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On Accurate Vessel Age Estimation based on the Acceleration Plethysmogram

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Abstract. This paper proposes a new estimation formula of the vessel age (VA), an index of the degree of atherosclerosis, based on parameters derived from acceleration plethysmogram (APG), which is the second-order derivative of the photoplethysmogram (PPG). The current estimation formula utilizes the sequence of five extreme values *a, b, c, d, e* observed in the APG waveform. The multiple regression analysis revealed that the parameters *c/a* and *d/a* play a significant role in estimating VA. To improve the estimation accuracy, the slope S_{bd} between two extreme values *b* and *d* is added to parameters *c/a* and *d/a* for the estimation. The parameter includes the information which reflects the APG waveform duration known to be an index to probe the large artery stiffness. The new vessel age estimation formula based on the multiple regression of these three parameters is evaluated by the PPG data collected from 347 healthy subjects aged 20-60 years (40.2 ± 12.4). The method will be effectively utilized for the early detection of the development of atherosclerosis.

Keywords: Vessel age; Photoplehysmography, Acceleration plethysmogram; Arteriosclerosis; Health monitoring;

1. Introduction

The leading cause of death worldwide is reported to be ischemic heart disease caused by atherosclerosis [1]. To prevent these incidences, the regular monitoring of the degree of atherosclerosis is recommended since moderate atherosclerosis doesn't accompany severe subjective symptoms. Toward this goal, this paper proposes an index to probe the degree of atherosclerosis based on the acceleration plethysmogram(APG). APG is the second-order derivative of photoplethysmogram (PPG), measurable by a simple device. PPG is primarily used for measuring the heart rate and blood oxygen saturation level(SpO2). In addition to these essential measurements, APG waveform has been utilized for various cardiovascular risk assessment such as the presence of atherosclerotic disorders, distensibility of the peripheral artery/carotid artery [2]-[4]. APG consists of 5 distinct peaks, extreme values, named *a, b, c, d,* and *e*. The characteristics and their age-dependency have been studied [2] [5-6]. The parameter *b/a* relates to the distensibility of the peripheral artery, which increases with aging. *c/a, d/a, e/a* decrease with aging, and *d/a* and *e/a* relate to the degree of atherosclerosis. *d/a* is also used as an index of left ventricle afterload. The clinical significance of *c/a* is unknown but is the major aging sensitive parameter as will be shown in this paper. From the age-dependency of these parameters, (*b- c- d- e)/a* has been suggested to be an index of vessel aging. The linear regression of subjects' age by the index leads to the definition of the vessel age (VA): VA=65.9+45.5(*b- c- d- e*)/*a* [5]. To search for a better VA estimation scheme, this paper quantitatively examines the significance of each APG parameter and explore to find

2. Material and Methods

2.1. Data acquisition

The PPG waveforms were collected from 347 healthy volunteer subjects aged 20-60 years (40.2 ± 12.4). The sensor platform MAX REFDES #100 (Maxim Integrated Co. Ltd.) has been utilized for the PPG waveform recordings. The platform is capable of measuring PPG waveform with green, red, and infrared LEDs, body temperature, 3-axis acceleration, and atmospheric pressure. During the data acquisition, subjects were in spine posture. The distance between sensor and fingertip has been kept constant (3mm) to record the consistent waveform for 20 seconds. The data were digitized in the platform and serially transferred to the PC. The PPG waveforms recorded by infrared LED were utilized for the analysis. Amplitude resolution and sampling frequencies were set at 12 bits and 200 Hz.

2.2. Parameter extraction

For attenuation of the high-frequency noise component in digitized PPG waveform, the 6th order Butterworth lowpass filter of the order six has been applied to the data. This prefiltering is essential since the accurate numerical derivative operation has to be applied for the APG peak estimation. After the prefiltering, APG and *3d*-PPG, defined as the third-order derivative of PPG, are numerically obtained. Fig. 1 shows the parameter extraction scheme. The instances t_a, t_b, t_c, t_d, t_e are identified by zero-crossing points of *3d*-PPG. Then the extreme values *a, b, c, d, e* of APG waveform are measured by the APG values at those instances. The advantage of the use of *3d*-PPG is to be able to detect the fused extreme values that sometimes appear for parameters *c* and *d*. The incident can be detected as the case where the *3d*-PPG values show small values ε close to zero. For example, if the *3d*-PPG value at time t_0 between t_b *and* t_e is smaller than a predetermined threshold θ , the extreme values *b* and *c* are assumed to be fused. In this case, the *APG* value at time t_0 can be assigned to the extreme values *b* and *c*.

