

Personalized Prognosis in Early/Intermediate Age-Related Macular Degeneration based on Drusen Regression

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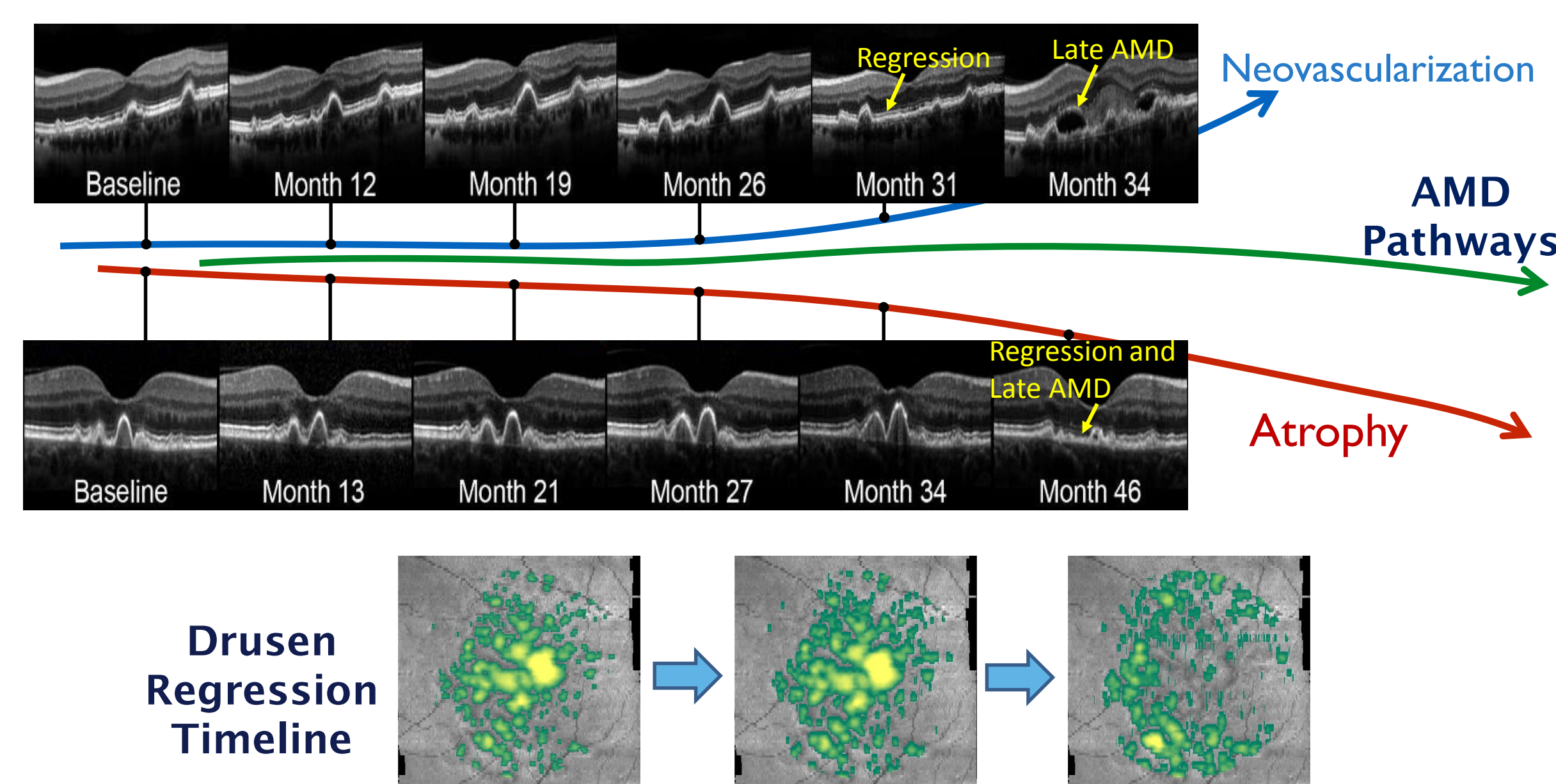
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Purpose and Motivation

- **Drusen are deposits** of cellular waste products that begin to accumulate between the retinal pigment epithelium (RPE) and the Bruch's membrane (BM).
- The presence of **drusen** is the **hallmark** of early/intermediate AMD, and their **sudden regression** is strongly associated with the onset of late AMD [1].
- The purpose is to develop a data-driven interpretable **predictive model of incoming drusen regression** from **longitudinal OCT datasets** using image-based features.

