Deep-learning-based Prediction of Late Age Related Macular Degeneration Progression

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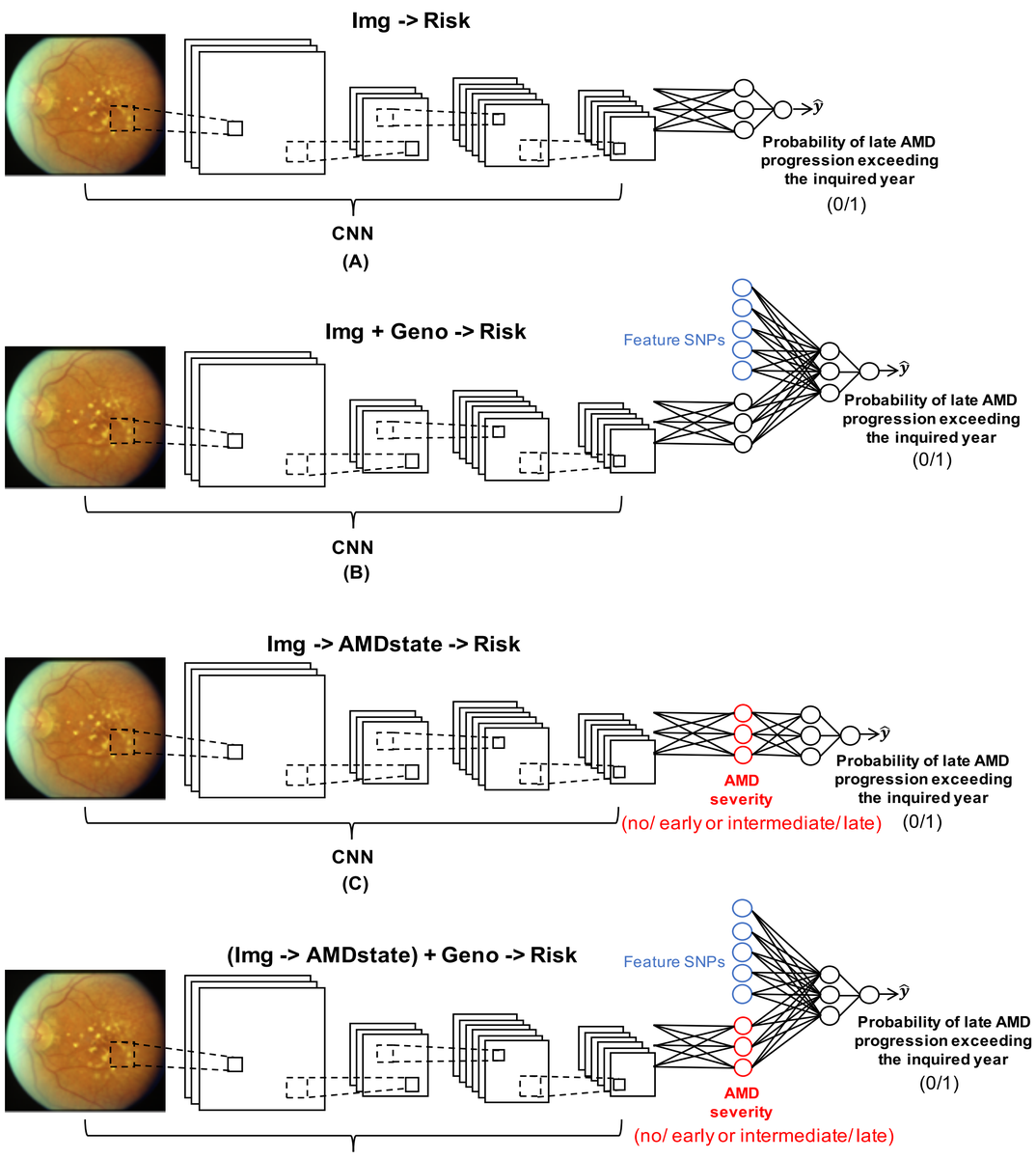
Background

- **A**ge-related **M**acular **D**egeneration (AMD) is a heritable neurodegenerative disease and a leading cause of blindness in the elderly population in the United States.
- AMD severity is mainly diagnosed by color fundus images and recent studies have shown the success of machine learning methods in predicting AMD progression using image data.
- We jointly used genotypes and fundus images to dynamically predict an eye as having progressed to late AMD with a modified deep convolutional neural network (CNN).
- Study Population: Caucasian patients from AREDS (Age-Related Eye Disease study)[1] including genotyping data, longitudinal color fundus photographs, and disease severity assessment over a period of 12 years.

