Relationship between Retinal Thickness Measurements and Visual Acuity in Progressing Cases of Dry Macular Degeneration

Research in progress by Brandon Klein and Dr. Lily Khadjavi.

Brandon Klein

Department of Biology
Loyola Marymount University
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Outline

- OCT imaging captures dry AMD pathology
  - Visualized pathology
  - Applications
- Extracted OCT data correlates to visual acuity
  - Pathology & central thickness
  - Multiple regression models
- Implications of the regression analyses
  - Clinical applications
  - Biological Interpretations
- Summary
- Future Directions

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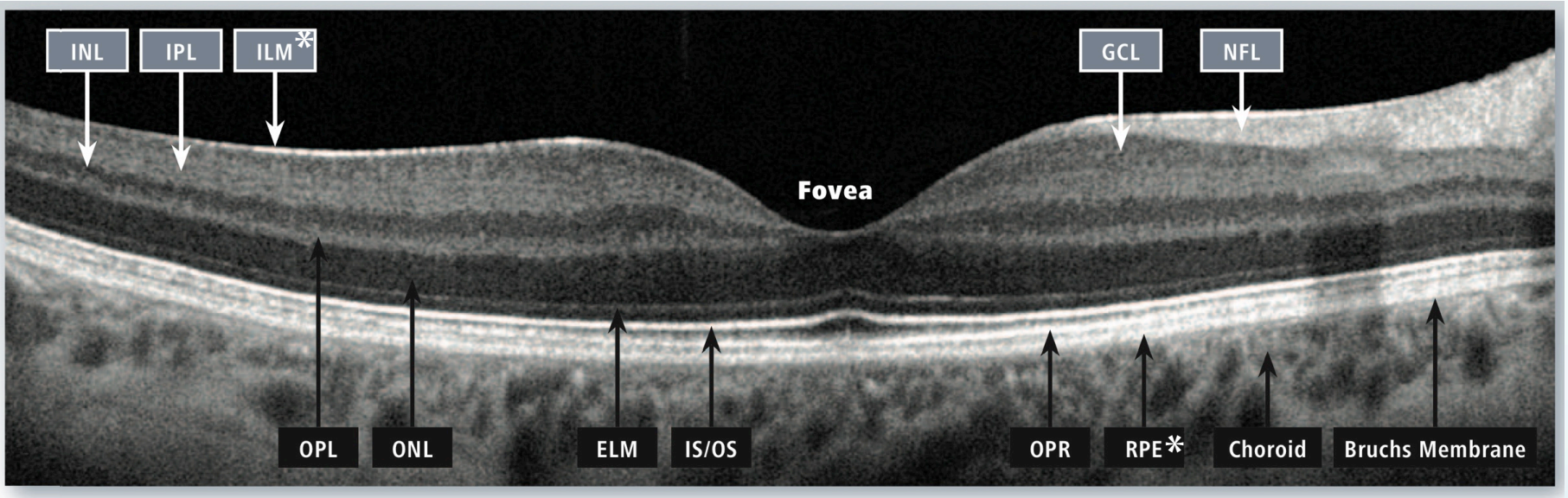
OCT Images Detail Microscopic Retinal Layers



ILM: Inner limiting membrane
IPL: Inner plexiform layer
INL: Inner nuclear layer
OPL: Outer plexiform layer
ONL: Outer nuclear layer

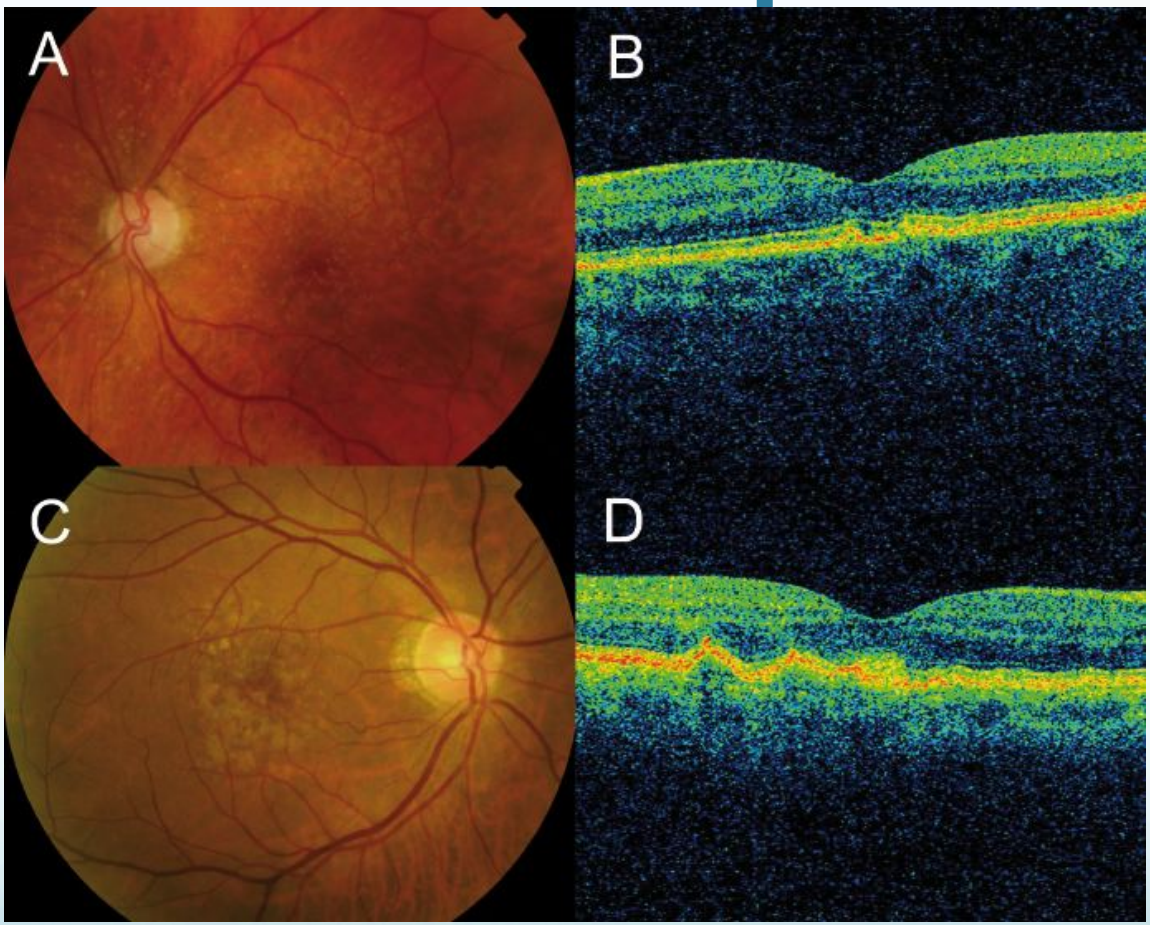
ELM: External limiting membrane
IS/OS: Junction of inner and outer photoreceptor segments
OPR: Outer segment PR/RPE complex