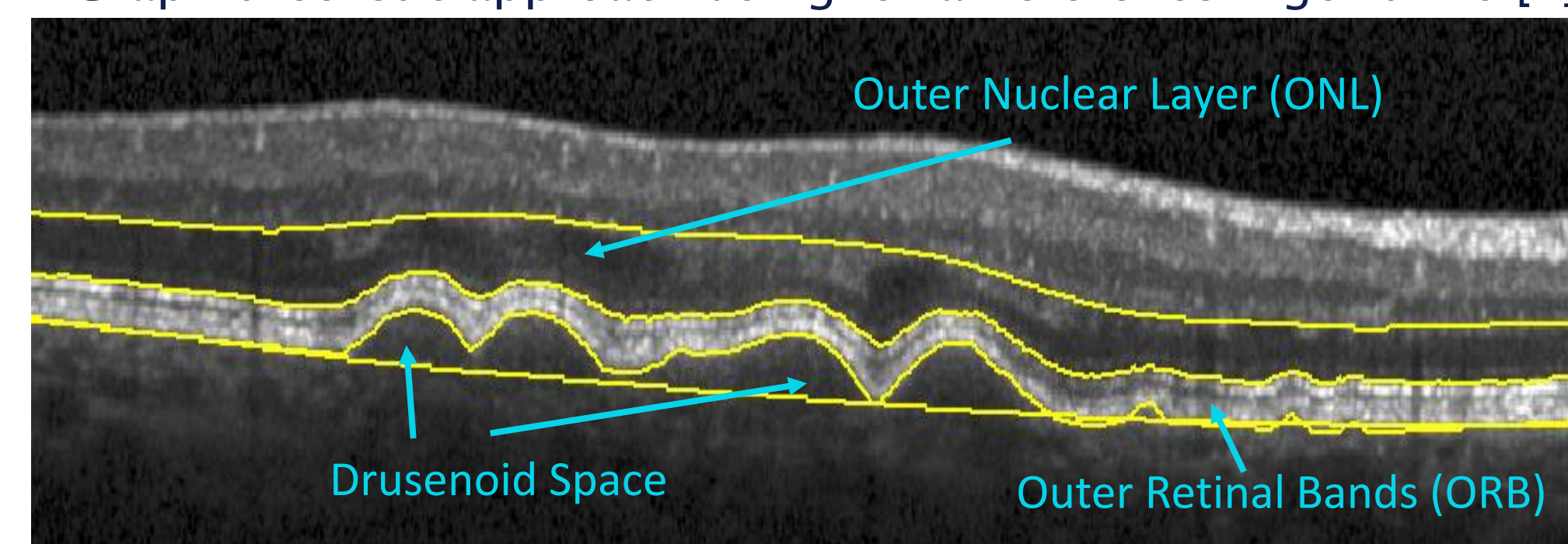


Methodology

- We developed a **machine-learning based method** that uses a large set of biomarkers to estimate the risk of regression at the level of an individual druse.
- The model relies on imaging biomarkers measured at **baseline and the first follow-up visit**, only three months apart.