Method



- Convolutional neural network (CNN) of retinal fundus images along with feature SNPs and AMD severity for the prediction of late-AMD progression exceeding certain inquired years.

Results

Table 1. Characteristics of the participants

	AREDS	Training	Test
Subject-level	1,351 subjects	1,223 subjects	128 subjects
Observation-level			
Fundus images used for prediction with progression cutoff			
2 years (n)	27,499	24,654	2,845
3 years (n)	25,862	23,170	2,692
4 years (n)	24,287	21,709	2,578
5 years (n)	22,435	20,041	2,394
6 years (n)	20,240	18,118	2,122
7 years (n)	18,066	16,172	1,894

References

1. Age-Related Eye Disease Study Research G. The Age-Related Eye Disease Study (AREDS): design implications. AREDS report no. 1. Controlled clinical trials. 1999;20(6):573-600.
2. Qi Yan, Daniel E. Weeks, Hongyi Xin, Heng Huang, Anand Swaroop, Emily Y. Chew, Ying Ding, Wei Chen. “Deep-learning-based Prediction of Late Age-Related Macular Degeneration Progression”. medRxiv preprint 19006171.

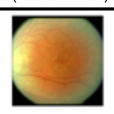
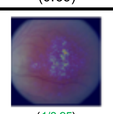
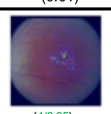
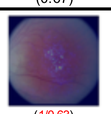
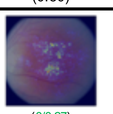
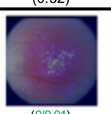
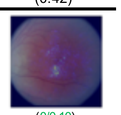
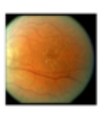
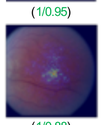
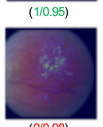
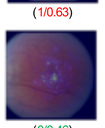
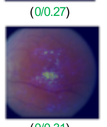
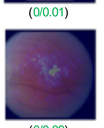
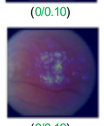
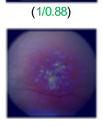
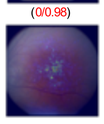
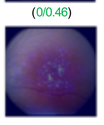
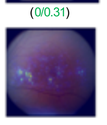
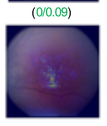
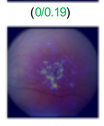
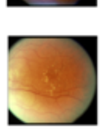
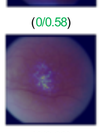
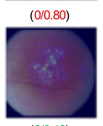
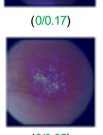
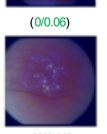
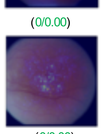
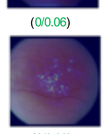
Results (continued)

Table 2. AUC values (95% CI) of the prediction of probability of late-AMD progression exceeding the inquired years for four models

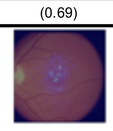
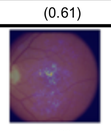
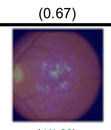
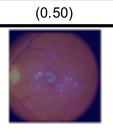
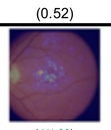
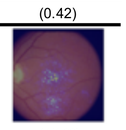
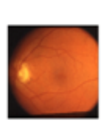
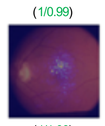
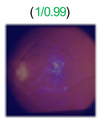
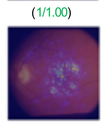
		2 years	3 years	4 years	5 years	6 years	7 years
AUC values	Image -> Risk*	0.81 (0.79-0.83)	0.81 (0.79-0.83)	0.81 (0.79-0.83)	0.79 (0.78-0.81)	0.83 (0.81-0.85)	0.84 (0.82-0.86)
	Image + Geno -> Risk	0.84 (0.83-0.86)	0.85 (0.83-0.86)	0.83 (0.82-0.85)	0.84 (0.82-0.85)	0.85 (0.83-0.86)	0.85 (0.83-0.87)
	Image -> AMDstate# -> Risk	0.81 (0.79-0.83)	0.80 (0.78-0.82)	0.79 (0.77-0.81)	0.82 (0.80-0.84)	0.82 (0.80-0.84)	0.84 (0.83-0.86)
	(Image -> AMDstate) + Geno -> Risk	0.85 (0.84-0.87)	0.86 (0.84-0.87)	0.86 (0.84-0.87)	0.85 (0.84-0.87)	0.85 (0.84-0.87)	0.85 (0.84-0.87)

