Investigating Structure-Function Relationship in Visual Pathway to Develop Optimized Measure for Visual Impairment in MS

Adam Shah; Peter Kosa, PhD; Bibiana Bielekova, MD

Neuroimmunological Diseases Section, NIH/NIAID

Objective

- The shortage of neurologists worldwide evokes a need for more efficient diagnostic & patient monitoring measures for neurological diseases
- Goal is to apply machine learning to understand relationships between different structural and functional visual outcomes
- **Derive single, optimized measurement of vision** that can eventually be used in self-administered smartphone test

Introduction

- Optical coherence tomography (OCT): structural integrity of the retina focusing on layer of axons and ganglion cells
- Visual evoked potentials (VEP): speed of electrical conduction from retina to visual cortex – prolonged with demyelination
- Brain parenchymal fraction (BPFr) and ventricular CSF volume: measures of global brain atrophy
- Vision is measured by visual acuity (VA) collected under different contrasts. Visual disability based on VA at 1.25% contrast used in multiple sclerosis (MS) clinical trials
- We hypothesize that fitting a linear model to these measurements will decrease measurement error; the area under the curve (AUC) will capture all contrasts, have greater dynamic range & less ceiling effect

Methods

1. Develop linear model of VA at different contrasts in healthy donors
2. Calculate VA AUC from regression of all VA contrasts
3. Validate AUC measure through ICC analysis and correlations with existing clinical outcomes
4. Use elastic net regression to generate a model for VA AUC using OCT, VEP, and atrophy data

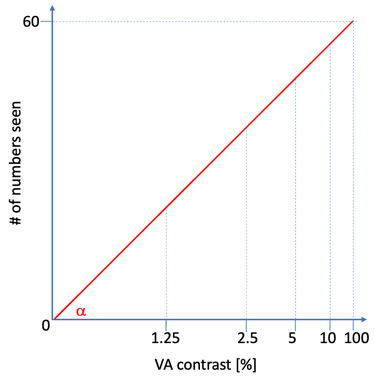


Figure 1: Theoretical linear regression model of VA contrasts to obtain AUC

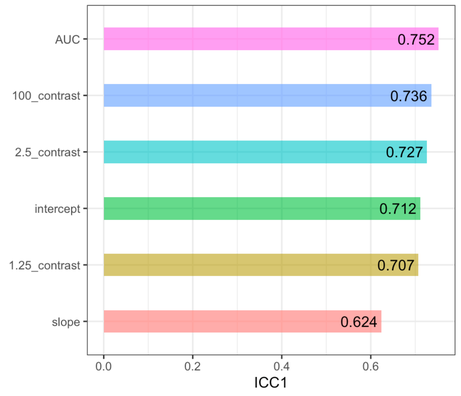


Figure 2: VA AUC outperforms other VA measures in intraclass correlation coefficient (ICC) analysis

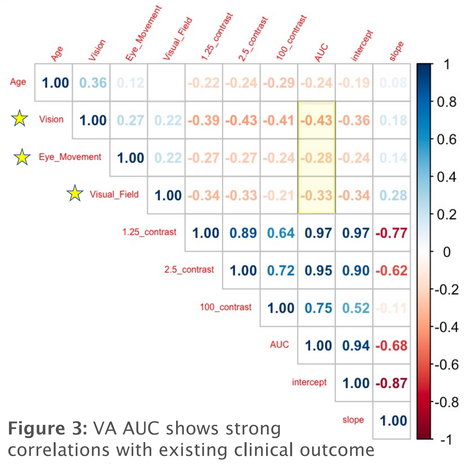
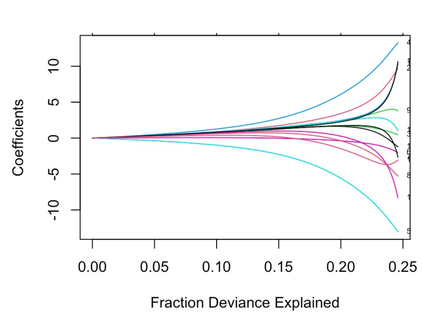
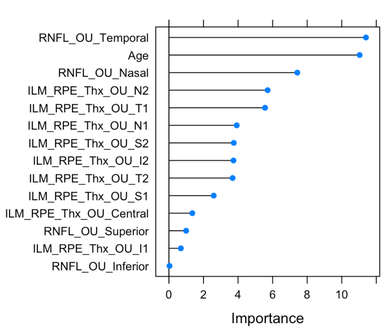
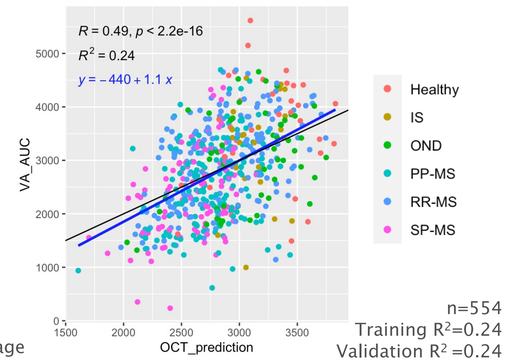


Figure 3: VA AUC shows strong correlations with existing clinical outcome measures ☆

Results







n=554
Training R^2=0.24
Validation R^2 =0.24

Figure 4: Model of VA AUC based on OCT parameters and age

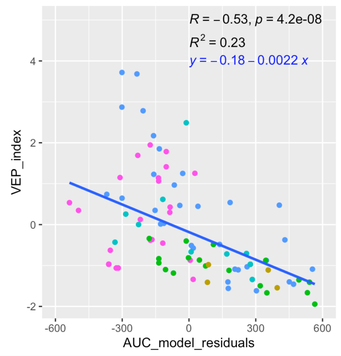
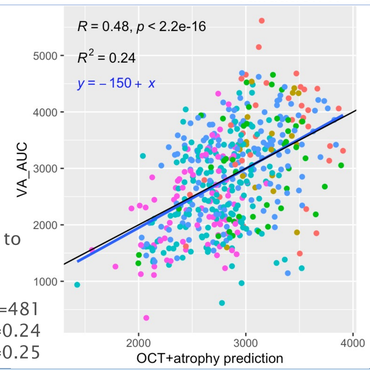


Figure 5: VEP explains portion of the residuals in OCT model

Healthy
IS
OND
PP-MS
RR-MS
SP-MS

n=92
Training R^2=0.22
Validation R^2=0.24

Figure 6: Adding atrophy parameters to the OCT model does not significantly increase variance explained



n=481
Training R^2=0.24
Validation R^2=0.25

Conclusions

- VA AUC has higher ICC, greater dynamic range and stronger correlations with clinician-derived outcomes of visual disability than currently used 1.25% contrast
- OCT and VEP measurements have mostly non-overlapping effect on explanation of variance in the model
- Brain atrophy measures and OCT outcomes explain overlapping portion of variance
- There is additional variance in VA AUC not explained by the model, likely due to diseases anterior to retina or posterior visual pathway not reflected by brain atrophy

Future Directions

- Diffusion tensor imaging data focusing on visual pathway might explain more variance than BPFr
- Assess use of VA AUC in clinical practice for tracking disease progression
- Compare VA AUC from clinic and NDS developed smartphone app for patient monitoring

Acknowledgements

I would like to thank Dr. Bielekova, Dr. Kosa, and all the NDS staff for this opportunity and for their support throughout this project.