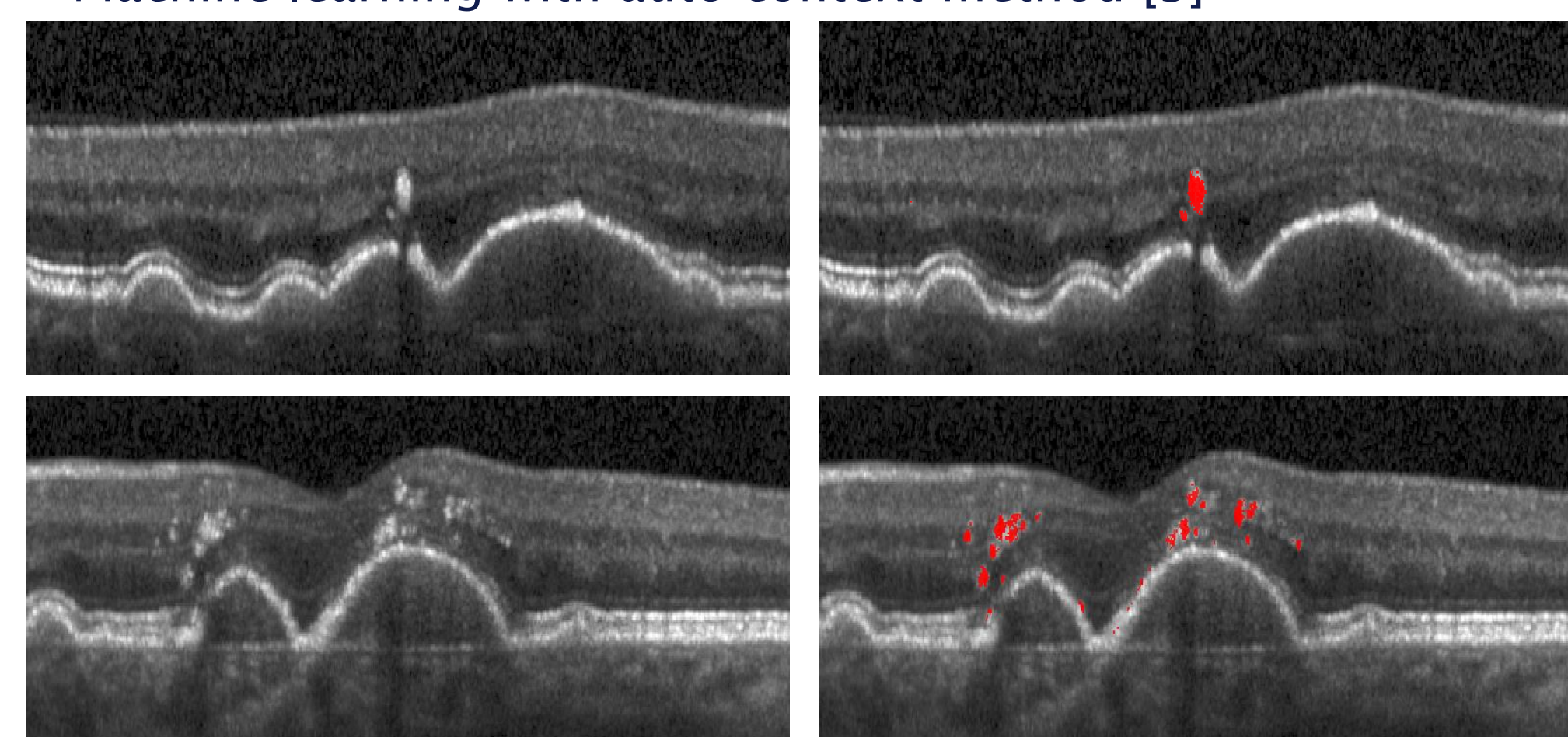
Outer Retina Segmentation

- Graph-theoretic approach using Iowa Reference Algorithms [2]