NFL: Nerve fiber layer
GCL: Ganglion cell layer
RPE: Retinal pigment epithelium + Bruch´s Membrane

All retinal layers can be distinguished in this high-resolution OCT image of a healthy individual. Note ILM-RPE region.

Desinee Drakulich. *OCT- What We Can See.* 2012.

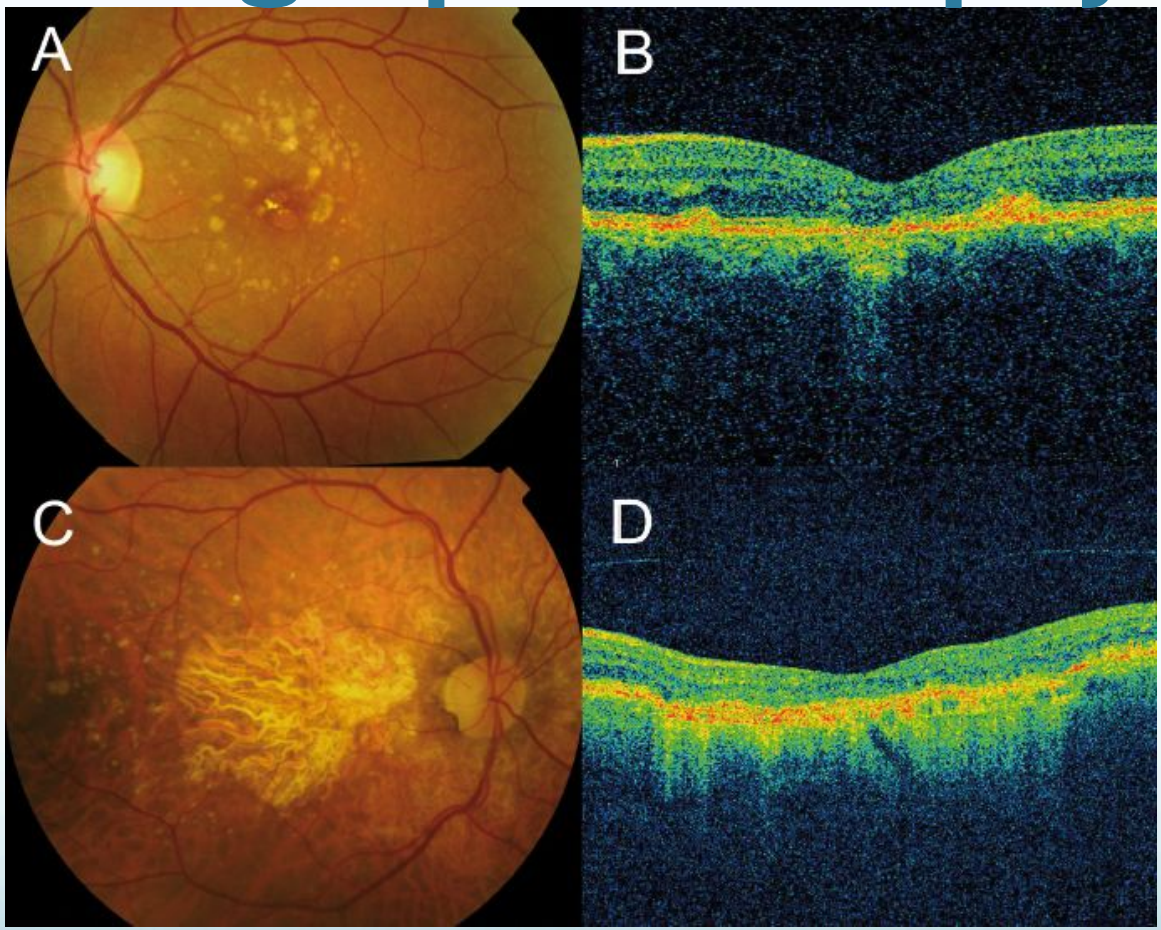
OCT Measurements Capture Drusen Complexes



Drusen, which present as undulations in the RPE, alter the thickness of the ILM-RPE.

