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).

LOADING PHASE
PRO RE NATA PHASE

M0 M1 M2 M3 M12

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 29 injections between M3 and M12, respectively.

75/351 patients with LOW (52) injection requirements.
52/351 patients with HIGH (29) 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.

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

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).

Fluid Segmentation
Based on deep learning [2].
Intraretinal and Subretinal fluid (IRF and SRF) volume and area.

Results – Classification of Low / High Treatment Needs

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

AUC = 0.66

AUC = 0.76

Results – Role of Retinal Fluids

Role of Retinal Fluid (IRF and SRF)

Role of Total Retinal Thickness (TRT)

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