Automatic Retinal image Analysis (ARIA) to Detect White Matter Hypertintensities in Stroke- and Dementia-free Healthy Subjects – A Cross-validation Study

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Introduction

Retinal imaging with artificial-intelligence assisted analysis has the potential to become a simple and reliable tool for screening population-at-risk of cerebrovascular disease and dementia.

Objective

To develop an algorithm with automatic retinal imaging in identifying asymptomatic subjects with high burden of white matter hyperintensities (WMH).

Methods

We performed automatic retinal image analysis (ARIA) in 180 community dwelling, stroke and dementia-free healthy subjects. ARIA is fully automatic and validated in separate disease cohorts. WMH on MRI brain was graded using ARWMC scale by an independent assessor. 126(70%) subjects were randomly selected for model building, 27(15%) for model cross-validation, and remaining 27(15%) for testing; all 180 subjects were used for evaluation of model accuracy to predict WMH burden.

ARIA – simple acquisition of retinal fundus image

Table 1. Summary of Demographic and Clinical Data Severe WMH (Global ARWMC ≥ 2)

	Global ARWMC 0-1	Global ARWMC 2-3	p-value
N	124	56	
Age (Median/IQR) ^a	69.00 (66.25 - 73.00)	71.00 (67.00 - 74.00)	0.083
Education (Median/IQR) ^a	7.00 (4.00 - 12.00)	7.00 (3.25 - 12.00)	0.932
Male (N/%) ^b	46 (37.1%)	24 (42.9%)	0.463
MoCA (Median/IQR) ^a	23.00 (21.00 - 26.00)	22.00 (19.00 - 25.00)	0.053
Hypertension (N/%) ^b	62 (50.0%)	44 (78.6%)	<.001
Diabetes Mellitus (N/%) ^b	17 (13.7%)	14 (25.0%)	0.063
Hyperlipidemia (N/%) ^b	30 (24.2%)	17 (30.4%)	0.383
IHD (N/%) ^c	5 (4.0%)	3 (5.4%)	0.705
Smoker (N/%) ^c			0.735
Non-smoker	105 (84.68%)	46 (82.14%)	
Past smoker	17 (13.71%)	8 (14.29%)	
Current smoker	2 (1.61%)	2 (3.57%)	
Alcoholism (N/%) ^c			
Non-drinker	105 (84.68%)	50 (89.29%)	0.477
Occasional (1 drink/wk - month)	8 (6.45%)	4 (7.14%)	
Modest drinker (1-6 /wk)	11 (8.87%)	2 (3.57%)	
WMH volume (Median/IQR) ^a	2.53 (1.64 - 4.34)	10.01 (4.89 - 18.17)	<.001
Log-transformed WMH volume (Mean/IQR) ^a	0.93 (0.50 - 1.47)	23.00 (1.59 - 2.90)	<.001
Presence of Lacunes (Median/IQR) ^c	2 (1.6%)	8 (14.3)	0.002
Presence of Microbleed (Median/IQR) ^b	31 (25.0%)	19 (33.9%)	0.281

Results

All 180 subjects completed ARIA with successful analysis. The mean age was 70.3 $\pm$ 4.5 years, 70(39%) were male. Risk factor profiles were: 106(59%) hypertension, 31(17%) diabetes, and 47(26%) hyperlipidemia. Severe WMH (defined as global ARWMC grading ≥ 2) was found in 56(31%) subjects. The performance (sensitivity, SN; and specificity, SP) for model building (SN 96.7%, SP 80.6%), model validation (SN 100%, SP 87.5%), and testing (SN 100%, SP 83.3%) was excellent. The overall performance was SN 97.6% and SP 82.1%, with PPV 94% and NPV 92%. There was good correlation with WMH volume (log-transformed) in the building ($R=0.92$), validation ($R=0.81$), testing ($R=0.88$) and overall ($R=0.90$) models, respectively.

Table 2. ARIA-SVD Model performance

Analysis 1 of 1		TARGET DISORDER			
		WMH grades 0-1 vs. 2-3			
		Present	Absent		
TEST	Positive	46	3	95% Confidence Intervals	
		a	b		
ARIA-WMH grade 0-1 vs. 2-3	Negative	10	121		
		c	d		
SENSITIVITY		a / (a+c)		82 %	72 to 92
SPECIFICITY		d / (b+d)		98 %	95 to 100
Pre-test Probability ("Prevalence"):		(a+c)/(a+b+c+d)		31 %	24 to 38
Positive Predictive Value:		a / (a+b)		94 %	87 to 100
Negative Predictive Value:		d / (c+d)		92 %	88 to 97
LIKELIHOOD RATIO +		sens / (1 - spec)		33.95	11.03 to 104.53
LIKELIHOOD RATIO -		(1 - sens) / spec		0.18	0.10 to 0.32

Table 3. Correlation with WMH volume (log-transformed)

Discussion and Conclusion

We developed a robust algorithm to automatically evaluate retinal fundus image that can identify community subjects with high WMH burden .

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