Abnormal retinal apoptosis morphometry in glaucoma and optic neuritis

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1. Introduction

Novai Ltd, a UK-based biotechnology company, has developed DARC technology (figure 1) for **in vivo detection** and localization of **dying** (apoptosis) and **stressed cells** in the **retina.** DARC uses a proprietary fluorescently labelled Annexin A5 biologic, near-infrared autofluorescence (NIRAF) imaging, and state-of-the-art AI to accurately identify these dying and stressed cells; an important early indication of disease activity in glaucoma, AMD, and central nervous system diseases [1].

DARC is currently being used as an exploratory biomarker in clinical trials (pre-clinical -> phase 2b).

Thus far, we have explored image characteristics at a global level by looking at measures such as total spot count, spatial distribution, and density [2]. Here, we **investigate local characteristics** at the **individual spot level**. Different diseases may have different DARC spot features. This can lead to a **more holistic overview of eye health** and a subsequent earlier-stage diagnosis.

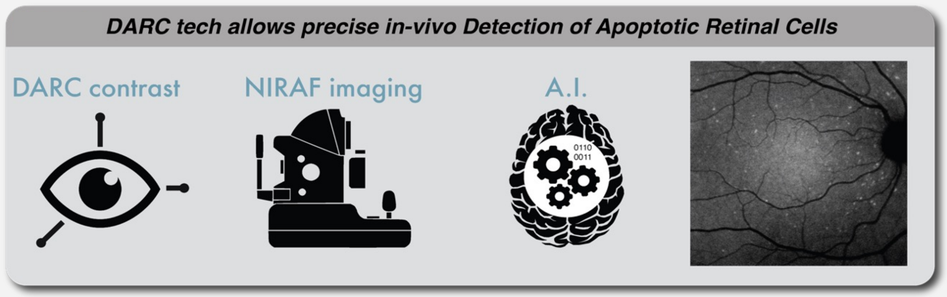
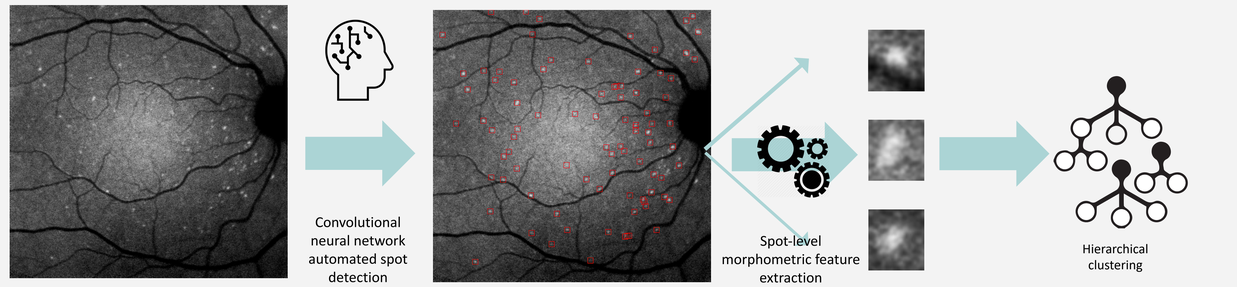


Figure 1. Novai's DARC technology - **D**etection of **A**poptosing **R**etinal **C**ells. Bright 'spots' in the right-hand image highlight regions of disease activity.

2. Methods

DARC NIRAF retinal imaging was conducted in healthy adults (N=36, mean age=45.97, SD=16.81) and in patients with glaucoma (N=20, mean age=61.74, SD=13.11) or multiple sclerosis (MS) optic neuritis (N=12, mean age=44.47, SD=10.82). DARC spots were automatically detected using a previously described A.I. algorithm [3].

For each DARC spot, hysteresis thresholding was applied to identify a perimeter from which a set of morphometrics were extracted (e.g., spot area, eccentricity, etc.). Data-driven hierarchical clustering of the morphometrics generated distinct populations of DARC spots that were then compared between the healthy and patient groups with a two-way chi-square test. Data analysis was performed in python.



3. Results

Hierarchical agglomerative clustering of DARC spot morphometry (Figure 2a) indicated 3 distinct DARC spot types (C0: Small regular, C1: Irregular, C2: Large regular – Figure 1b). The most common DARC spot type in each eye (Figure 1c) significantly differed between the groups (two-way chi2: 13.312, p=0.038). The most common spot type in al eyes was cluster 1. No spots from cluster 0 were found in eyes with optic neuritis.

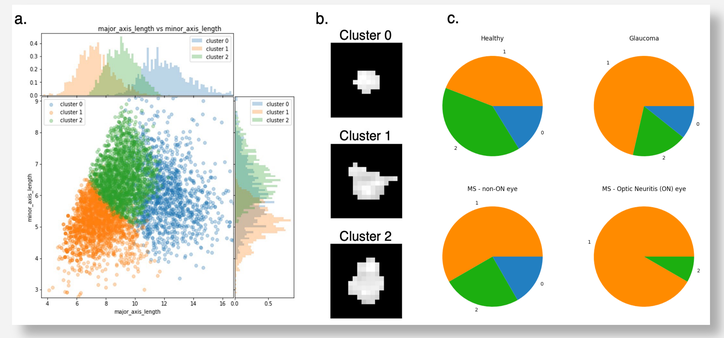


Figure 2. DARC spot morphometry differs between healthy & patient groups**.** a) Major vs minor DARC spot axis length labelled by hierarchically identified clusters. b) Example DARC spots types c) Proportions of most frequent DARC spot type within each group.

4. Conclusions

This investigation presents evidence indicating that **distinct** types of **DARC spots** can be **observed in vivo**. An increased proportion of irregularly shaped DARC spots was associated with Glaucoma and ON. ON also displayed no small round spots. While this is suggestive of distinct cellular processes, we are conducting further preclinical and histological work to confirm the validity of these in vivo findings.

5. References

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3. Normando, Eduardo et al. "A CNN-aided method to predict glaucoma progression using DARC (Detection of Apoptosing Retinal Cells)" *Expert Review of Molecular Diagnostics* (2020)

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