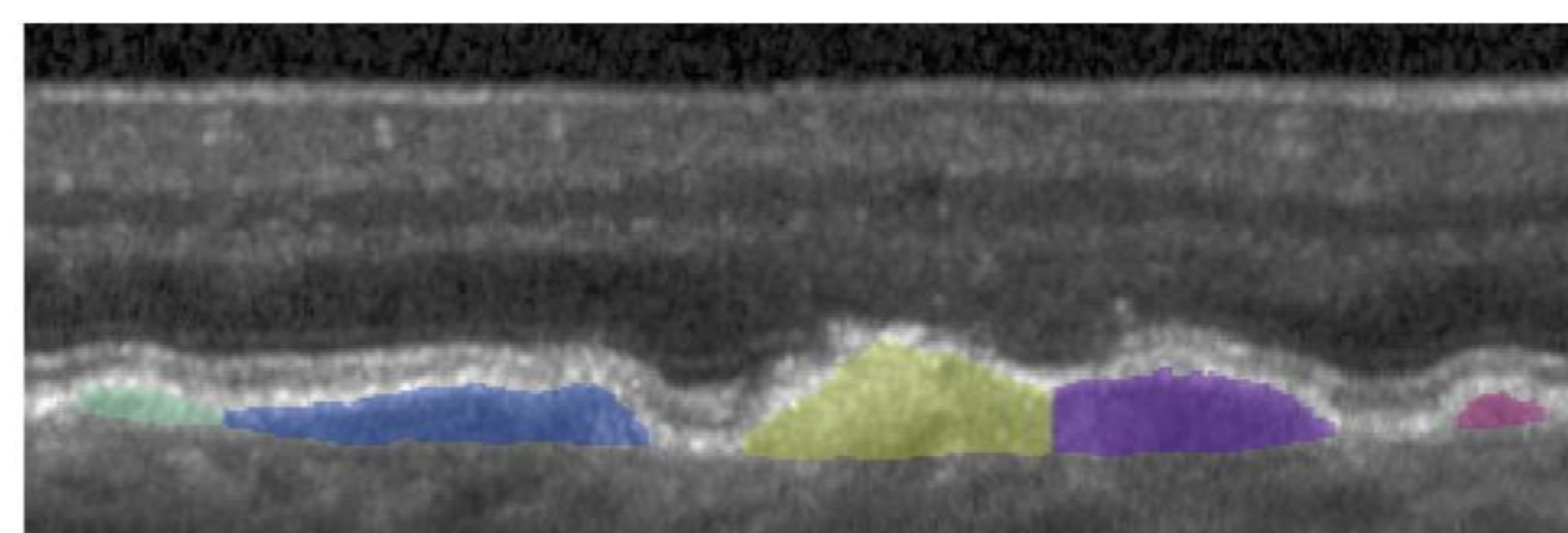
Hyperreflective Foci (HRF) Segmentation

- Machine learning with auto-context method [3]



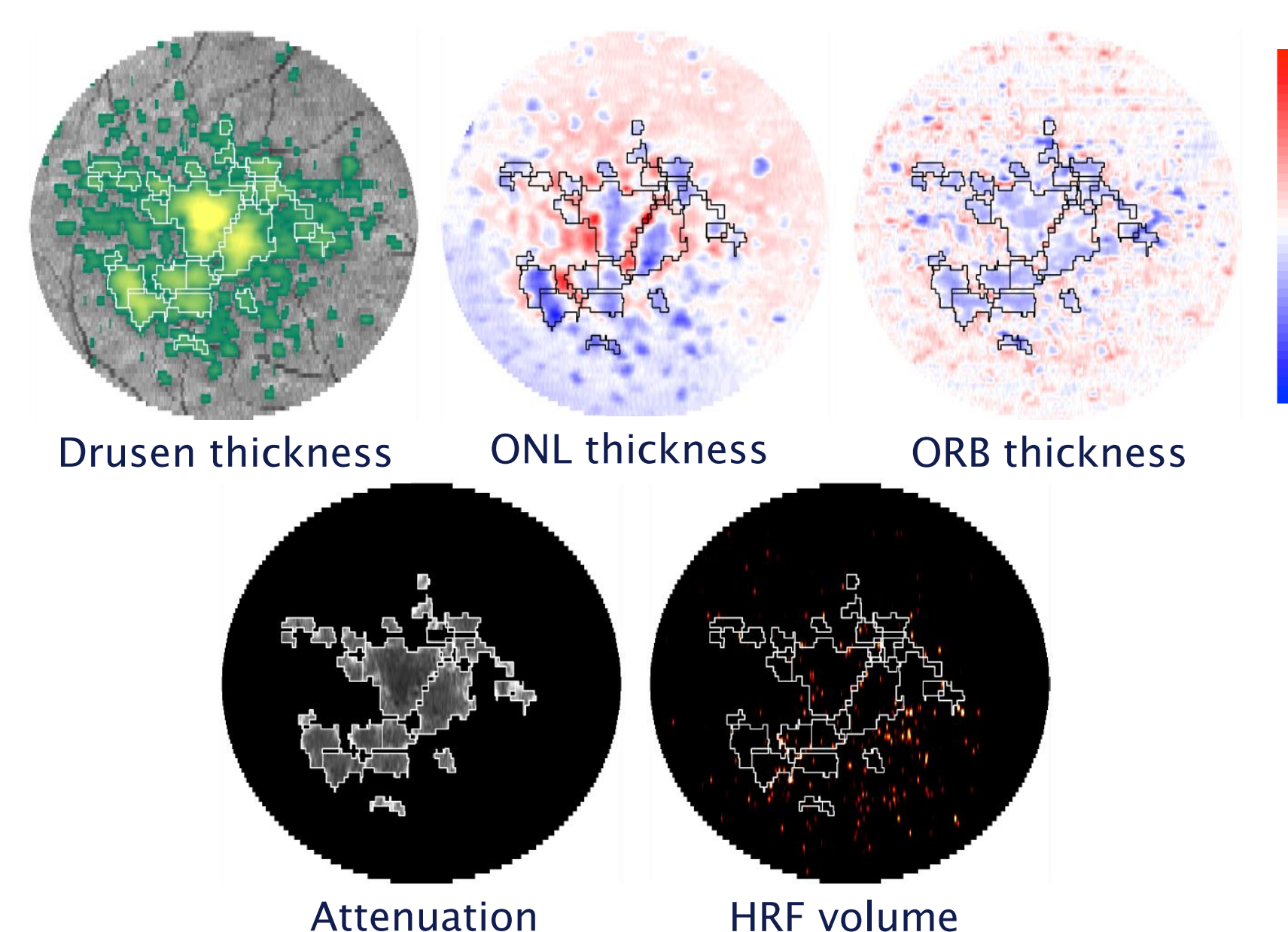
Individual Drusen Segmentation

- Confluent drusen separated into individual drusen
- Defines **individual drusen footprint**



