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AUTOMATIC CORNEAL DENDRITIC CELL DENSITY & MORPHOLOGY EVALUATION IN CONFOCAL MICROSCOPY IMAGES USING DEEP LEARNING

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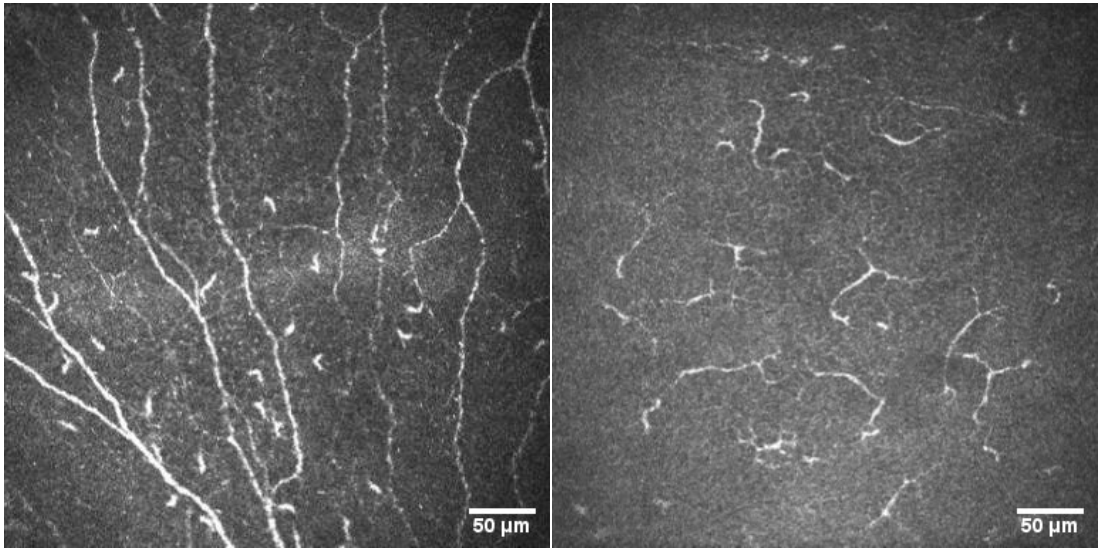
Motivation & Purpose

- Dendritic cells (DCs) are distributed throughout the cornea, reflecting the inflammatory state of ocular surface disease
- In Vivo Confocal Microscopy (IVCM) provides high resolution images of corneal dendritic cells
- To analyze DC numbers, density, size, and to differentiate immature from mature DCs manual grading techniques are available
- Semi-quantitative analysis of DCs in numerous images/patient is time consuming, non-reproducible, and a laborious task



Corneal Confocal microscopy images, Prof. Philipp Steven

Aim: To develop a convolutional neural network-based automatic segmentation and quantification system for DCs in IVCM images

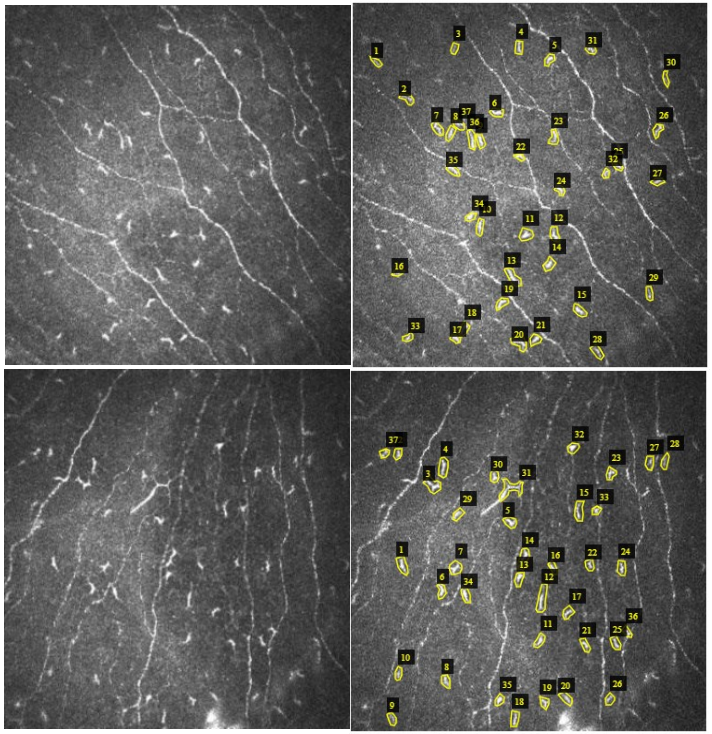
1. Hamrah et al. 2003 J Leukoc Biol; 2. Moein at al. 2020 Ocul Surf; 3. Benitez et al. 2004 Investig Ophthalmol Vis Sci

