Artificial intelligence to predict optimal treatment intervals in treat-and-extend (T&E)

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Purpose: Treat-and-extend (T&E) is an increasingly popular treatment regimen in anti-VEGF therapy in neovascular age-related macular degeneration (nAMD). An extension longer than the ideal interval between injections puts patients at risk for recurrence and vision loss. We developed and evaluated a predictive model based on machine learning to determine a priori the optimal interval in a T&E regimen using clinical information and optical coherence tomography (OCT) based biomarkers.

Methods: SD-OCT volume scans (512x128x1024 voxels, Cirrus, Zeiss, or 512x49x496 voxels, Spectralis, Heidelberg Engineering) were processed at baseline and after the first anti-VEGF injection (Month 1). First, automated segmentations were performed (Figure 1) in which intraretinal and subretinal fluids were segmented using a deep learning convolutional neural network. Retinal layers were segmented with a graph-theoretic approach. Second, a set of quantitative features from the segmented layers and fluid regions was computed across an Early Treatment Diabetic Retinopathy Study (ETDRS) grid to describe the retinal pathomorphology both quantitatively and spatially. Finally, using the computed set of features, a predictive model of future treatment intervals was built using machine learning and was evaluated with cross-validation.

Results: Clinical trial data of 210 evaluable patients receiving standardized ranibizumab T&E therapy for 1 year according to the protocol specified in the TREND study were used. The maximum treatment intervals ranged from 4 to 12 weeks; 107/210 patients reached and maintained long (8, 10, 12 weeks) and other 103/210 had short (4, 6 weeks) treatment intervals. The model predicted (Figure 2) the maximum treatment interval in an individual patient within 4.7 weeks (95% confidence interval (CI)) and it identified the interval groups with a mean accuracy of 0.72 (CI: 0.64-0.79) area under the curve (AUC). The amount of SRF remaining at Month 1 was found to be the most important predictive feature.

Conclusions: We proposed and evaluated artificial intelligence methodology to predict the T&E treatment intervals from OCT images. The results of this pilot study are a promising step toward image-guided prediction of optimal treatment intervals in nAMD therapy and may help to personalize anti-VEGF therapy while minimizing the risk of undertreatment.
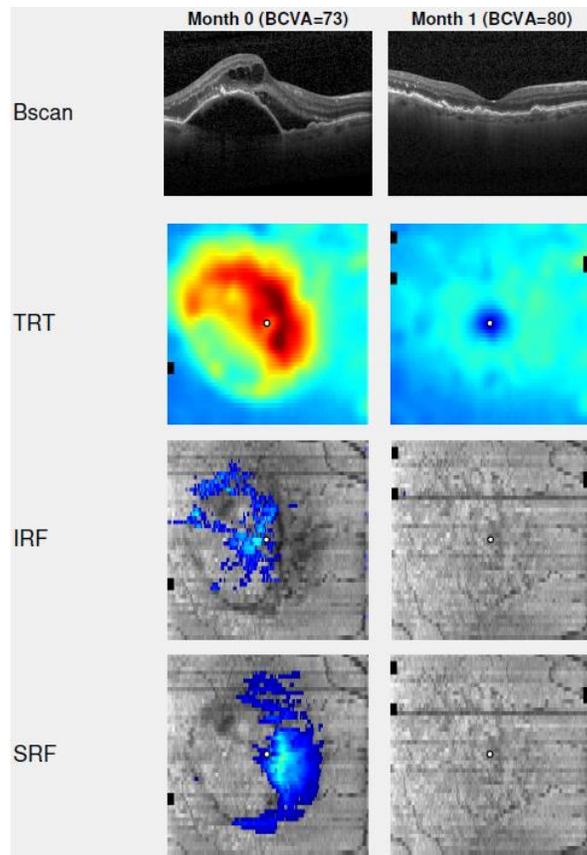
Figure 1. Segmented morphological features: Total retinal thickness (TRT), intraretinal fluid (IRF), and subretinal fluid (SRF).
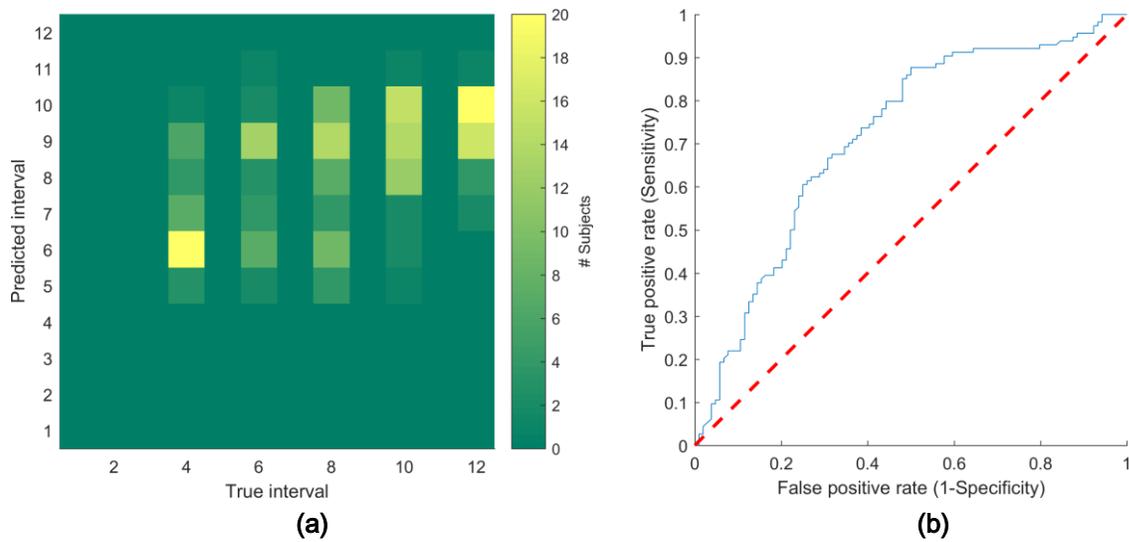
Figure 2. (a) Scatter plot of maximum interval predictions. (b) Receiver operating curve for interval group identification.