Alfredo Garcia-Layana et al. *AMD Book*. 2011.

OCT Measurements Capture Geographic Atrophy



Geographic atrophy is characterized by retinal thinning, but also greater beam penetration into the choroid.

Alfredo Garcia-Layana et al. *AMD Book*. 2011.

Possible Use of OCT Metrics to Predict AMD Outcomes

- Numerical OCT outputs in patients with AMD are heavily influenced by disease pathology.
  - Nonneovascular (dry) AMD pathology is progressive and limited in scope.
  - OCT analyses are becoming important parts of clinical evaluation for AMD patients.
- **Question:** Can numerical data computed from OCT images be used to understand AMD pathology and predict patient outcomes?

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Data was Extracted from Clinical OCT Analyses

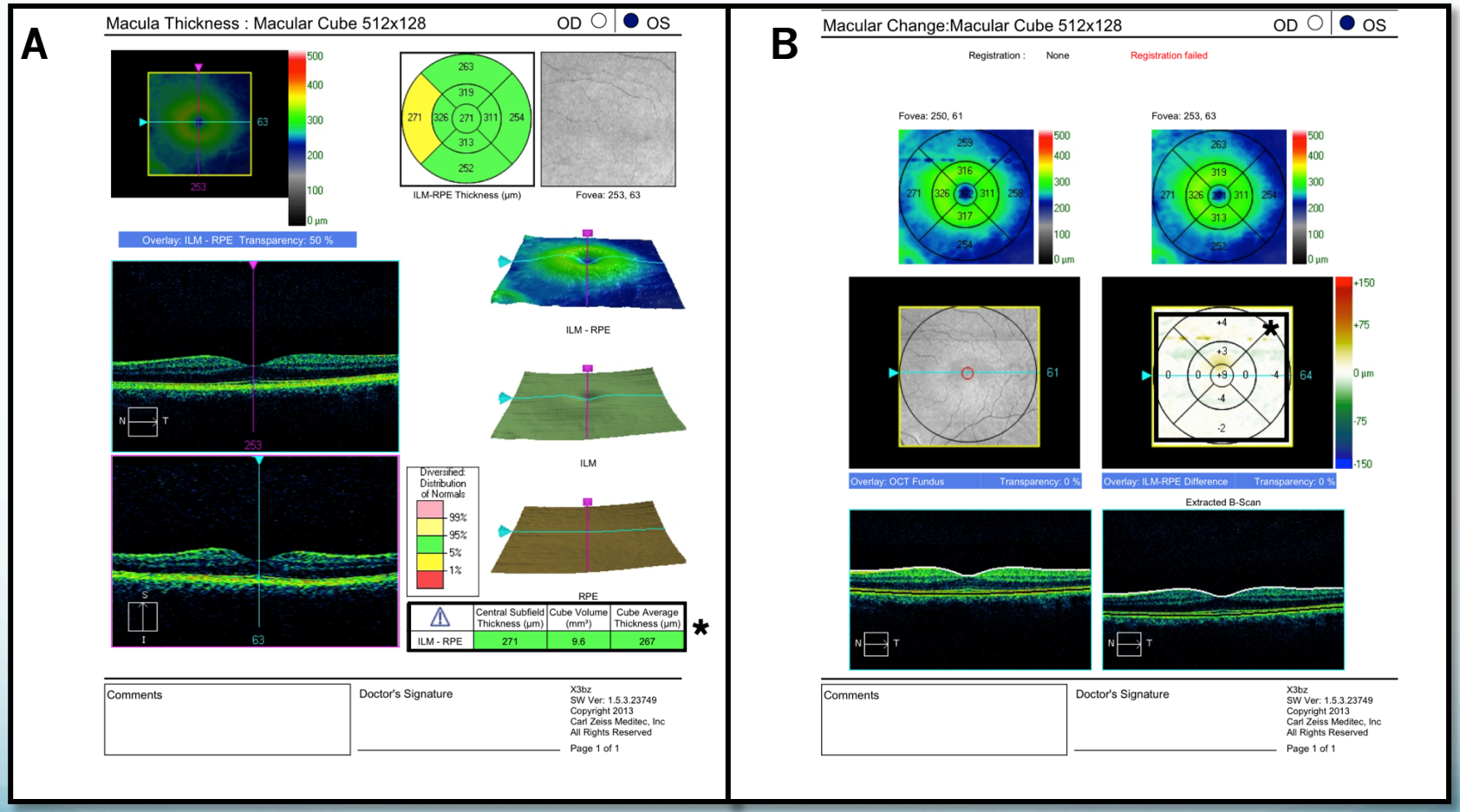

Figure 1 pictures the format of raw data from which thickness measurements (1A) and change measurements (1B) were synthesized.