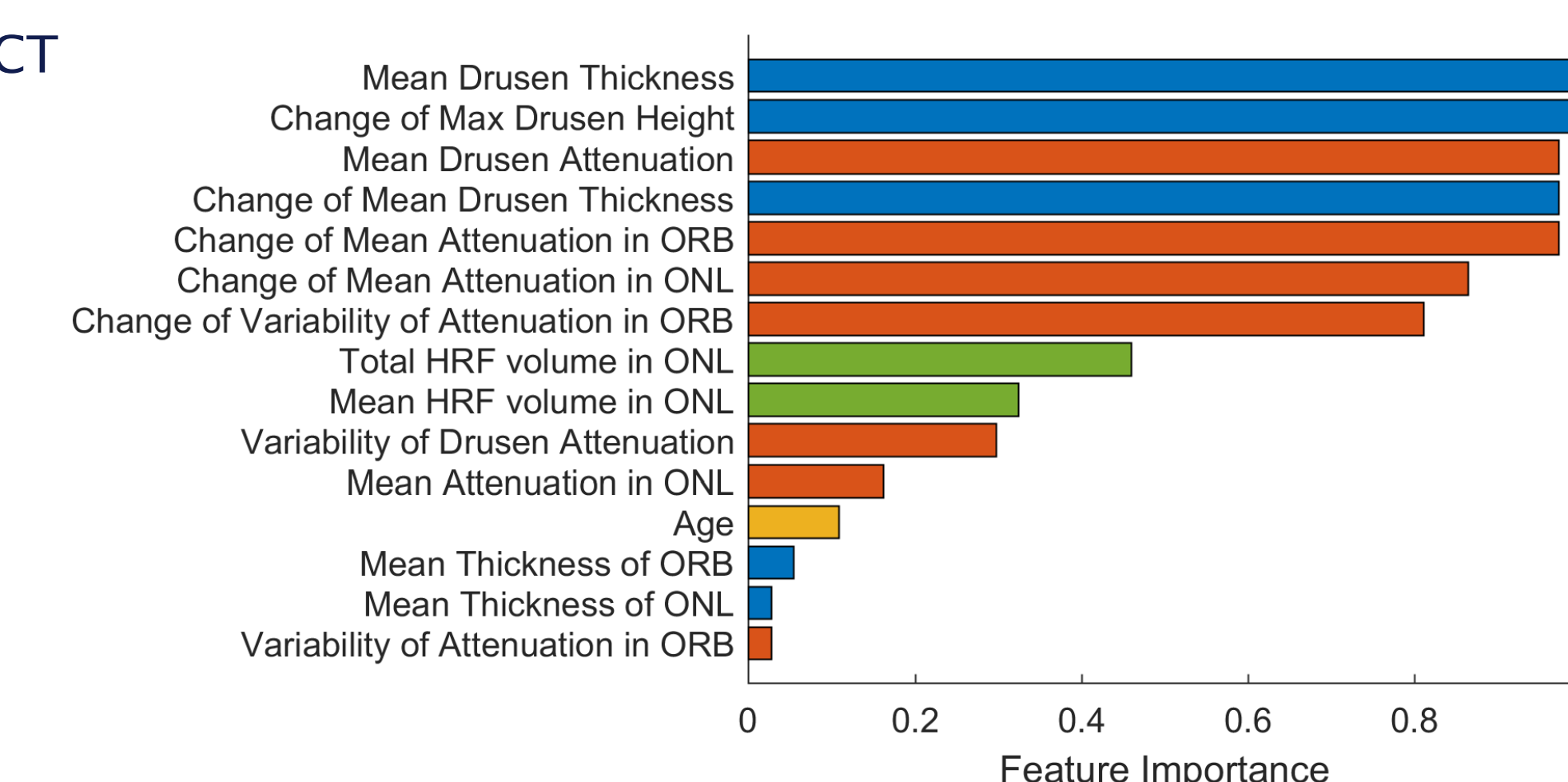
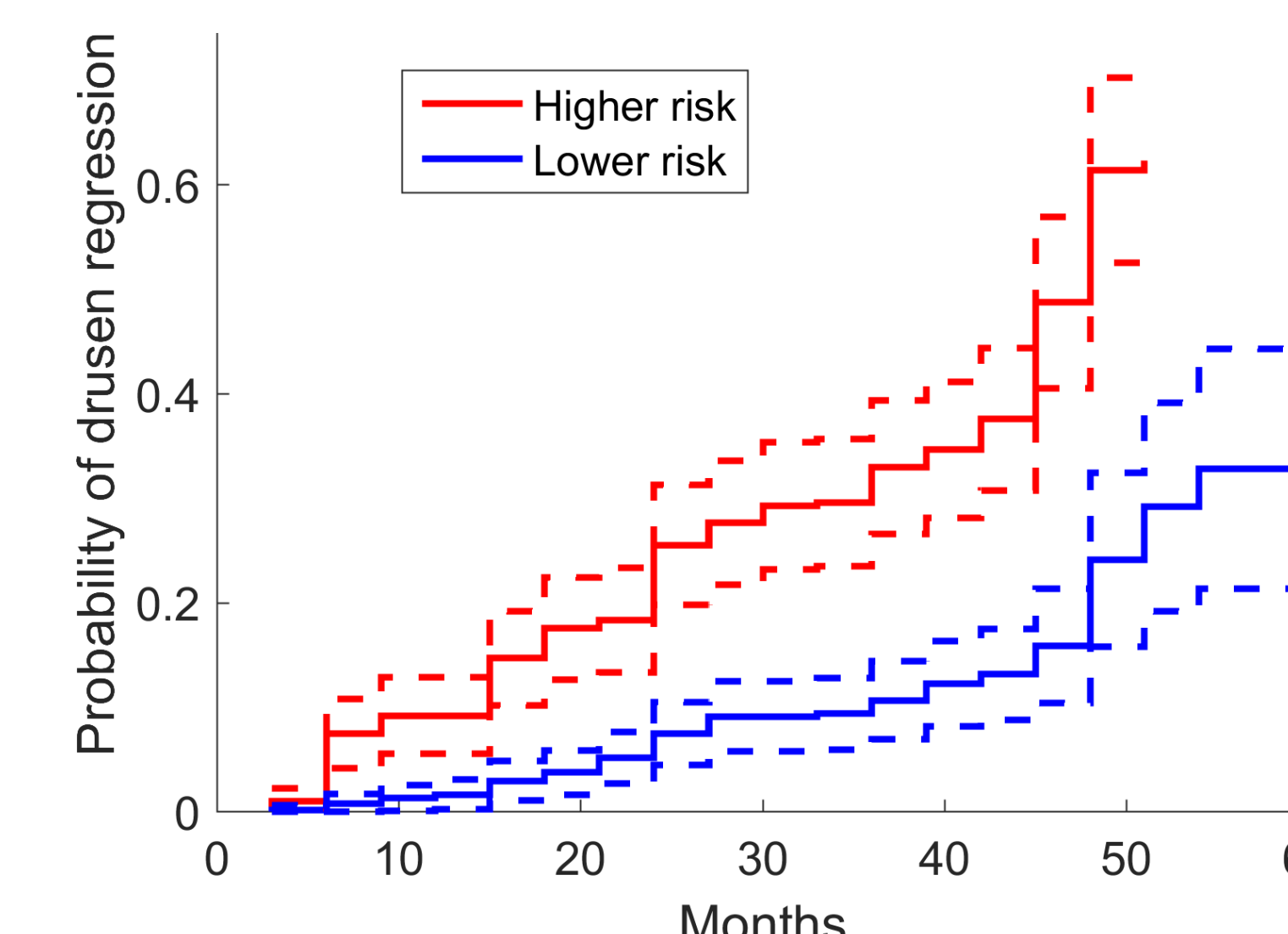
Predictive Model

