Retinal Vascular Geometry: Novel Biomarkers of Progression from Diabetes to Diabetic Retinopathy

Georgios Leontidis
Computer and Data Scientist
School of Computer Science
University of Lincoln, UK

Correspondence email: gleontidis@lincoln.ac.uk
Introduction

• Diabetic retinopathy (DR) remains a major cause of blindness in the developed countries [1].

• Geometric and Haemodynamic features are still not widely investigated, especially as biomarkers of progression to DR.

• Most studies rely on disease vs control design, which introduces errors and limitations, given the diversity of the retinal vascular geometry (small and large vessels).

• Our studies have mainly focused on investigating the vascular changes within the same patients during a four year period that includes the last three years of pre-DR and 1st year of DR (onset).

Investigated Features

<table>
<thead>
<tr>
<th>Geometric</th>
<th>Haemodynamic</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Widths</td>
<td>• Blood flow velocity</td>
</tr>
<tr>
<td>• Angles</td>
<td>• Blood flow rate</td>
</tr>
<tr>
<td>• Tortuosity</td>
<td>• Reynolds number</td>
</tr>
<tr>
<td>• CRVE/CRAE and AVR</td>
<td>• Wall shear stress</td>
</tr>
<tr>
<td>• Branching coefficient</td>
<td>• Pressure</td>
</tr>
<tr>
<td>• Angle-to-BC ratio</td>
<td>• Descriptive statistics of the above</td>
</tr>
<tr>
<td>• Asymmetry index</td>
<td></td>
</tr>
<tr>
<td>• Fractal dimension</td>
<td></td>
</tr>
<tr>
<td>• FD-to-Lacunarity ratio</td>
<td></td>
</tr>
<tr>
<td>• Lacunarity</td>
<td></td>
</tr>
</tbody>
</table>
Tools and Methods

- Automated tools for the segmentation and the extraction of the investigated features [2].

- Mathematical modelling (0D lumped models) in order to simulate and estimate haemodynamic parameters [3].

Figure 1. Two segmented retinal images.

Figure 2. Example of the tool for the estimation of haemodynamic parameters in vascular trees.


Tools and Methods

- Extraction of arterial and venular bifurcations and modeling in connected trees.

- Areas of Interest [4] for individually studying some of the geometric features (widths, angles and tortuosity).

Tools and Methods

- Statistical evaluation based on linear mixed effects models – metric based on AIC, BIC, log-likelihood and p-values (full vs restricted models [5]).

- Machine learning (Elastic-net logistic regression and random forests) for the feature selection and classification process [5].

---

Results

• Arterial and venular widths, tortuosity, fractal dimension, blood flow velocity, blood flow rate, pressure and wall shear stress were found to significantly differ across the whole four year period.

• Post-hoc comparisons showed that the changes are primarily found for the combination “three years pre-DR and 1st year of DR”.

• Classification models created for various combinations, such as 3y/2y/1y pre-DR vs 1st year of DR (onset), patients with diabetes vs DR patients and progressors vs non-progressors vs DR patients.
Results

- Best five features for the discrimination of the classes within all the combinations of the classification models are SD of arterial angles, CRVE [6], CRAE [6], Angle-to-BC ratio and venular pressure.

![Graphs showing ROC curves](Image)

Figure 6: Area under the Receiver operating characteristic (ROC) curve (AUC) for the combination “non-progressed patients with diabetes vs DR patients”.

Summary

• Early screening of diabetic retinopathy, before any lesions appear, can be identified, relying on geometric and haemodynamic features.

• Robust statistical analysis is crucial for identifying the biomarkers that can be used in classification models.

• Machine learning techniques for the feature selection process and for the classification models can help to identify the progression to DR.

• This can be used as an indication of the progression (or not) of the disease (within each patient’s annual retinal screening) and possibly investigate the condition further, if needed.
Research supported by a Marie Skłodowska-Curie grant from the European Commission in the framework of the REVAMMAD ITN Project number 316990.
QUESTIONS

THANK YOU FOR YOUR ATTENTION