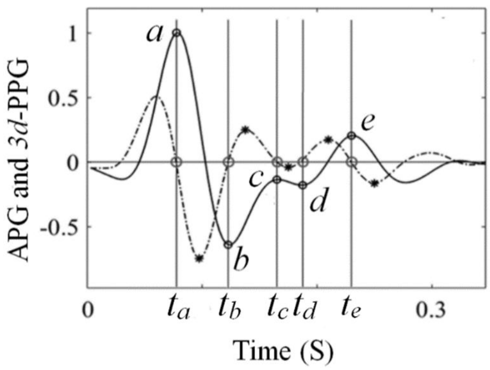

Fig. 1. APG parameter extraction based on APG and *3d*-PPG
Solid line: APG; Dotted line: *3d*-PPG

By careful measurement, keeping the subjects' spine resting condition constant, the measured APG waveforms are consistent and stable. However, the parameters *a-e* still have a certain amount of beat to beat fluctuations. To obtain the nominal parameter for the subsequent analysis, the mean parameter vector *p* consisting of five parameters *a-e* is calculated and the iterative procedure is applied to excludes the parameter vector of a beat showing the largest Euclidean distance from *p*.

3. Results

3.1. Multiple regression VA estimation

Conventional VA estimation formula includes all normalized APG extreme values *b/a, c/a, d/a, e/a* with equal weight. To improve the estimation accuracy, the multiple regression method has been applied to the VA estimation. The VA predicting formula became $VA=36.89+(6.62b -27.05c-24.68 d+2.44e)/a$. The formula gives the adjusted coefficient of determination R^2 value 0.482 and error standard deviation of 8.9 years. It is noted that the weights for parameters *c/a* and *d/a* have significantly larger weights than *b/a* and *e/a*. The conventional estimation formula VA=65.9+45.5(*b*-*c*-*d*-*e*)/*a* gives the error standard deviation of 16.3 years.

3.2. Parameter selection

Multiple regression analysis revealed that *c/a* and *d/a* showed a significant contribution to the estimation of the subjects' age ($p<10^{-3}$), whereas *b/a* and *e/a* don't ($p>0.05$). This observation suggests selecting two parameters *c/a* and *d/a*, for the VA estimation. In addition to these parameters, a combined index $(d-b)/(t_d-t_b)$ is proposed to be utilized for the VA estimation. Because it is well recognized that the parameters *b/a* and *-d/a* increase as age progresses, and the reciprocal of APG waveform duration is reported to be a measure of artery stiffness[7]. The proposed index S_{bd} shows the slope of two extreme values *b* and *d*, hence denoted as S_{bd}. Based on these considerations, three parameters *b, d,* and S_{bd} are suggested to be utilized for the VA estimation.

3.3. VA estimation by plausible parameters

The aging trend of the three selected parameters is shown in Fig. 2. Correlation coefficients between subjects' age and parameters *c/a*, *d/a and* S_{bd}. are shown to be 0.594($p<10^{-3}$), 0.580 ($p<10^{-3}$) and 0.492 (p<10-3).