- **Cox Proportional Hazards (CPH) Survival Model**
- Features of individual drusen describing: **Shape and size, attenuation, and overlying HRF volume**
- 16 features from the baseline + 16 difference to follow-up



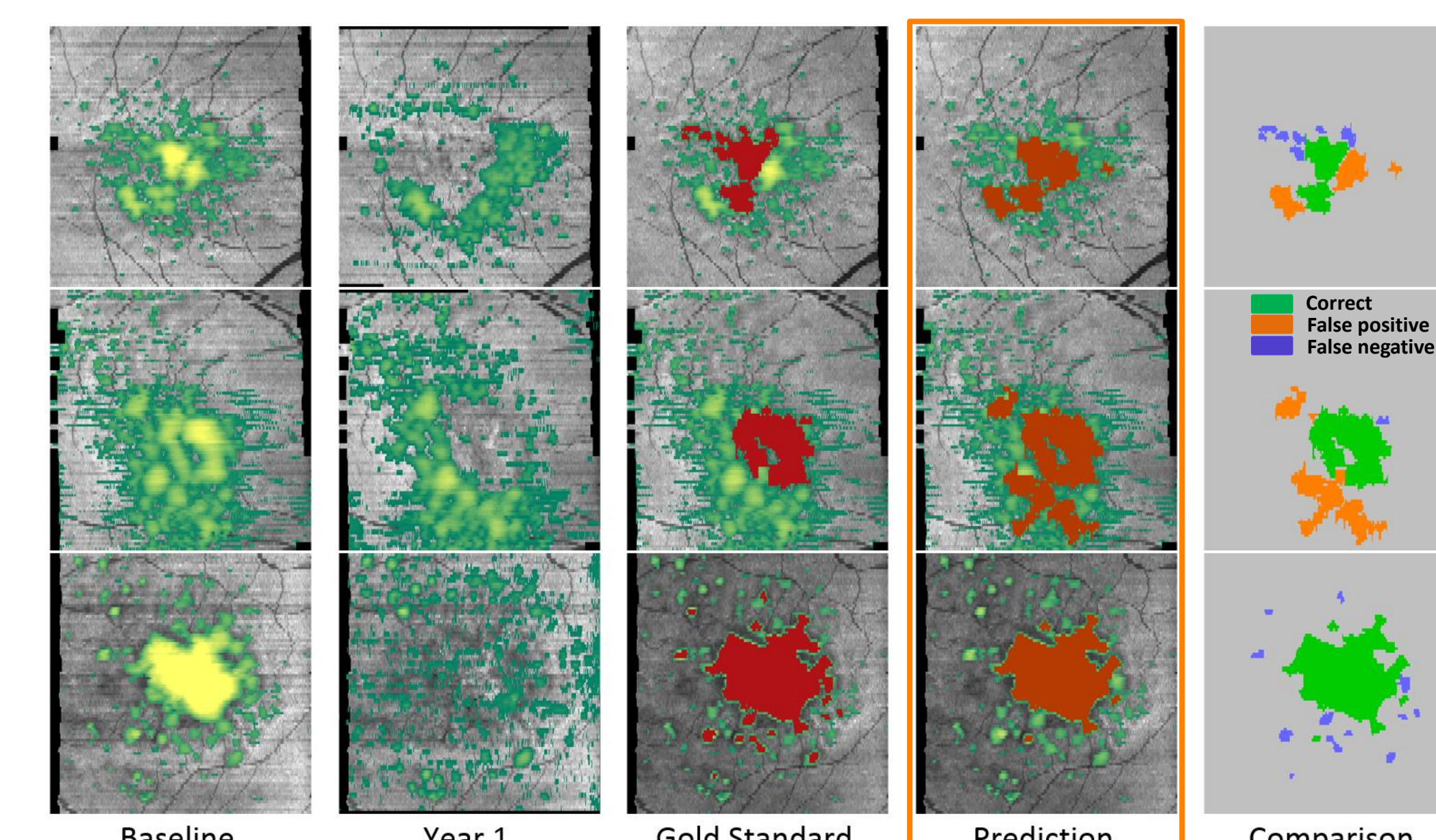
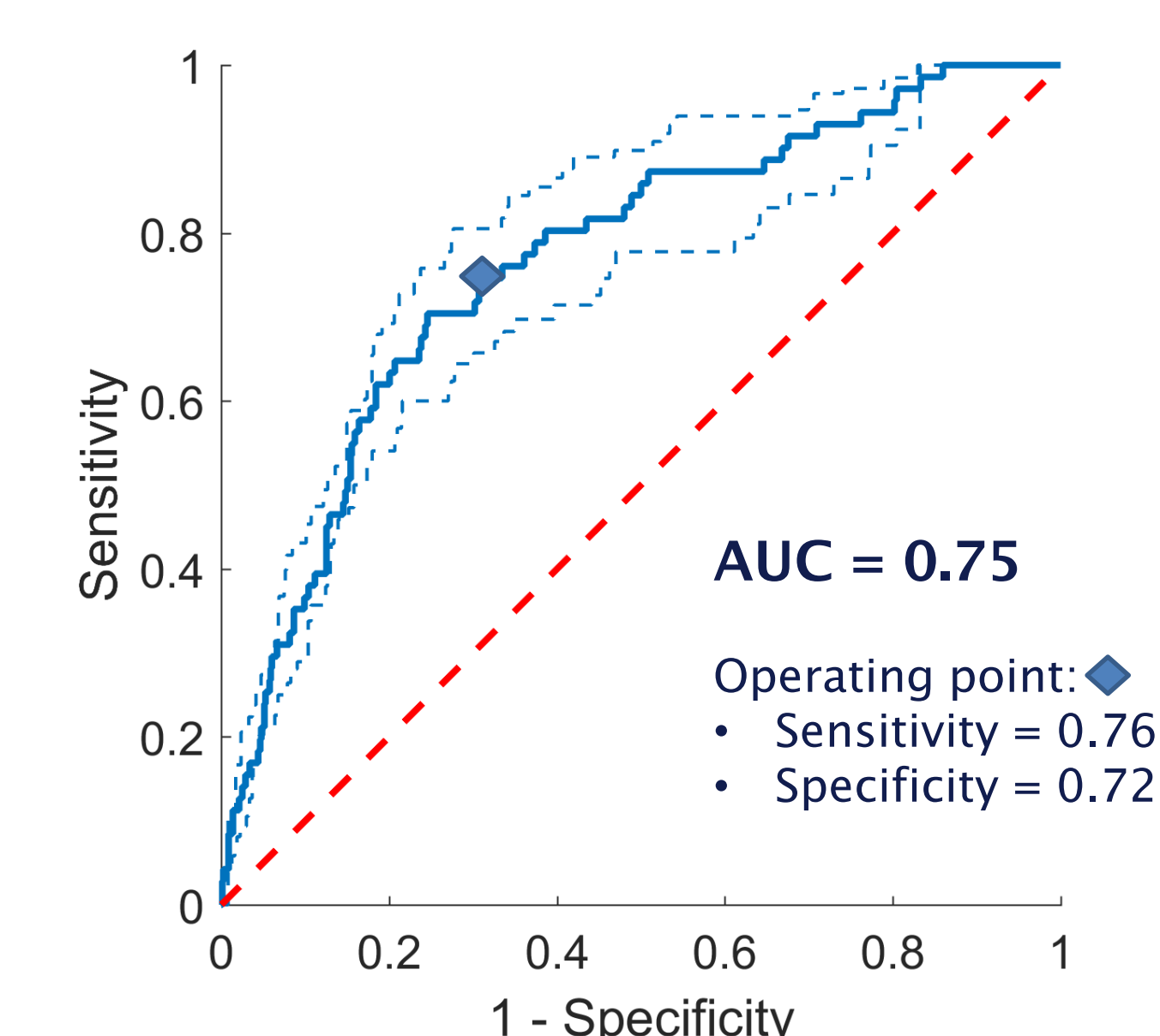
Results – Risk Stratification