- The probability of late-AMD progression exceeding the inquired years.
- # No, early or intermediate, or late AMD (3 levels).

- This subject progressed to late AMD after 4.8 years of follow-up.

Visit year	Time left to censored time (4.8 years)	Original images	Saliency maps (true label/predicted probability)					
			0: <2 years 1: >=2 years	0: <3 years 1: >=3 years	0: <4 years 1: >=4 years	0: <5 years 1: >=5 years	0: <6 years 1: >=6 years	0: <7 years 1: >=7 years
		(Youden index)	(0.69)	(0.61)	(0.67)	(0.50)	(0.52)	(0.42)
0	4.8		 (1/0.95)	 (1/0.95)	 (1/0.63)	 (0/0.27)	 (0/0.01)	 (0/0.10)
2	2.8		 (1/0.88)	 (0/0.98)	 (0/0.46)	 (0/0.31)	 (0/0.09)	 (0/0.19)
4	0.8		 (0/0.58)	 (0/0.80)	 (0/0.17)	 (0/0.06)	 (0/0.00)	 (0/0.06)
5.9	0		 (0/0.03)	 (0/0.10)	 (0/0.05)	 (0/0.05)	 (0/0.00)	 (0/0.00)

- This subject was censored after 11.1 years of follow-up.

Visit year	Time left to censored time (11.1 years)	Original images	Saliency maps (true label/predicted probability)					
			0: <2 years 1: >=2 years	0: <3 years 1: >=3 years	0: <4 years 1: >=4 years	0: <5 years 1: >=5 years	0: <6 years 1: >=6 years	0: <7 years 1: >=7 years
		(Youden index)	(0.69)	(0.61)	(0.67)	(0.50)	(0.52)	(0.42)
0	11.1		 (1/0.99)	 (1/0.99)	 (1/1.00)	 (1/0.99)	 (1/1.00)	 (1/1.00)
1.9	9.2		 (1/1.00)	 (1/0.99)	 (1/0.99)	(1/0.99)	(1/1.00)	(1/1.00)
3.8	7.3		(1/0.99)	(1/1.00)	(1/0.99)	(1/0.99)	(1/1.00)	(1/1.00)
5.8	5.3		(1/0.99)	(1/1.00)	(1/0.99)	(1/0.99)	(NA/1.00)	(NA/1.00)

- This subject developed late AMD before enrollment.

Visit year	Time left to late AMD progression (0 years)	Original images	Saliency maps (true label/predicted probability)					
			0: <2 years 1: >=2 years	0: <3 years 1: >=3 years	0: <4 years 1: >=4 years	0: <5 years 1: >=5 years	0: <6 years 1: >=6 years	0: <7 years 1: >=7 years
		(Youden index)	(0.69)	(0.61)	(0.67)	(0.50)	(0.52)	(0.42)
0	0		(0/0.00)	(0/0.01)	(0/0.07)	(0/0.03)	(0/0.01)	(0/0.06)
1.9	0		(0/0.01)	(0/0.02)	(0/0.04)	(0/0.05)	(0/0.00)	(0/0.02)
7.8	0		(0/0.00)	(0/0.01)	(0/0.00)	(0/0.00)	(0/0.00)	(0/0.00)
10	0		(0/0.01)	(0/0.01)	(0/0.01)	(0/0.00)	(0/0.00)	(0/0.00)
12	0		(0/0.01)	(0/0.00)	(0/0.01)	(0/0.02)	(0/0.00)	(0/0.00)

Implementation and Availability

- The prediction models[2] are available at https://github.com/QiYanPitt/AMDprogressCNN
- A web-based application is also available at http://www.pitt.edu/~qiy17/amdprediction.html