



Unsupervised deep learning to identify markers in OCT of AMD

Sebastian M. Waldstein^{1*}, Philipp Seeböck^{1,2*}, René Donner², Bianca S. Gerendas¹, Amir Sadeghipour¹, Georg Langs^{1,2}, Aaron Osborne³, Ursula Schmidt-Erfurth¹

¹Christian Doppler Laboratory for Ophthalmic Image Analysis, Department of Ophthalmology and Optometry, Medical University of Vienna

²Computational Imaging Research Lab, Department of Biomedical Imaging and Image-guided Therapy, Medical University of Vienna

³Genentech, Inc, South San Francisco, CA, United States

*contributed equally

Introduction

Robust and sensitive imaging biomarkers remain an unmet medical need in the management of macular disease. Classical OCT biomarkers such as fluid are defined based on human intuition and experience. However, these conventional markers may not represent a comprehensive vocabulary to capture all important information in OCT images. Furthermore, they are inherently limited by pre-made hypotheses.

Patients and Methods

To complement the classical vocabulary of OCT biomarkers, we propose unsupervised deep learning to identify features inherent in OCT data in a completely unbiased fashion. We use auto-encoder methodology to automatically identify and categorize relevant features without human prior knowledge.

Approach:

- First we apply our method on the (local) A-scan level to capture fine-grained features in the image.
- Second, we auto-encode on (global) volume levels to capture simplified descriptions of entire OCT volumes.

Our method is trained on clinical trial data of 1,098 patients with treatment-naïve neovascular age-related macular degeneration. We evaluate the resulting biomarkers by correlating them with measures of visual function and markers of disease activity.

	BCVA	LLVA	CRT	IRC volume	SRF volume	PED volume	Lesion area	Leakage area
A-scan (local) level								
R ²	0.26	0.44	0.65	0.09	0.44	0.20	0.27	0.22
MAE	9.3 + 7.1	10.3 + 6.5	10.6 + 11.0	62 + 48	333 + 3.3e6	300 + 248	1.2 + 1.0	1.3 + 1.0
Volume (global) level								
R ²	0.29	0.46	0.64	0.19	0.27	0.28	0.21	0.15
MAE	8.9 + 7.3	9.7 + 7.0	10.9 + 11.0	54 + 50	342 + 412	286 + 237	1.4 + 1.0	0 + 1.1

Tab. 2: Multivariate regression analysis of (locally averaged) A-scan features and global volume features versus functional and morphologic variables. (MAE, mean absolute error)

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Results: Local features

The deep learning system identified 20 distinct (local) A-scan features that correlated well with retinal function and known OCT- and FA-markers of disease activity. Individual correlation coefficients reached from $r=0.36$ to $r=0.40$ (Table 1). Some markers (Figure) corresponded to known findings such as retinal fluid (a17) or subretinal hyperreflective material (a5), while another strongly predictive marker (a4) did not reveal an obvious link to known morphologic features. In a multivariate regression analysis, the markers achieved good correlation with visual function ($R^2=0.26$ (BCVA) and $R^2=0.44$ (LLVA), Table 2).

Results: Global features

On the global level, unsupervised learning resulted in a compact 20-dimensional description of the OCT volume. Correlation with visual function was superior to the A-scan level (multivariate $R^2=0.29$ (BCVA) and 0.46 (LLVA), Table 2), and stable for morphologic descriptors of disease activity.

Conclusion

Unsupervised deep learning enabled an unbiased identification and categorization of clinically important markers in OCT imaging that correlated well with visual acuity. Furthermore, it successfully achieved a compact (20-dim) representation of volumetric OCT data. The presented methodology makes big-data OCT analysis feasible by summarizing relevant imaging biomarkers, while discarding unnecessary information provided in the image.

	Functional		OCT							Fluorescein Angiography
	Best Corrected Visual Acuity	Least Luminescence Visual Acuity	Retinal Thickness	Intra-Retinal Cysts	Subretinal Fluid	Pigment Epithelial Detachment	Total Area of Lesion (Disk Area)	Total Area of Leakage from CNV (Disk Area)		
a1	-0.21	-0.19	0.30	0.07	0.25	0.15	-0.08	0.07		
a2	-0.20	-0.17	0.36	0.20	0.32	0.15	0.16	0.19		
a3	-0.10	-0.08	0.39	0.18	0.27	0.10	-0.27	0.17		
a4	0.30	0.36	-0.32	-0.07	-0.22	-0.24	0.34	-0.20		
a5	-0.31	-0.40	0.30	0.20	0.33	0.19	0.41	0.43		
a6	-0.10	-0.03	0.31	0.07	0.19	0.12	-0.17	-0.02		
a7	-0.08	-0.20	-0.05	-0.00	0.17	0.17	0.55	0.10		
a8	-0.08	-0.04	0.29	0.14	0.24	0.11	0.21	0.11		
a9	-0.17	-0.21	0.27	0.05	0.15	0.09	-0.30	0.27		
a10	-0.29	-0.27	0.54	0.20	0.41	0.24	-0.05	0.19		
a11	-0.05	-0.03	0.03	-0.02	0.11	0.07	-0.02	-0.08		
a12	-0.08	0.00	0.49	0.18	0.26	0.10	-0.35	0.06		
a13	-0.22	-0.26	0.41	0.27	0.39	0.22	0.73	0.43		
a14	0.05	0.03	-0.31	-0.04	-0.04	-0.09	0.43	-0.06		
a15	0.03	0.02	0.01	-0.04	0.08	-0.01	0.15	0.12		
a16	-0.02	-0.01	0.08	-0.04	0.16	0.10	0.01	-0.07		
a17	-0.28	-0.23	0.73	0.37	0.45	0.32	0.01	0.22		
a18	-0.23	-0.26	0.18	0.00	0.24	0.17	-0.00	0.13		
a19	-0.19	-0.16	0.28	0.10	0.28	0.15	0.02	0.01		
a20	-0.22	-0.19	0.39	0.18	0.33	0.21	0.07	0.14		

Tab. 1: Spearman correlation coefficients between the 20 identified local features (mean activation, central 1.5mm area) and functional variables as well as OCT- and FA- measures of disease activity.

■ = negative ■ = positive

Figure: Example patients for selected unsupervised features (maps) in comparison to known features (IRC, SRF, PED, retinal thickness).