Methods (Data collection & Ground truth)

- A total 754 clinical images were collected from patients with dry-eye disease, diabetes, and corneal neuropathic pain syndrome
- Confocal microscopy was performed using a Heidelberg Retina Tomograph (HRT3) with Rostock Cornea Module (RCM)

HRT3-RCM,
Heidelberg Engineering GmbH

Original image | Ground truth masks



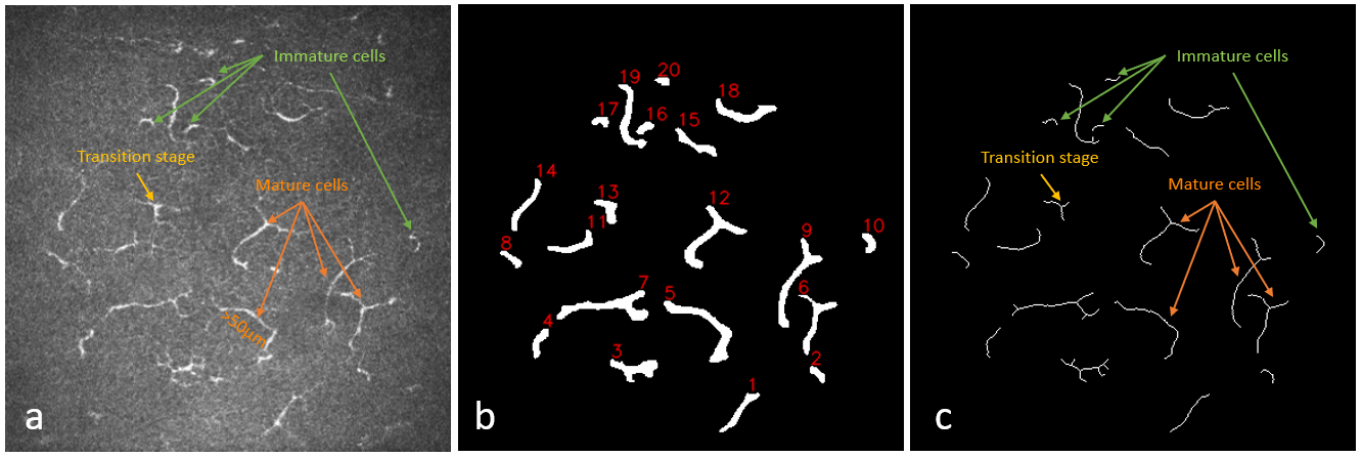
Manual annotation of the DC

- All DCs were manually annotated and verified by an experienced ophthalmologist before model training and testing
- Data augmentation was used to increased number of training images
- Among the 754 images, 654 images were used for training while 100 images were used for testing

Methods (Morphometric parameter assessment)

- DC size calculation: total area of cell body and dendrites, reported as μm^2
- Stratification parameters for immature, transition stage, and mature DCs: total cell length and presence of dendrites were
- Calculation of cell length and dendrites: Skeletonization of binary segmented image