Visible Pathology Correlated with Patient Visual Acuity

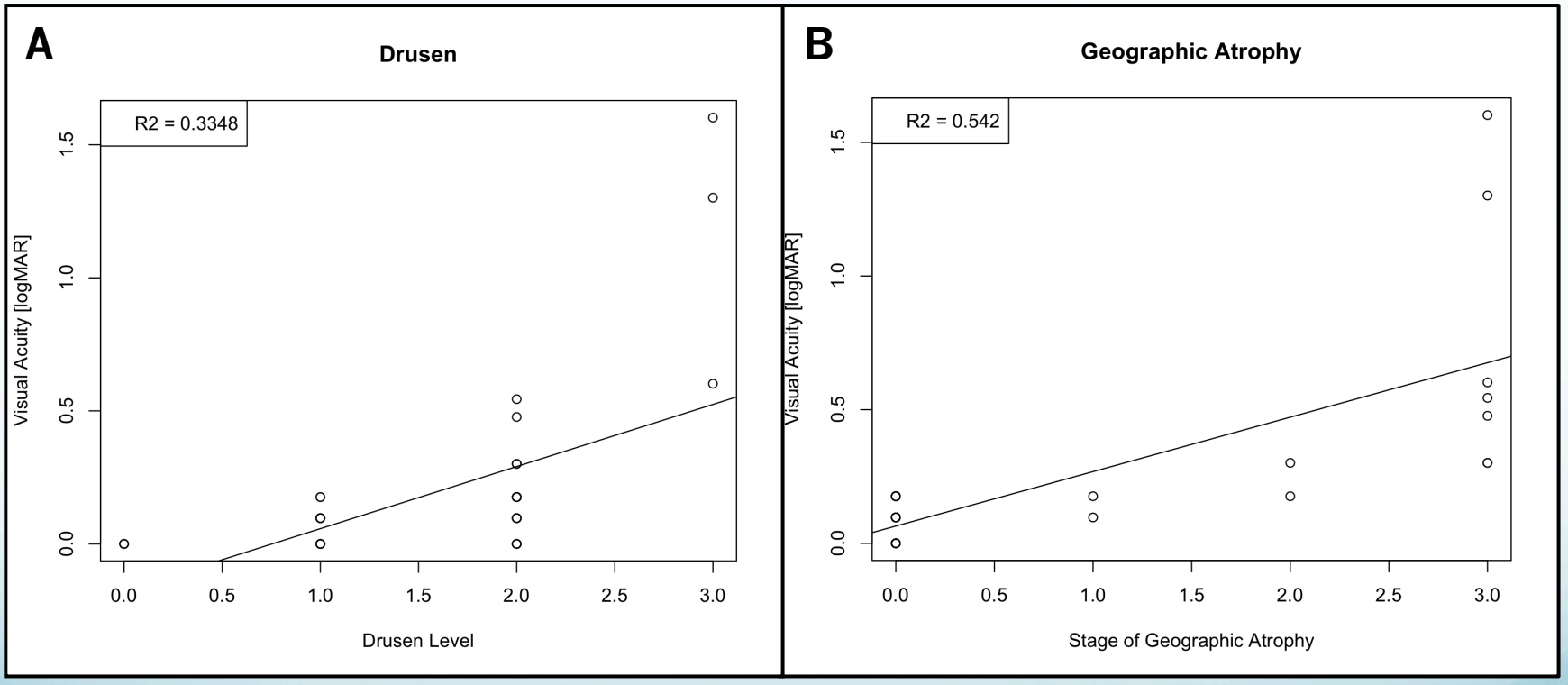

Figure 2. Both visible drusen (2A) and geographic atrophy (2B) correlated with visual acuity. Interaction between them seems apparent.

