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Modulation of VAMPIRE retinal vasculature analysis software to extend utility and provide secondary value from optical coherence tomography imaging

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INTRODUCTION

Retinal image analysis is emerging as a key source of biomarkers of chronic disease affecting the cardiovascular system and brain.

The rapid development and increasing diversity of commercial retinal imaging systems presents a challenge to image analysis software providers. In addition, clinicians are looking to extract maximum value from the clinical imaging taking place.

We describe how existing and well established retinal vasculature segmentation and measurement software for fundus camera images has been modulated to analyse scanning laser ophthalmoscope retinal images generated by the dual modality Heidelberg SPECTRALIS® instrument which also features optical coherence tomography.

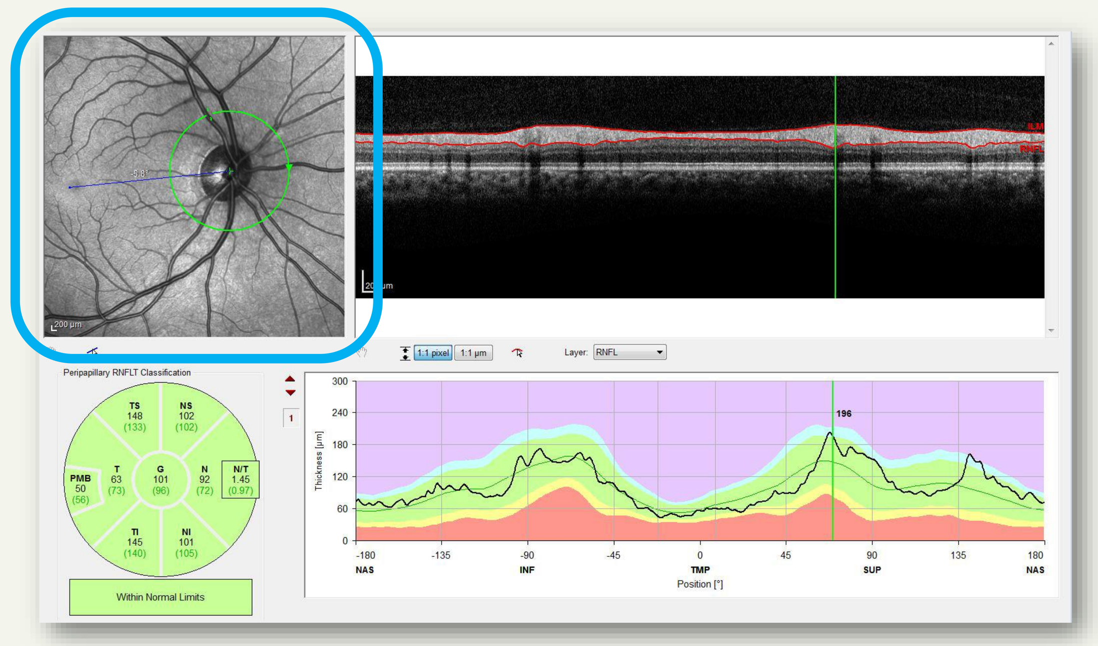

FIGURE 1
OCT peripapillary circular scan
Heidelberg SPECTRALIS OCT

A standard peripapillary OCT scan protocol, usually used for evaluation of the RNFL.

Note the fundal image in the top left hand corner: this represents the SLO image captured simultaneously, and can be extracted from the scan, for separate analysis.

BACKGROUND

VAMPIRE (Vascular Assessment and Measurement Platform for Images of the REtina) is a semi-automatic software platform, for the analysis of the retinal vasculature morphology, in colour fundus photographs.

Modulation of the software to be able to analyse other types of retinal image, such as those produced by a scanning laser ophthalmoscope (SLO) is also a goal of the VAMPIRE project.

The Heidelberg SPECTRALIS OCT is a popular imaging device in clinical ophthalmology. Simultaneously with the OCT image, it acquires a sharp, high-contrast confocal SLO image, with a 35° field of view and an image size of 1536x1536 pixels. [Fig. 1] It is primarily used for guiding location of the OCT imaging and enabling image registration for follow-up scans,. However, there is potential to evaluate the retinal vessels appearing in these SLO images in much the same way as other work with colour fundus photos.

This would add value to the already acquired patient imaging, and provide a unique opportunity for the development of dual-mode image analysis derived from a single instrument and a single imaging event.