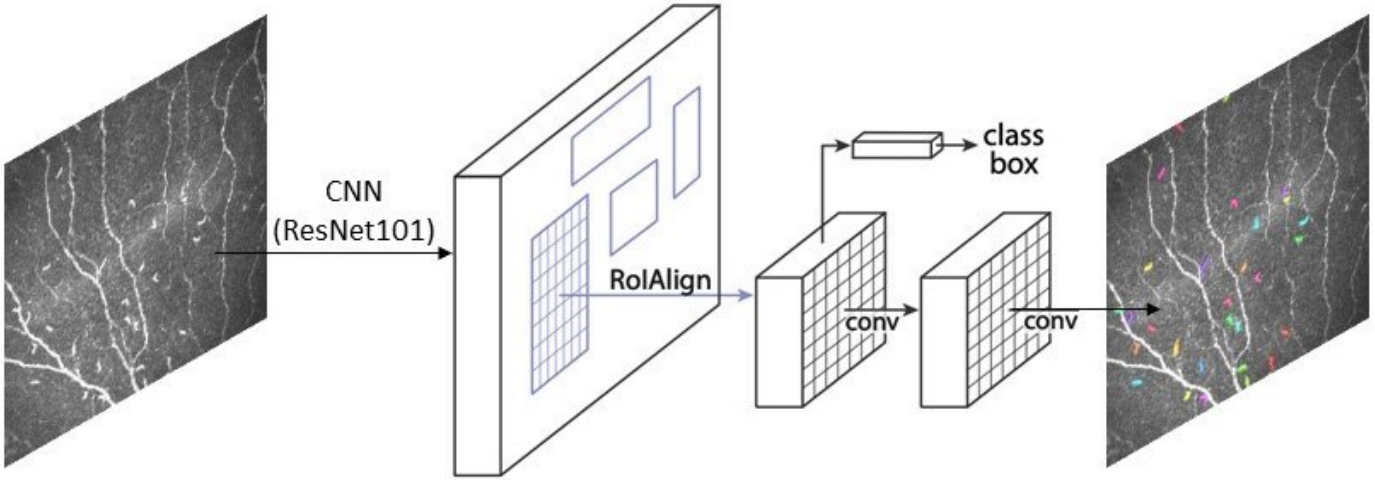
Cell types	Presence of dendrites	Cell length threshold
Immature	**No**	**< 50 µm**
Transition-stage	**Yes**	**< 50 µm**
Mature	**Yes / No**	**> 50 µm**



Morphometric parameter assessment. (a) original image, (b) Binary segmentation with cell identification number, and (c) Skeletonized image (one pixel width)

1. Zhivov et al. 2005 Graefe's Arch Clin Exp; 2. Ferdousi et al. 2019 Sci Rep; 3. Khan et al. 2021 Transl Vis Sci Technol

Methods (Deep learning model design & Training)