Provided Central Thickness had a Weaker Relationship with VA than was Expected

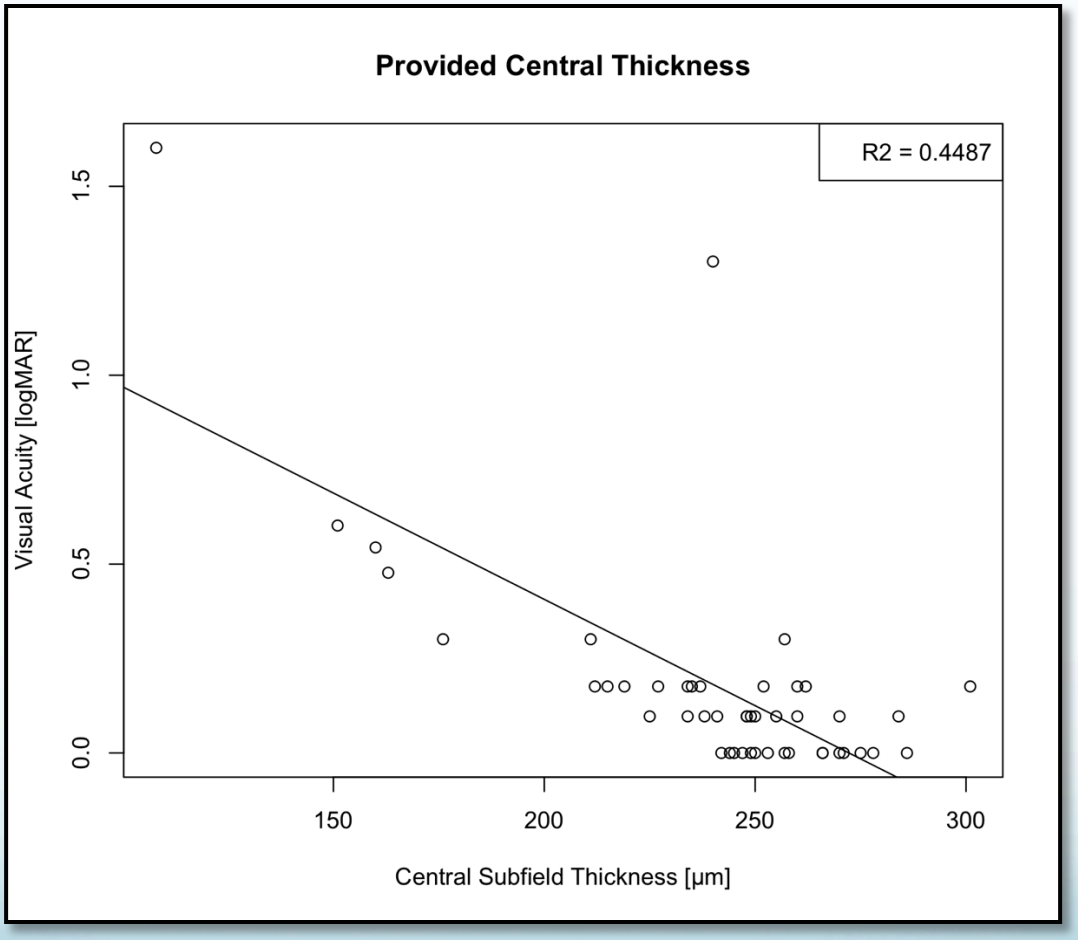

Figure 3 demonstrates that central thickness was not as an efficient of a predictor as visible pathology. Note the extreme outliers.