ACKNOWLEDGEMENTS

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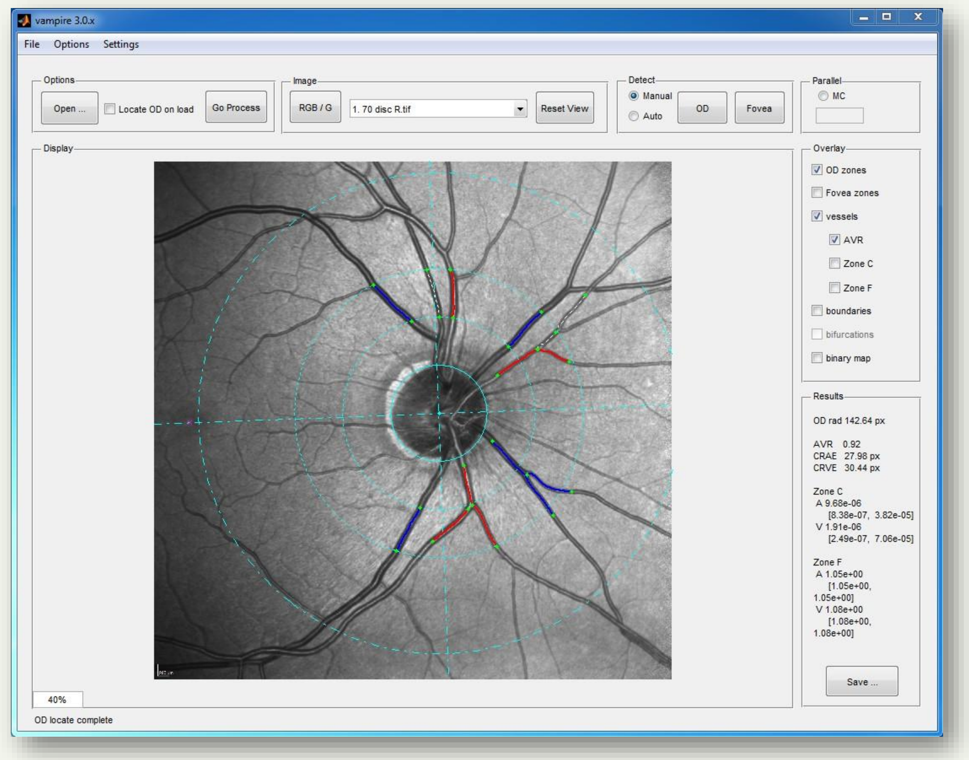
Anne Rowling Regenerative Neurology Clinic

SOFTWARE MODULATION

For automatic detection of vessels, a 2-D Gabor wavelet approach for fundus camera images was adapted to emphasize the appearance of vessels captured with SLO, followed by supervised pixel classification with a Bayesian classifier. This vascular detection algorithm was retrained to work on the SLO images by manually delineating vessels, taking 1,000,000 samples of pixels with 6 features (original grayscale intensity and response to Gabor filters of size 2-6 pixels) to create a supervised classifier which is applied to new images to automatically create pixel-by-pixel maps of the vessels.



Vampire

FIGURE 2
VAMPIRE 3.1

This is the modulated software, accurately segmenting the SLO image and deriving the standard retinal vascular morphology metrics.

Further post-processing based on mathematical morphology was also adapted to vessels in SLO images where the central reflex is more evident, causing misclassified gaps in vessels with the supervised classification technique; this effect was lessened by removing such regions with size<200 pixels to create an improved map of the vessel.

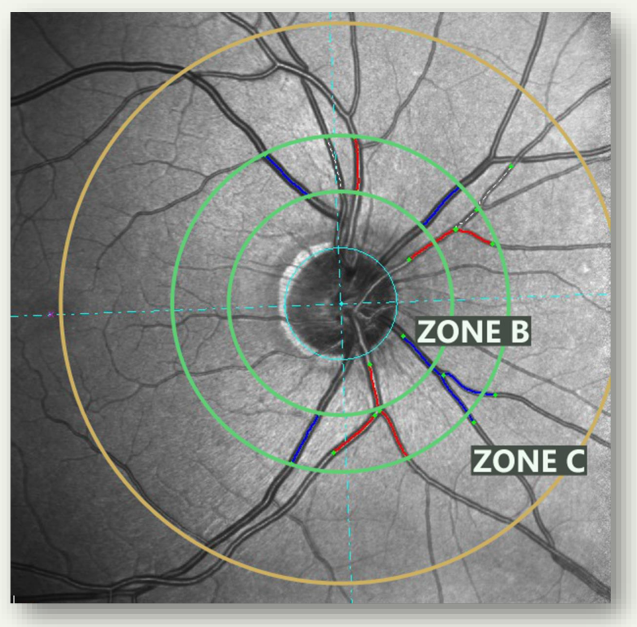


FIGURE 3
SLO image ZONES

The standard set of circular measurement zones commonly used in the analysis of fundus camera images is also shown – zone B which is the ring 0.5-1 optic disc diameters away from the centre, and Zone C which is the ring extending from optic disc boundary to 2 optic disc diameters away.