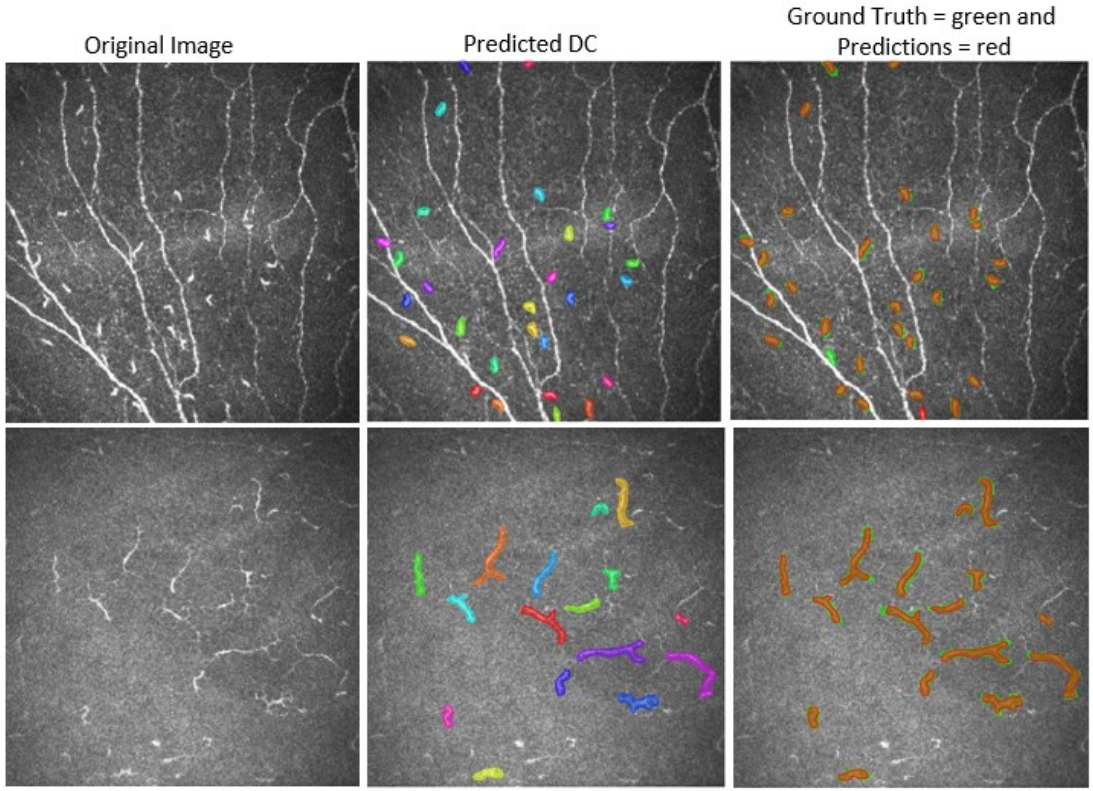


MASK R-CNN architecture

- The convolutional neural network (CNN) was developed based on a region-based instance segmentation architecture, MASK R-CNN
- The two step CNN process of MASK R-CNN enables more precise object localization than the typical one step CNN process of U-Net architecture
- MASK R-CNN has the potential to identify objects more accurately than U-Net even in the conjugate cells

1. He at al. 2017 IEEE Int Conf Comput Vis; 2. Luola et al 2019 IEEE Proc Int Symp Biomed Imaging

Results (Deep learning model training performance)

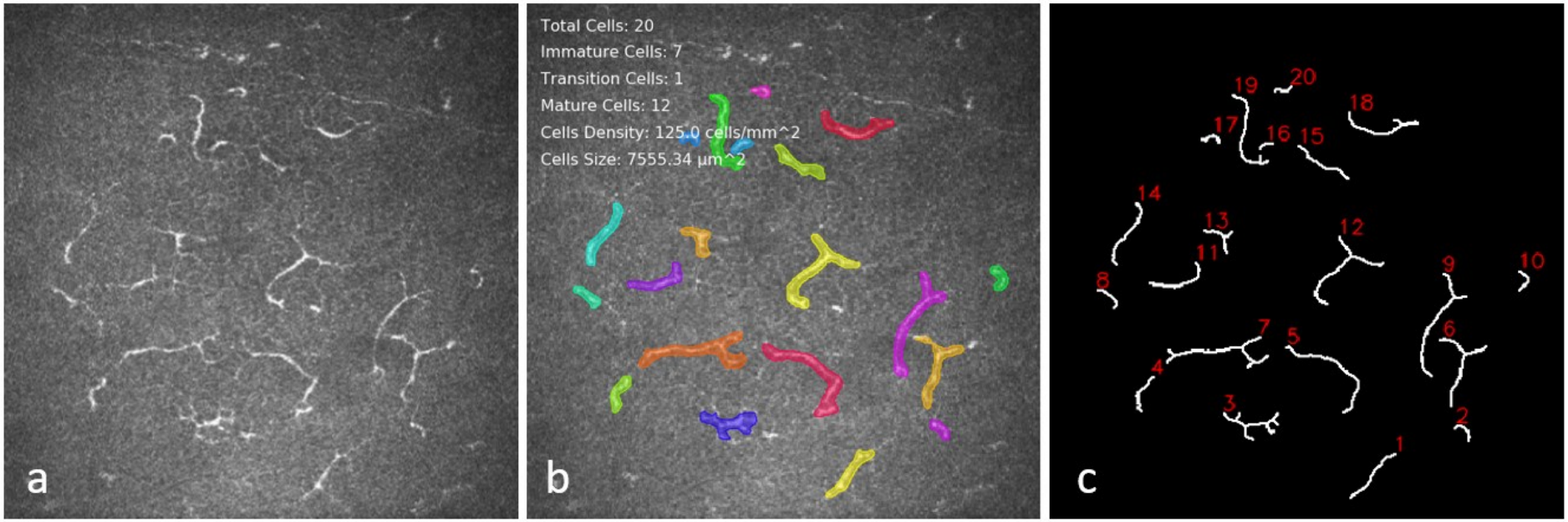


DC segmentation and comparison with manual annotations

Precision	Recall	F1 Score	Single image processing time
92%	95%	93%	3 sec

Results (Morphometric parameter assessment)

- The morphometric parameters of DC number, size (μm^2), density (cells/mm^2), and number of immature, transition stage, and mature cells were computed directly from the binary segmented image