- 61 eyes from 38 patients with **intermediate AMD**.
 - **3 month follow-up** for 1-5 years with Spectralis SD-OCT
- 944 drusen at baseline, out of which 249 regressed (26 %) during the follow-up and 74 (7.8 %) over the first year



Ranking of features involved in the risk estimate. Shape-based (blue), attenuation-based (red), HRF-based (green), and demographic-based (yellow). Mean drusen thickness, maximum drusen height and the attenuation had the greatest impact.

Results – Prediction at Year 1



Examples of drusen thickness maps and the **drusen regression prediction within one year period**. Each row represents one example eye.

Conclusions

- Prediction of drusen regression is possible (AUC~0.75).
- A promising step toward **identification of imaging biomarkers** of incoming drusen regression.
- Enables **prognostic value at the individual level**.
- The results are expected to:
 - **Advance our understanding** of AMD.
 - **Help identify patients at greater risk** of progression and thus adjust their personalized screening schedule.
 - **Help develop therapies** for early treatment before AMD advances, currently a large unmet clinical and social need.

References

- [1] Schlanitz et al. Drusen volume development over time and its relevance to the course of age-related macular degeneration. *Br J Ophthalmol*, 101:198-203 (2016)
- [2] Garvin et al. Automated 3-D Intraretinal Layer Segmentation of Macular Spectral-Domain OCT Images. *IEEE Trans Med. Imaging*, 2009; 28(9):1436-47
- [3] A. Montuoro, S. M. Waldstein, B. S. Gerendas, U. Schmidt-Erfurth, and H. Bogunović, "Joint retinal layer and fluid segmentation in OCT scans of eyes with severe macular edema using unsupervised representation and auto-context," *Biomed. Opt. Express* 8, 1874-1888 (2017)

Acknowledgments

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