Population-wide Disease Modeling to Predict Macular Thickness and Treatment Response in Longitudinal OCT Data

Wolf-Dieter Vogl1,2,3, Sebastian M. Waldstein1, Bianca S. Gerendas1, Jing Wu1, Alessio Montuoro2, Ana-Maria Gliodan2, Dominika Podkowinski2, Christian Simader2, Ursula Schmidt-Erfurth1 and Georg Langs1

1Computational Imaging Research Lab (CIR), Department of Biomedical Imaging and Image-guided Therapy, Vienna Reading Center, Department of Ophthalmology and Opthalmometry, Christian Doppler Laboratory for Ophthalmic Image Analysis (OPTIMA), Medical University of Vienna, Austria

Introduction

Motivation: The ability to predict the future development of a disease is an extremely important goal both in clinical and scientific practice, as well as in the general health care setting.

Aim: Predict future treatment response and disease path from longitudinal spectral domain optical coherence tomography (SD-OCT) images.

1. Total Retinal Thickness Maps
   - Normalize scans to compensate for anatomical and scan position variations.
   - Use total retinal thickness maps as feature describing the development of the underlying retinal structure and pathology.
   - Total retinal thickness maps are computed as distance between ILM and RPE layer. Layers are automatically segmented using Iowa reference algorithm.
2. Spatio-temporal Features in a Joint Reference Space
   - Transformation of scans and thickness maps into a joint reference space via: (1) Intra-patient registration by aligning the vessel structures and (2) Inter-patient registration by aligning fovea center and optic disk center landmarks.

Data

Training and Validation Set:
- 155 patients with macular edema secondary to central retinal vein occlusion.
- Retinal SD-OCT baseline scan + 12 monthly follow-up scans from two vendors (Heidelberg Spectralis, Zeiss Cirrus). 2,015 scans overall.
- 28 patients showed no recurring edema within 12 month follow-up.

Treatment:
- Three month induction phase with monthly ranibizumab injections, followed by a PRN (pro re nata = per need) regimen.

Methods

1. Total Retinal Thickness Maps
   - Total retinal thickness maps are computed as distance between ILM and RPE layer. Layers are automatically segmented using Iowa reference algorithm.
2. Spatio-temporal Features in a Joint Reference Space
   - Transformation of scans and thickness maps into a joint reference space via: (1) Intra-patient registration by aligning the vessel structures and (2) Inter-patient registration by aligning fovea center and optic disk center landmarks.

Results

Validation
- 5-fold cross validation setup.
- Compare elastic net regression and logistic regression with other regression methods (Random forest, LASSO, Cox...).
- Performance measures:
  - Mean absolute error (MAE) in µm for thickness prediction.
  - Sensitivity / specificity, and ROC Area under curve (AuC) for recurrence prediction.

Prediction of Total Retinal Thickness

<table>
<thead>
<tr>
<th>Method</th>
<th>Parameter</th>
<th>Median MAE [µm]</th>
<th>Mean (std) MAE [µm]</th>
<th>R²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elastic Net</td>
<td>λ = 500, t = 0.1</td>
<td>13.64</td>
<td>20.26 (20.86)</td>
<td>0.45</td>
</tr>
<tr>
<td>LASSO</td>
<td>λ = 100</td>
<td>14.71</td>
<td>20.88 (21.50)</td>
<td>0.40</td>
</tr>
<tr>
<td>Ridge Regression</td>
<td>λ = 1.4 × 10²</td>
<td>14.83</td>
<td>21.47 (21.97)</td>
<td>0.43</td>
</tr>
<tr>
<td>Random Forest</td>
<td>trees = 100</td>
<td>16.03</td>
<td>21.91 (19.48)</td>
<td>0.43</td>
</tr>
</tbody>
</table>

Conclusion

- We propose a method for prediction of future development of disease under treatment using sparse machine learning models based on longitudinal SD-OCT imaging data.
- The method predicts the outcome of two variables: (1) total retinal thickness after induction phase, (2) non-recurrence vs. recurrence of edema within twelve month follow-up.
- Sparse feature selection via elastic net in a multivariate generalized linear model setting yields accurate predictions and interpretable results.

References


Financial disclosures: None

Department of Ophthalmology | http://optima.meduniwien.ac.at  wolf-dieter.vogl@meduniwien.ac.at

Financially supported by the Austrian Federal Ministry of Science, Research and Economy and the national Foundation for Research, Technology and Development

Optical Imaging