=0.001**). The change in number of DONFL defects from three to six months was not significantly correlated with ILM peel metrics.
- The change in DONFL over time was not significantly correlated with age (r=0.259, p=0.122), minimum linear diameter of the MH (r=0.280, p=0.121) or duration of the MH (r=0.122, p=0.480).

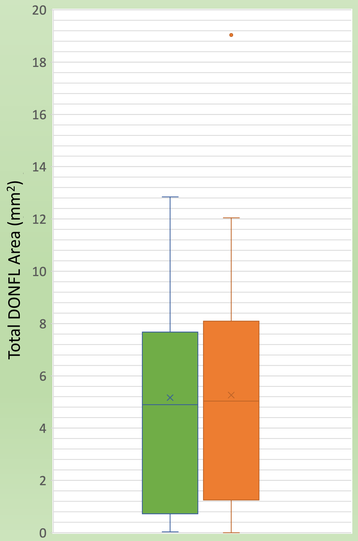


Figure 6: Box and whisker plot of total DONFL area at 3months (green) and 6months (orange)

Discussion

- The extent of **DONFL did not appear to change over time**, this was in line with existing literature which states that once established, the size of lesions do not increase over time [4].
- The **mean number of DONFL lesions was ~36** and the **median percentage of DONFL coverage within the ILM surgical peel outline was ~20%.** The latter metric is particularly useful as it provides a clear indication to the extent of DONFL coverage.
- The **strong association between number of DONFL lesions and ILM peel metrics** is in line with existing literature and further supports the hypothesis that DONFL is not due to instrument trauma, instead being caused by widespread damage to Muller cells from the peeling process [5].
- There were **clearly some mistakes in the thresholding technique**, as evidenced by some patients have a result of 0% DONFL coverage and others having 90% coverage. It should be noted that ANOVA and Brown-Forsythe analysis showed that these outliers on both extremes did not disproportionally distort the sample.

Conclusion

- The use of ImageJ and MaxEntropy to quantitatively identify the extent of DONFL presence was a **success though further improvement in the method is possible** and this should be investigated, potentially by using ILM-RNFL posterior pole slabs.

References

[1] Tadayoni R, Paques M, Massin P, Mouki-Benani S, Mikol J, Gaudric A. Dissociated optic nerve fiber layer appearance of the fundus after idiopathic epiretinal membrane removal. Ophthalmology. 2001;108(12):2279-83.
[2] Schindelin J, Arganda-Carreras I, Frise E, Kaynig V, Longair M, Pietzsch T, et al. Fiji: an open-source platform for biological-image analysis. Nat Methods. 2012;9(7):676-82.
[3] Legland D, Arganda-Carreras I, Andrey P. MorphoLibJ: integrated library and plugins for mathematical morphology with ImageJ. Bioinformatics. 2016;32(22):3532-4.
[4] Alkabes M, Salinas C, Vitale L, Bures-Jelstrup A, Nucci P, Mateo C. En face optical coherence tomography of inner retinal defects after internal limiting membrane peeling for idiopathic macular hole. Invest Ophthalmol Vis Sci. 2011;52(11):8349-55.
[5] Spaide RF. "Dissociated optic nerve fiber layer appearance" after internal limiting membrane removal is inner retinal dimpling. Retina. 2012;32(9):1719-26.