Characterising DARC (Detecting Apoptosing Retinal Cells) spots in Optic Neuritis (ON) and healthy eyes

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1. Introduction:

ON:

Ocular manifestation of MS

Common initial symptom of MS (around 25%) [1]

Symptomatic and asymptomatic ON could occur in up to 90% of MS patients during disease [1]

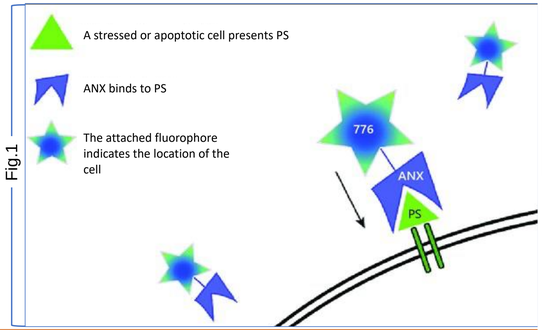
DARC Technology:

Fluorescent labelled DARC molecule binds to externalized phosphatidylserine (PS) on the membranes of cells in initial stages of cell stress or apoptosis [2] (Fig.1)

Confocal scanning laser ophthalmoscope used to image the eye live to visualise apoptosing cells as fluorescent white spots

Here we analyse the DARC spots identified using the CNN previously described [3-5] from the Phase 2 DARC clinical trial (ISRCTN10751859)

Fig.1



Key Question:

Are there differences in morphological parameters of DARC spots in healthy and ON subjects?

2. Methods:

DARC images

obtained from ON eyes (n=12) and healthy volunteers (n=68). Fig.2(A)

SCAN ME

DARC spot count

previously developed convolutional neural network - algorithm [3-5]. Fig.2(A)

Descriptive measures (DMs)

per DARC spot defined by shape/intensity characteristics [6-8]

13 DMs were obtained and analysed per spot. Fig.2(B,C)

Statistical analyses

t-tests, Kolmogorov-Smirnov tests performed (R studio) to answer our key question

Fig. 2 (A)

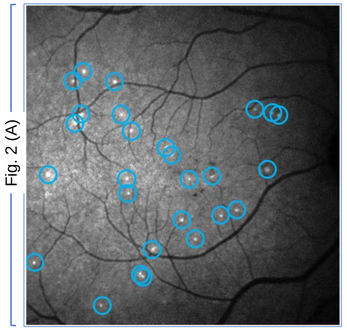
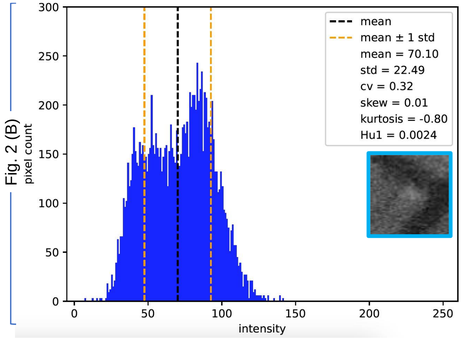


Fig. 2 (B)



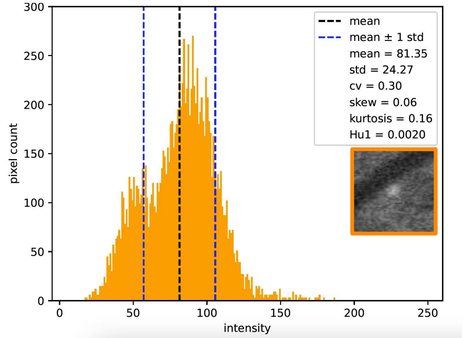


Fig. 2 (C)

Mean: Average pixel intensity of a spot [9]

Standard deviation (Std): Variation of the means [9]

Coefficient of variant (CV): A measure of relative variability (Std/mean) [10]

Skew: Symmetry of histogram [9]

Kurtosis: Flatness of the histogram [9]

Hu moments: moments invariant to translation, scale, rotation and reflection [6,7]

Figure.2
DARC image (A) with automatically identified DARC spots (blue circles, A). DMs obtained from histograms (B) of pixel intensities per spot (insert images, B). Blue = healthy. Orange = ON. Definitions of DMs (C).

3. Results:

Table.1

Descriptive Measure	Mean	CV	Kurtosis	Hu1	Std
T-test (Healthy *vs* ON)	**** p≤0.0001	****p≤ 0.0001	**** p≤0.0001	*** p≤0.001	*** p≤0.001
KS-test (Healthy *vs* ON)	**** p≤0.0001	**** p≤0.0001	**** p≤0.0001	**** p≤0.0001	**** p≤0.0001

Table.1
Significant differences between healthy and ON DARC spot DMs: mean, cv and kurtosis ($p \leq 0.0001$) hu1 and std ($p \leq 0.001$) using t - test and KS -test distributions for the same DMs ($p \leq 0.0001$).

4. Conclusions:

Key message:
These preliminary results suggest that there are differences in morphological parameters between ON and healthy DARC spots. This highlights the potential of DARC as a diagnostic tool in ON.

Future implications:
Further work is needed and more data on definitively differentiating ON disease from health for which we plan to use artifical intelligence (AI) to investigate spatial patterns and morphological characteristics to enable further analysis in future, planned clinical trials. Until now, a CNN has only been used to identify DARC labelling.

5. References:

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