Analysis of Outliers Demonstrated Segmentation Errors

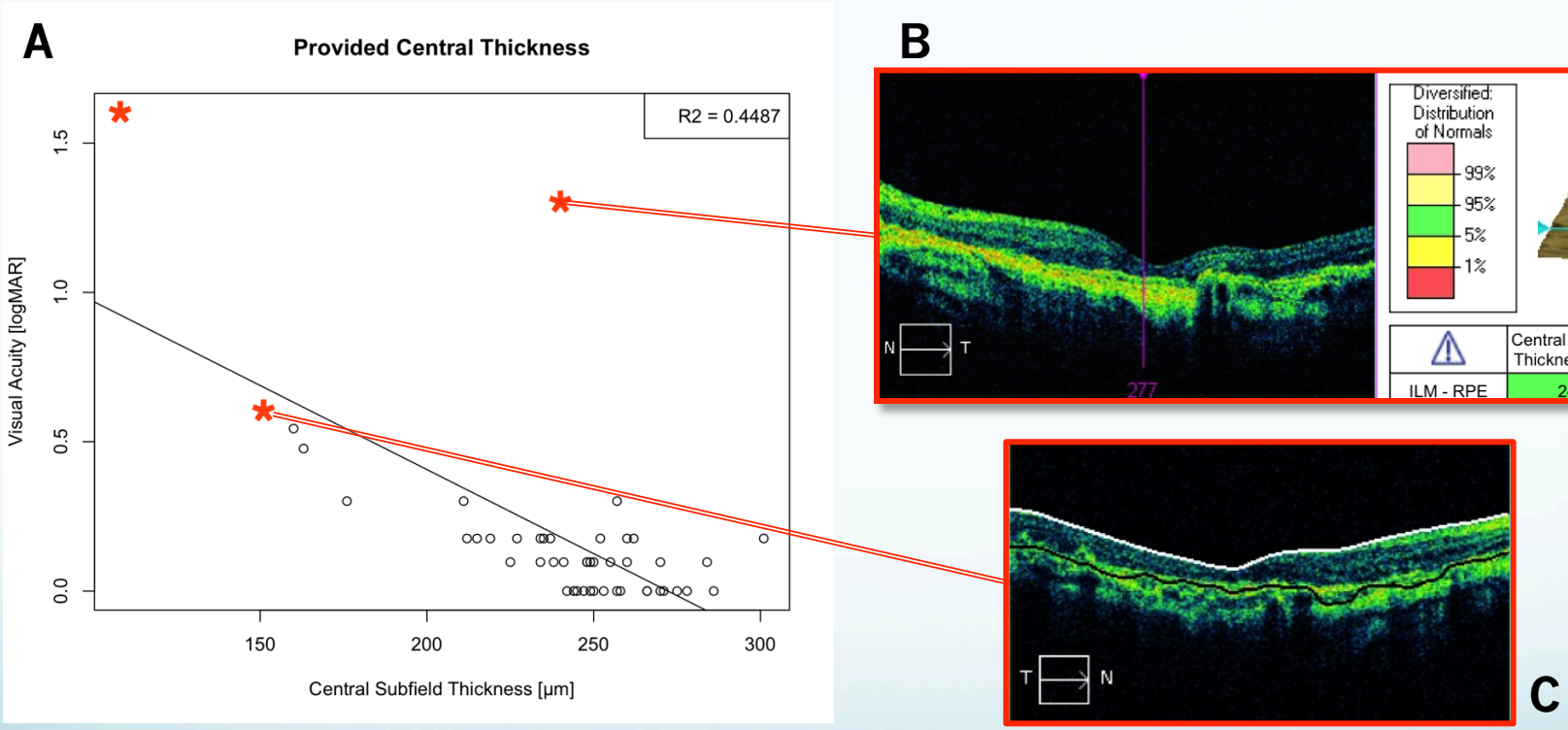

Figure 4 illustrates segmentation errors (4C) that manifested as improper thickness measurements (4B) in severe cases of GA.

Improper Thickness Measurements were Manually Corrected

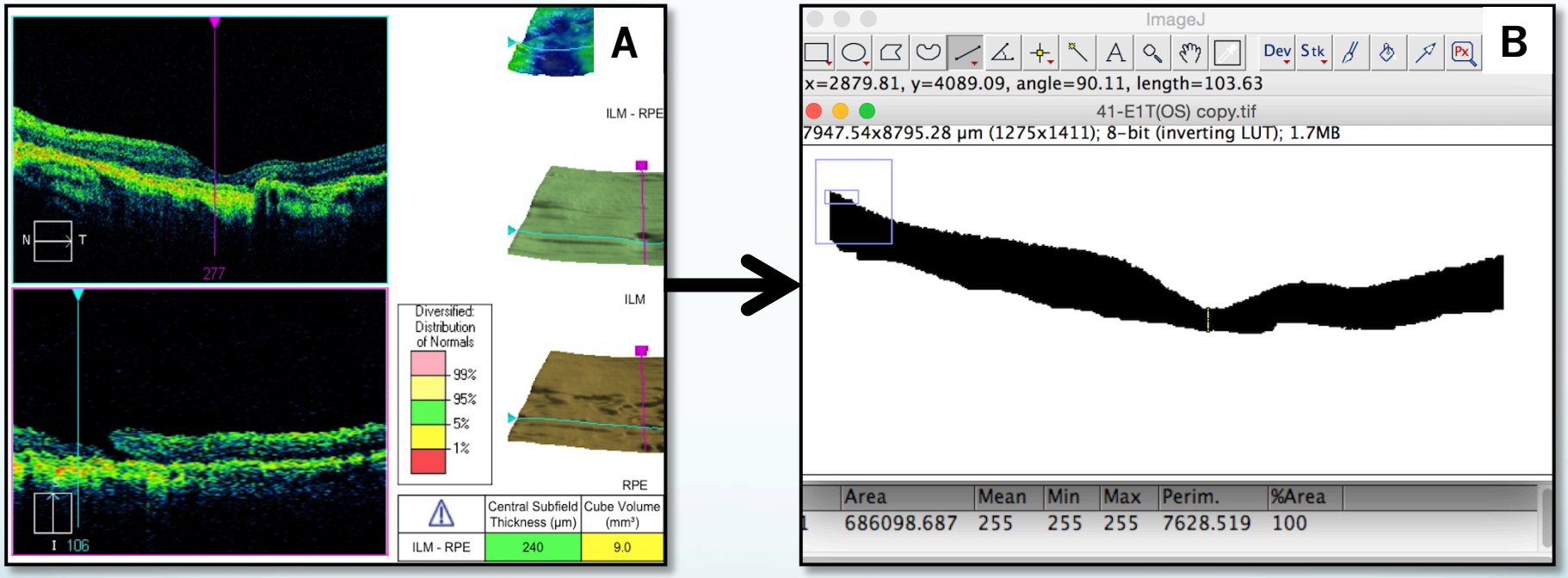

Figure 5 depicts the process in which improper thickness calculations (5A) were revised using *ImageJ* (5B) and image resolution values.