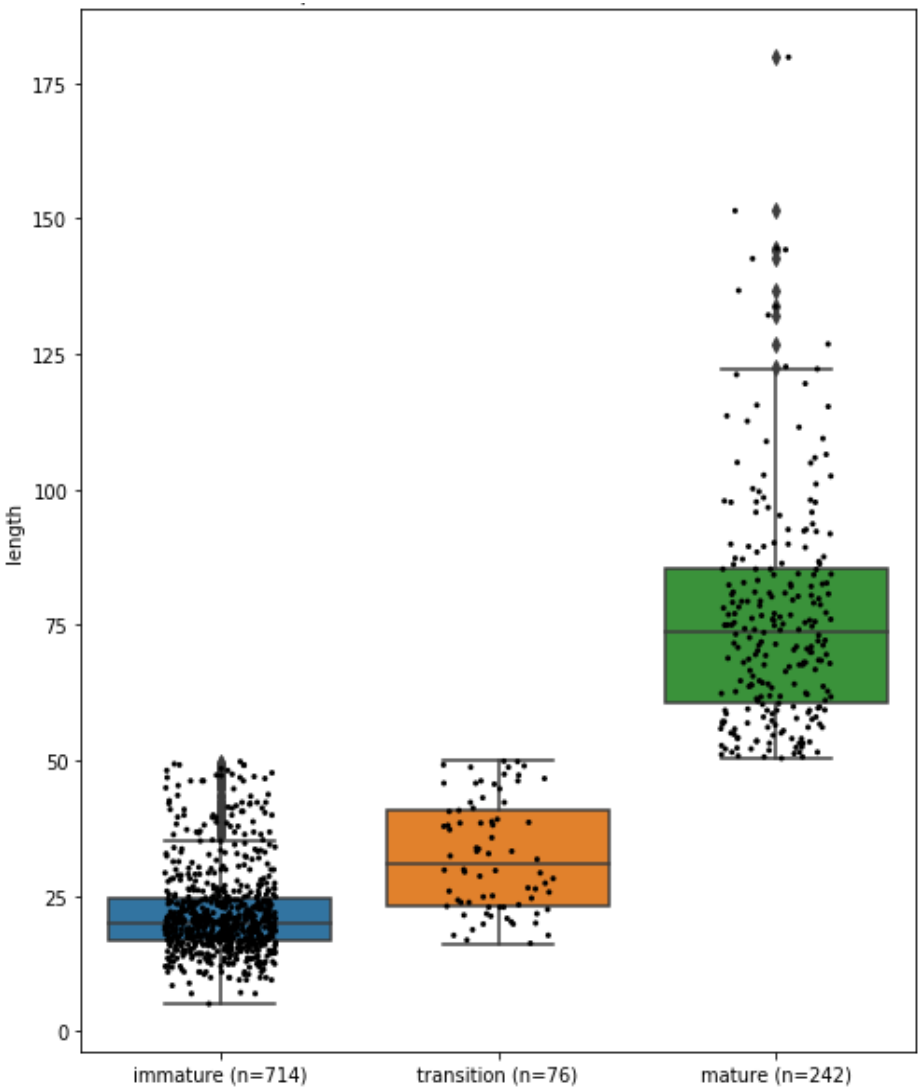
DC segmentation and morphometric evaluation. (a) Original image, (b) Overlay of automatic segmentation with morphometric evaluation information, and (c) Skeletonized image (one pixel width) with the cell identification number.

Results (Model performance on test dataset)

- Interclass correlation coefficient between manual and automatic segmentation of total DC number and size were 0.98 and 0.96 respectively

Parameters	Manual	Automatic
DC number	11.38 ± 6.70	11.81 ± 6.72
DC size (μm^2)	2277.45 ± 1346.78	2072.67 ± 1210.65

- To segment and quantify ~ 1000 DC in 100 test images our system took only ~5 mins
- Most of the immature cell's length were in between 20 to 25 µm while the length of mature and transition stage cells were homogeneous



Box-Scatter plot of immature, transition stage, and mature DC

Conclusion

- Convolutional neural network-based method demonstrated high consistency between manual annotation and automatic segmentation with rapid speed
- The proposed method reduce observer variability and time to analyze large volume of clinical patient images
- This method has the potential to be implemented into commercial devices and has the potential to enable clinicians and researchers to rapidly quantify DCs in the cornea for better diagnosing and treating ocular surface disease

THANK YOU FOR YOUR ATTENTION

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