Prediction of Low and High Anti-VEGF Treatment requirements During the PRN Phase from Early OCT Images in Neovascular Age-Related Macular Degeneration

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Introduction

In **anti-VEGF therapy of neovascular AMD**, inter-individual treatment requirements are vastly heterogeneous. **Tools and biomarkers to predict** these individual requirements represent an **unmet medical and socioeconomic need**.

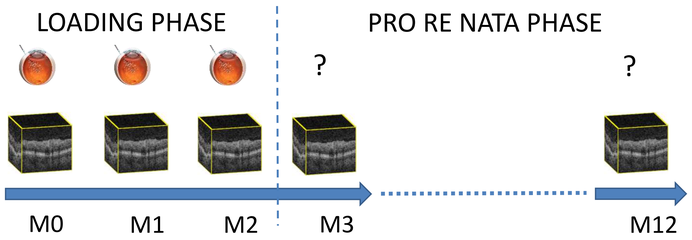
The aim of this retrospective study was **to predict anti-VEGF injection requirements during the pro re nata (PRN)** phase, using a set of OCT images acquired during the loading phase of the **HARBOR** study in treatment-naïve patients with neovascular AMD.

Patients and Data

Clinical trial data of **351 patients receiving 3 monthly loading injections** followed by PRN ranibizumab (0.5 mg or 2 mg) therapy

PRN is undertaken according to the protocol specified criteria in the **HARBOR** study.

SD-OCT images (512x128x1024 voxels, Cirrus, Zeiss) were analyzed from the loading phase:
Baseline (M0), Month 1 (M1), and Month 2 (M2).



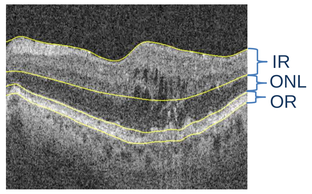
The number of injections during the PRN phase until month 12 ranged from 0 to 10.

Groups of low and high injection requirements were defined as ≤2 and ≥9 injections between M3 and M12, respectively.
75/351 patients with **LOW (≤2) injection requirements.**
52/351 patients with **HIGH (≥9) injection requirements.**

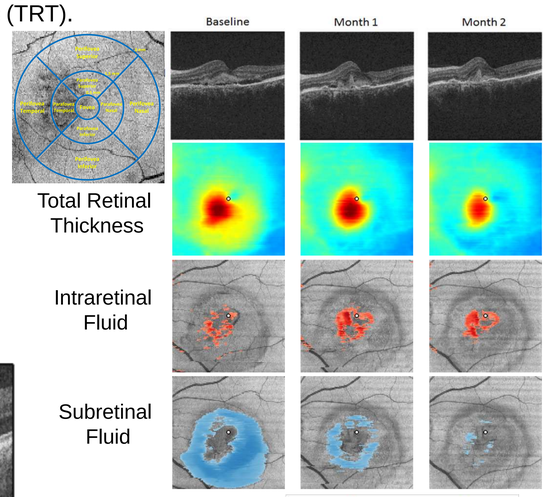
Methodology – Quantitative Analysis and Learning

Quantitative features based on automated segmentation of layers and fluid regions were extracted to describe the retinal microstructure. **Machine learning was used to predict** the injection requirements

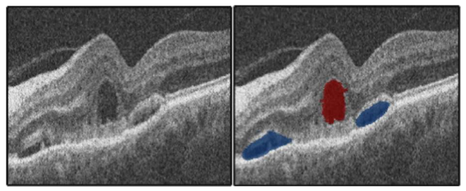
LAYER SEGMENTATION
Based on Iowa Reference algorithms [1].
Inner retina (IR), outer nuclear layer (ONL), photoreceptor outer segments with retinal pigment epithelium (OR), and total retinal thickness (TRT).



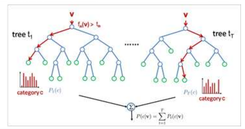
FEATURE EXTRACTION
Local Spatio-Temporal features computed on ETDRS grid.
Total number of features = 312 (8x13x3)



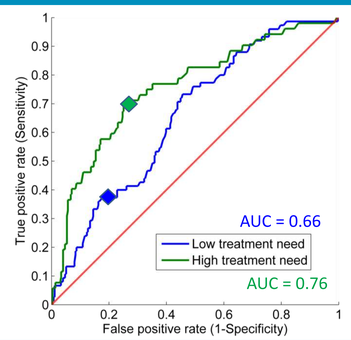
FLUID SEGMENTATION
Based on deep learning [2].
Intra- and Subretinal fluid (IRF and SRF) volume and area.

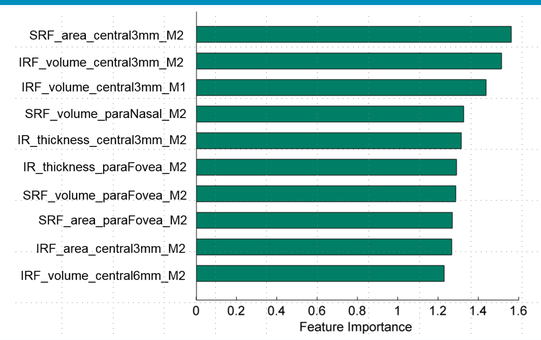


MACHINE LEARNING
Random forest classification. Evaluation with 10-fold cross validation.



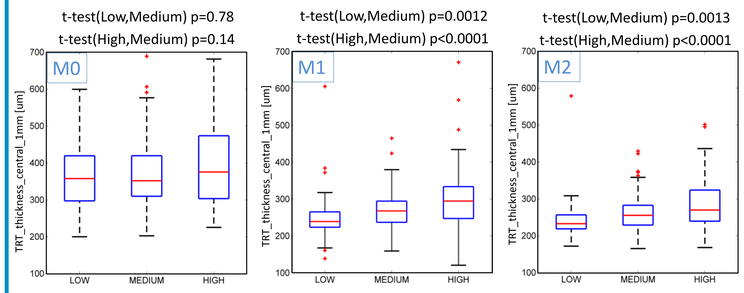
Results – Classification of Low / High Treatment Needs



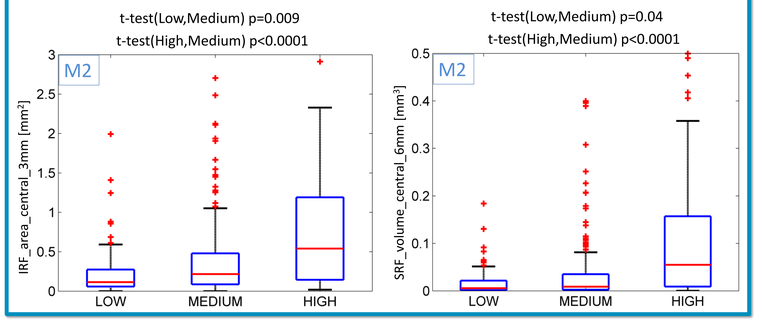


Results – Role of Retinal Features

Role of Total Retinal Thickness (TRT)



Role of Retinal Fluid (IRF and SRF)



Conclusions

The proposed machine learning system predicted:
- **Low requirements patients with 80% specificity and 35% sensitivity.**
- **High requirements patients with 70% specificity and sensitivity.**

Total retinal thickness in the central 1 mm, intraretinal fluid area in the central 3 mm, and subretinal fluid volume in the central 6 mm were the most discriminative features.

The results indicate potential for imaging to guide monitoring and treatment intervals.

References

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[2] Schlegl et al. Predicting Semantic Descriptions from Medical Images with Convolutional Neural Networks. In Inf Process Med Imaging, 2015; 24:437-48

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