Correcting Central Thicknesses Meaningfully Improved their Correlation with VA

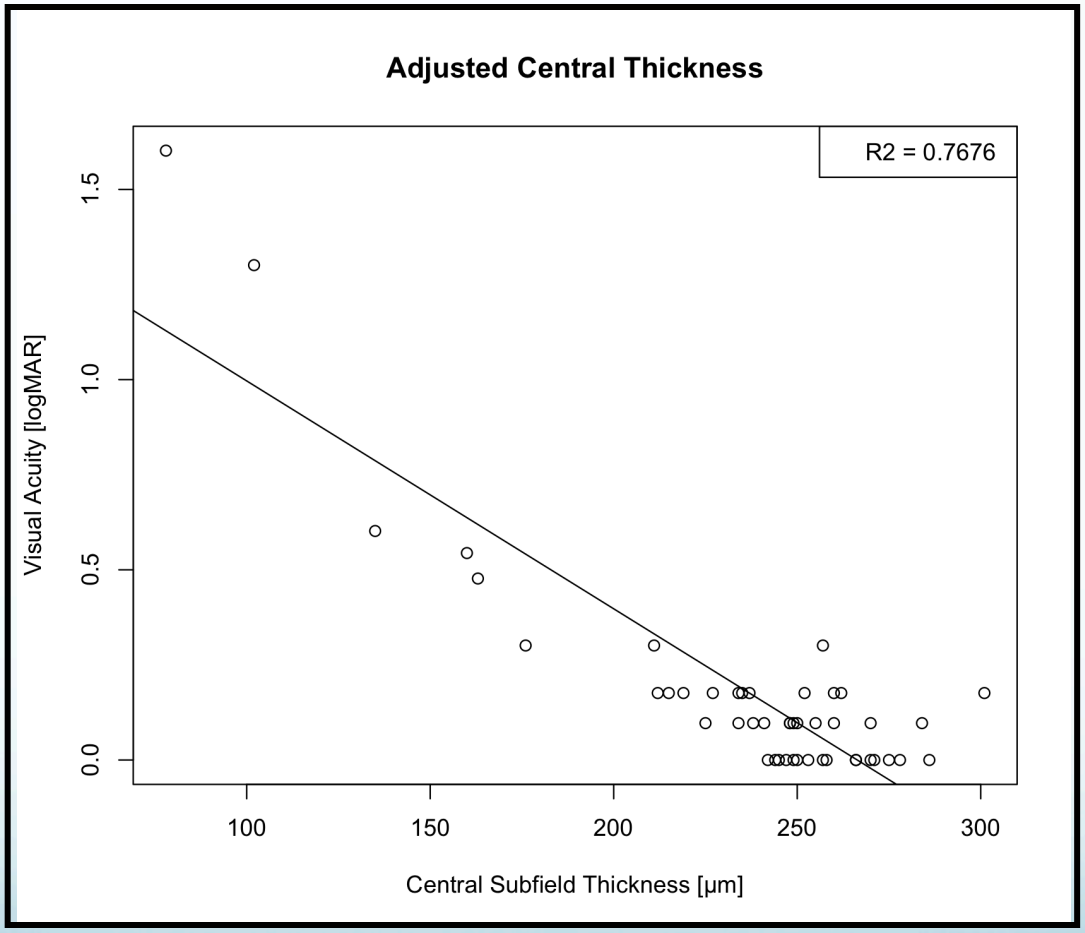

Figure 6 demonstrates the high correlation between adjusted central thickness values and best corrected visual acuity.

Adding Drusen to the CT Logistic Model Improves Predictive Ability

	Coefficient Estimate	Std. Error	t value	Pr(>|t|)	Significance
(Intercept)	1.286991	0.1471753	8.745	3.53E-11	***
Drusen	0.0893324	0.0292676	3.052	0.00384	**
Central Thickness	-0.0052628	0.0005049	-10.423	1.84E-13	***

	Multiple R2	Adjusted R2	F-statistic	p-value	Significance
Model Fit	0.8124	0.8039	95.27	2.20E-16	***

Figure 6 reveals that a significant predictive model of VA can be created when the influence of drusen on central thickness is weighted.

Relative Subfield Change Values for Longitudinal Data Correlate Well to VA

A

	Coefficient Estimate	Std. Error	t value	Pr(>|t|)	Significance
(Intercept)	0.1103453	0.0458939	2.404	0.02465	*
Net Central Change	-0.0308883	0.0086488	-3.571	0.00162	**
Net Inner Change	0.0004667	0.0082847	0.056	0.95556	
Net Outer Change	0.0057753	0.0103106	0.56	0.5808	

	Multiple R2	Adjusted R2	F-statistic	p-value	Significance
Model Fit	0.4894	0.4228	7.349	0.001263	**

B

	Coefficient Estimate	Std. Error	t value	Pr(>|t|)	Significance
(Intercept)	0.096412	0.033902	2.844	0.00919	**
Relative Central Change	-0.037204	0.010656	-3.491	0.00197	**
Relative Inner Change	-0.012398	0.014278	-0.868	0.3942	
Relative Outer Change	0.008143	0.019497	0.418	0.6801	

	Multiple R2	Adjusted R2	F-statistic	p-value	Significance
Model Fit	0.7192	0.6826	19.64	1.542e-06	***

Figure 7 demonstrates that net change values extracted from OCT analyses (7A) were less predictive of VA than relative change values (7B).

Final Model Using Only OCT Explanatory Variables was Highly Predictive of Visual Acuity

	Coefficient Estimate	Std. Error	t value	Pr(>|t|)	Significance
(Intercept)	1.3638098	0.2409477	5.66	9.21E-06	***
Central Thickness	-0.0025567	0.0006493	-3.937	0.000657	***
Volume	-0.0647024	0.0319215	-2.027	0.054415	.
% Central Change	-0.0249007	0.0043303	-5.75	7.40E-06	***

	Multiple R^2	Adjusted R^2	F-statistic	p-value	Significance
Model Fit	0.9087	0.8962	76.29	4.21E-12	***

Figure 8 reveals that OCT metrics in longitudinal studies can be used exclusively in model construction and yield high goodness-of-fit.

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Clinical Applications

- Highlights the interaction between drusen and geographic pathology in dry AMD cases.
- Suggests potential of improvements to OCT segmentation software.
  - Improved central thickness measurements in geographic atrophy cases yield more predictive results.
  - Use of relative change improves predictive results.
- Predictive models for best corrected visual acuity have clinical applications.
  - Can help determine when a patient is operable.
  - Importance of biological imaging moving forward.

