Quantifying the Effect of Image Centering Towards Standardization of Retinal Vascular Measurements

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Aim

Vascular measurements from retinal fundus images have been used for years to identify biomarkers from the morphology of the retinal vasculature, and its changes, for a variety of conditions (e.g., complications of diabetes, dementia, and cardiovascular disease). The values of such measurements are however affected by many factors. Here, we investigate the changes induced specifically on by centering acquisition on either the optic disc or on the macula.

Materials and Methods

- Dataset: 4 fundus-camera images of each of 20 subjects (2 per eye, macula and OD-centered, 80 images in total) were sourced from the Edinburgh Type 2 Diabetes Study (ET2DS), a population-based cohort study designed to investigate potentially modifiable risk factors for cognitive decrements in type 2 diabetes [1]. Images were acquired with a TOPCON TRC-50FX digital fundus camera at 350 FOV after pupil dilation using 1% tropicamide. Ethical approval for the ET2DS was granted by the Lothian Research Ethics Committee, and written informed consent was obtained from all participants [2].

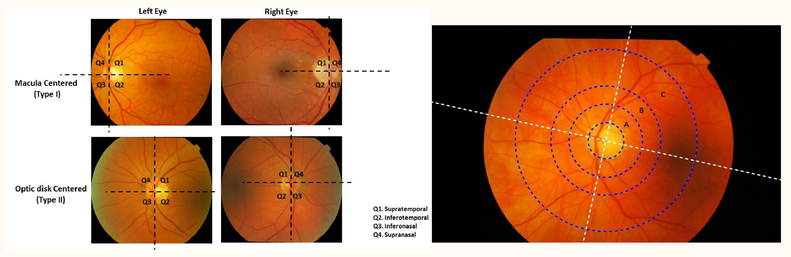


Fig. 1. Illustration of quadrants and retinal coordinates centered on the OD and circular zones used to compute retinal measurements.

- Retinal measurements: VAMPIRE computes 151 measurements and their basic statistics (mean, median, standard deviation, max, min) for each image [3, 4]. Measurements are computed by vessel type (arteriole or venule), by region (zone, whole image, quadrant (Fig. 1)) and vessel (path, generation). We considered the 149 measures describing vessel morphology: 39 widths and functions thereof (e.g. Central Arterial Equivalent (CRAE), Central Venular Equivalent (CRVE), Arteriole to Venule Ratio (AVR), basic statistics, width gradients, different width estimation algorithms by artery and vein, average ratio length-diameter at branching points), 104 tortuosity measurements, and 6 Fractal Dimension (FD) coefficients (3 per vessel network type, arterial or venous).

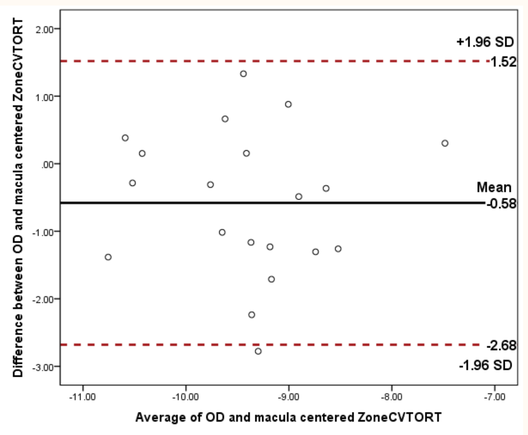
- Statistical analysis: Two-way mixed model Intra-Class Coefficients (ICC) and Pearson's correlation were used to examine agreement between macula- and OD-centered images (right and left eye separately). In addition, we also analyzed measurement (e.g., CRAE) symmetry between right and left eye (macula and OD-centered images separately) [5, 6].

Results

- In the right eye, 5 **width-related measurements** (of 39) showed at least moderate correlation, association and significance (defined for our purposes as $r > 0.5$, $ICC > 0.6$, $p < 0.1$) between OD- and macula-centered image (Fig. 2).

- **Tortuosity measures** with at least moderate correlation and *ICC* (defined as above) between OD- and macula-centered images were only 17 (of 104) in the right and 20 in the left eyes Of these, only 10 satisfied our conditions in both eyes: 8 arterial and 2 venular tortu-osity measures, including 7 taken in Q1 and mean arterial tortuosity in Zone C.

- **FD measures** (3 for arteries, 3 for veins), only 2 of 20 images of the right eye supported full computation, leading to excellent but obviously not significant correlation and association; but in the left eyes, all 6 measures could be computed on the full set (20 images). Good and significant correlation ($r \sim 0.7$, $p < 0.01$) and moderate association ($ICC \sim 0.7$) was found for arterial measures only.



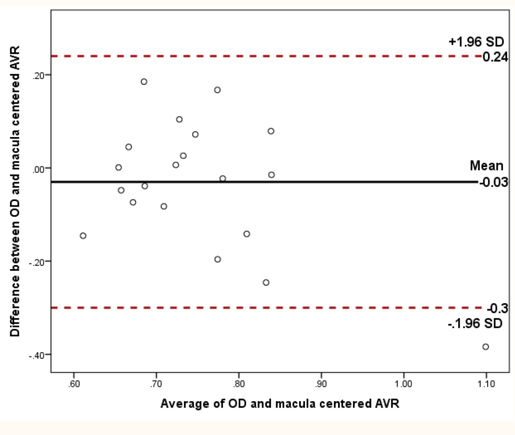


Fig. 2. Bland-Altman plots visualizing, for illustration, the association of venular tortuosity in Zone C (top) and AVR (bottom) between OD- and macula-centered images (right eyes).

Summary and Next Steps

- Our results suggest that different centering induces substantial differences. The important risk is that this could lead, potentially, to fragile statistical conclusions in biomarker studies. Such studies should, ideally, consider both centering types and discuss the differences in associations for Type I and Type II images separately.

- We plan to extend our analysis to larger samples from independent populations to better understand the effects of centering on morphometric vascular measurements in the retina.

- Ultimately, the many aspects of a protocol for reliable biomarker studies, of which centering is only one, require in our view an international collaborative standardization effort, which we strongly auspicate.

References

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