Using this vessel map, VAMPIRE creates a tree-like representation of the vasculature as a pre-processing step for performing vascular measurements. [Fig. 2] From the vessel tree the software automatically selects the 6 widest arterioles and venules crossing zone B and measures vessel calibres using a supervised algorithm that was retrained on SLO images by manually annotating widths at 200 locations in 5 images.

These measurements were used to calculate the well-recognized summary parameters – central retinal arteriole equivalent (CRAE) and central retinal venule equivalent (CRVE) – yielding the arteriole to venule width ratio (AVR). Similarly, for tortuosity, VAMPIRE selects the 6 widest arterioles and venules crossing zone C, evaluates the tortuosity for each using an established technique, and calculates the median values (plus standard deviation and range). [Fig. 3]

EVALUATION

The modulated software was evaluated by assessing inter-operator reliability.

We obtained optic disc centred images from 78 participants - 48 males, 30 females, and an age range of 39-69 years – using the SPECTRALIS device.

Two operators separately uploaded and processed the image set. This required them to manually select the optic disc boundary (two opposite points) and the fovea (single click). This creates a circular approximation to the optic disc outline and also places the standard measurement zones B&C.

The software then processed the segmentation and measurements, outputting the final data. The two operators were blinded to each other's use of the software and a comparison between their results was assessed as an outcome measure of the successful modulation of VAMPIRE to these SLO retinal images.

Inter-operator reliability was assessed using intraclass correlation coefficients (ICC) and a Bland-Altman approach to display the extent of agreements.

RESULTS

The ICCs were >0.9 for all metrics [Fig. 4] demonstrating very high reliability and repeatability of these measurements with the modulated software. The Bland-Altman analysis demonstrated a high level of consistency between the operators [Fig. 5].

	AVR	CRAE	CRVE	A tortuosity	V tortuosity
Intraclass Correlation Coefficient	0.961	0.936	0.961	0.955	0.958
95% CI	0.939-0.975	0.900-0.959	0.938-0.975	0.930-0.971	0.934-0.973

FIGURE 4
Intraclass Correlation Coefficients (and 95% confidence intervals) for absolute agreement between two operators, of the retinal parameters.

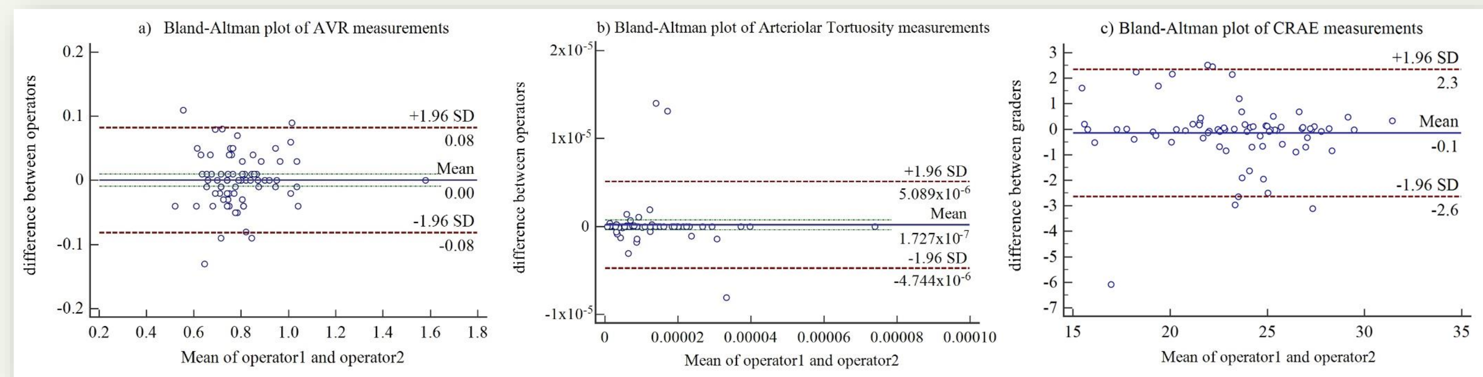


FIGURE 5
Bland-Altman plots of agreement between two operators (with 95% CIs for limits of agreement) for a) AVR, b) arteriolar tortuosity and c) CRAE

CONCLUSION

- We have successfully modulated the VAMPIRE software to accept and analyse the SLO retinal images acquired by the SPECTRALIS machine.
- Our initial evaluation has demonstrated a high reliability and repeatability of the vascular measurements that can be made on these images.
- This development of retinal image analysis holds potential for use as part of multi-modal retinal analysis, from one single patient acquisition, using the patient-friendly SPECTRALIS device.

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