Biological Interpretations

- Suggests net cellular degradation effects when drusen and geographic atrophy overlap.
- Lower visual acuities and geographic atrophy associated with higher rates of retinal thinning.
  - Suggests possible positive feedback mechanism for geographic atrophy.
- Potential to generate complete dry AMD progression models from clinical longitudinal studies.

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Summary

- **Introduction**: Statistical analysis of OCT outputs can be of clinical use in treating AMD patients.
- **Methods/Results**: Using a database of progressing AMD cases, predictive models for VA were yielded from OCT measurements.
- **Discussion**: Models such as those found in this study can improve clinical care and biological understanding of AMD.

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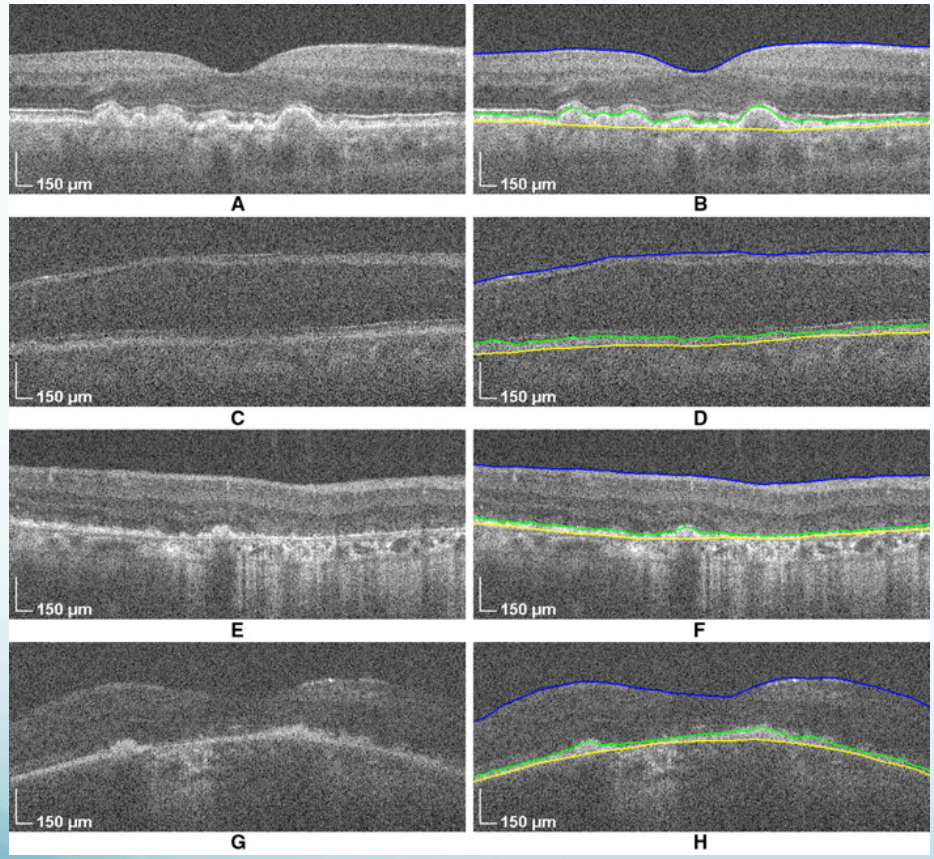
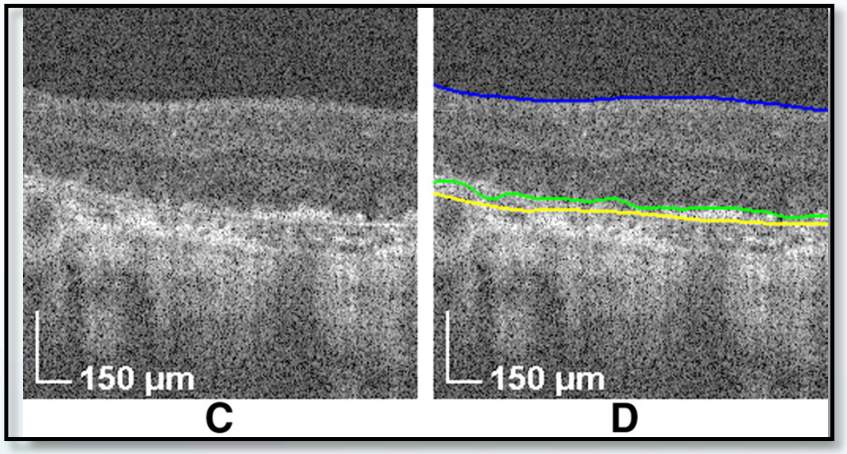
Acquiring More Precise Variables for Study



- AMD segmentation software can be used to calculate drusen volume.
- RPE thickness data can also provide more precise metrics of GA.
- Using these improved metrics in similar studies may reveal new and improved relationships.

Stephanie Chiu et al. *Invest Ophthalmol Vis Sci*. 2012.

Segmentation Limitations



- As in this study, segmentation often encounters issues in cases of advanced GA.
- This presents an interest in developing better methods for segmenting areas of GA moving forward.

Stephanie Chiu et al. *Invest Ophthalmol Vis Sci*. 2012.

Acknowledgments

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