Ensemble Machine Learning for Alzheimer's disease Classification from Retinal Vasculature

Hely Lin*, Ruogu Fang

J. Crayton Pruitt Family Department of Biomedical Engineering, University of Florida, Gainesville, FL, 32611

Introduction: Alzheimer's disease (AD) causes progressive irreversible cognitive decline and is the leading cause of dementia. Therefore, a timely diagnosis is imperative to maximize neurological preservation. However, current treatments are either too costly or limited in availability. In this project, we explored using retinal vasculature as a potential biomarker for early AD diagnosis. This project focuses on stage 3 of a three-stage modular machine learning pipeline which consisted of image quality selection, vessel map generation, and classification [1]. The previous model only used support vector machine (SVM) to classify AD labels which limited its accuracy to 82%. In this project, random forest and gradient boosting were added and, along with SVM, combined into an ensemble classifier, raising the classification accuracy to 89%.

Materials and Methods: Subjects classified as AD were those who were diagnosed with dementia in "Dementia Outcome: Alzheimer's disease" from the UK Biobank Electronic Health Records. Five control groups were chosen with a 5:1 ratio of control to AD patients where the control patients had the same age, gender, and eye side image as the AD patient. In total, 122 vessel images from each group (AD and control) were used. The vessel maps were then segmented from fundus images through U-net.

A t-test feature selection was first done on the training folds and the selected features was fed into the classifiers with a p-value threshold of 0.01. Next, 20 repetitions of 5-fold cross validation were performed where the hyperparameters were solely tuned on the training data. An ensemble classifier consisting of SVM, gradient boosting tree, and random forests was built and the final prediction was made through majority voting and evaluated on the test set.

Results and Discussion: Through ensemble classification, accuracy increased by 4-12% relative to the individual classifiers, precision by 9-15%, sensitivity by 2-9%, specificity by at least 9-16%, and F1 score by 712%.

Performance for Classification of Alzheimer's Disease versus Control Group Patients					
Classifier	**Accuracy**	**Precision**	**Sensitivity**	**Specificity**	**F1 Score**
SVM	0.8201	0.80	0.85	0.79	0.82
Random Forest	0.7687	0.76	0.78	0.75	0.77
Gradient Boosting	0.8456	0.82	0.81	0.82	0.81
Ensemble	**0.8852**	**0.91**	**0.87**	**0.91**	**0.89**

Figure 1 - Accuracies, Precision, Sensitivity, Specificity, and F1 Score of Classifiers

Conclusions: Overall, a relatively high classification accuracy was achieved using machine learning ensemble classification with SVM, random forest, and gradient boosting. Although the results are very promising, a limitation of this study is that the requirement of needing images of sufficient quality decreased the amount of control parameters that can be implemented. However, through retinal vasculature analysis, this project shows machine learning's high potential to be an efficient, more cost-effective alternative to diagnosing Alzheimer's disease.

Clinical Application: Using machine learning for AD diagnosis through retinal images will make screening available for a broader population by being more accessible and cost-efficient. Mobile device based screening can also be enabled at primary screening in resource-deprived regions. It can provide a pathway for future understanding of the association between biomarkers in the eye and brain.

Acknowledgements: This work was partially supported by the National Science Foundation, IIS-1908299 III: Small: Modeling Multi-Level Connectivity of Brain Dynamics.

References: [1] Tian, J., Smith, G., Guo, H. et al. Modular machine learning for Alzheimer's disease classification from retinal vasculature. Sci Rep 11, 238 (2021). https://doi.org/10.1038/s41598-020-80312-2