

Appearance-based Approach to Extract an Age-related Biomarker from Retinal Images

R. Bock¹, J. Meier¹, L. G. Nyúl¹, S. Wärntges², G. Michelson², J. Hornegger¹

¹Institute of Pattern Recognition

²Department of Ophthalmology

University of Erlangen-Nuremberg,

Erlangen, Germany

email: ruediger.bock@informatik.uni-erlangen.de

Background

The concept of biological age was established to quantify the true global state of an aging organism. Because of the complexity of aging, the biological age is commonly understood as a combination of several biomarkers [1].

Valid biomarkers correlate with chronological age and are influenced by risk factors.

Purpose

We show that purely data-driven approaches are able to extract medically relevant information. We apply this technique to extract a valid biomarker from color fundus images of the human eye.

Materials

For the evaluation, we used fundus images from a population-based screening project called TalkingEyes. The color images were acquired by a Kowa nonmyd-alpha digital fundus camera (1600x1216 pixels, 45° FOV, optic nerve head centered positioning).

Methods

The appearance-based feature extraction applies Principal Component Analysis on the intensities [2] of the retinal images. Each principal axis assigns a weight to each pixel and can be illustrated as an eigenimage. The computed feature value corresponds to the weighted sum of the pixel intensities. We selected the principal component with the highest correlation with age for further investigations. This purely data-driven approach is novel in the domain of retina image processing.

We used the Spearman-Rho coefficient to quantify the correlation of the feature value with age. The intra-class correlation coefficient of reliability was graded by Cronbach-Alpha with a 95% confidence interval (six healthy participants, five images of each, acquired at one minute intervals).

Results

The algorithm achieves a high reliability with a Cronbach alpha = 0.953. The correlation of the retinal biomarker with age in the male control was $\rho = -0.284$ ($p = 0.017$) and in the female control: $\rho = -0.374$ ($p = 0.001$).

As the selected principal axis can be visualized as eigenimage, an anatomical analysis of the eye ground is possible (see Figure 1). The temporal parapapillary area and the optic nerve head have a strong influence to the age-related feature. These regions are medically relevant as they are known to change with increasing age.

Additionally, cardio-vascular risk factors have an influence to the extracted feature. The difference of the proposed biomarker between the control group and the participants is significantly influenced by risk factors (see Table 1). The existence of cardiovascular risk factors causes lower mean feature values.

As the feature correlates with age and cardiovascular risk factors have an influence, we can

declare the feature a *biomarker*.

Conclusion

We found a purely image driven feature of the retina correlating with age. In addition, cardiovascular risk factors (arterial hypertension, smoking) changed the age-related feature significantly. The algorithm identifies the temporal parapapillary region as relevant for the proposed age-related biomarker. Although the approach does not use any medical a priori information, we were able to extract an age-related biomarker that is strongly influenced by a medically relevant region.

References

- [1] Klemra, P. et al. A new approach to concept and computation of biological age. *Mech Ageing Dev* **127** (3), 240-248 (2006)
- [2] Turk, M. et al. Eigenfaces for recognition. *J Cogn Neurosci* **3** (1), 71-86 (1991)
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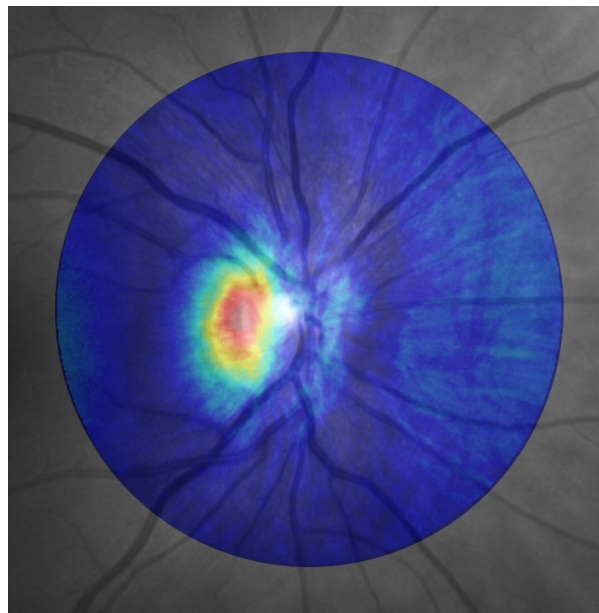


Figure 1: The pixel weights are depicted as a color overlay onto a gray-scaled representation of the retina fundus image. Warm colored regions have a strong influence to the proposed biomarker and are located at the temporal parapapillary area and the optic nerve head.

	Hypertension	Control	Significance
Men	-0.10 ± 0.84	0.57 ± 0.95	0.01
Women	-0.46 ± 1.23	0.06 ± 0.99	0.09

	Smoking	Control	Significance
Men	-0.16 ± 1.29	0.72 ± 0.92	< 0.001
Women	-0.12 ± 1.10	0.24 ± 0.98	0.048

Table 1: Feature values for hypertensive and smoking participants