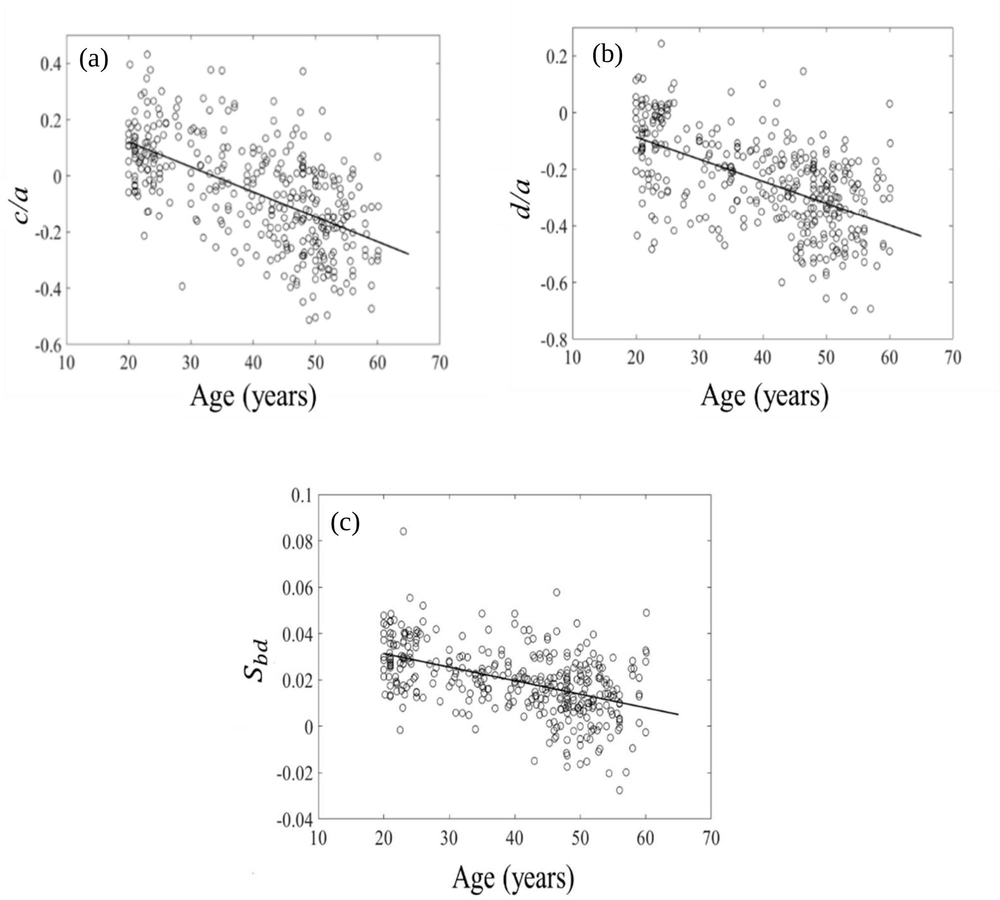

Fig. 2 The aging trend of the prameters to be utilized for the VA estimation
(a) *c/a* (r=0.594, $p<10^{-3}$); (b) *d/a* (r=0.580, $p<10^{-3}$); (c) S_{bd} (r=0.492, p< 10^{-3})

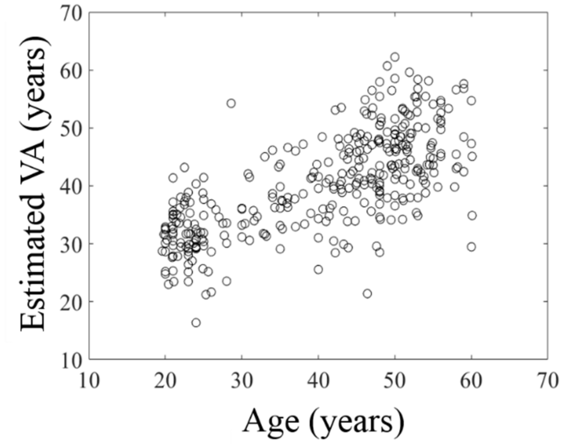

Fig. 3 The scatter diagram of the subject's age and estimated VA
(R^2=0.488, Error *s.d.* = 8.8 years)

Fig. 3 shows the result of VA estimation by the multiple regression analysis. The obtained VA estimation formula is $VA=36.92-(30.33c-17.78d)/a-14.78S_{bd}$. All parameters showed statistical significance ($p<10^{-3}$). The adjusted coefficient of determination R^2 and error standard deviation was 0.488 and 8.8 years, respectively.

4. Discussion

The two new VA estimation formulae are examined to improve the accuracy and interpretability of the formula. The first formula is a simple extension of the conventional one [5]. Instead of assigning equal weight for the single regression analysis, the multiple regression scheme has been examined. Comparing the standard deviation of the age estimation error showed an improvement from 16.3 to 8.8 years. By updating the original formula's regression parameters based on the dataset for this study, the error standard deviation became 9.3. To establish a reliable VA estimation scheme, an extensive bigdata collection with a precision standardized sensor module may be necessary.

By the multiple regression analysis, two parameters *c/a* and *d/a* are shown to be statistically significant ($p<0.05$) and important for the age estimation. Based on this observation, the second VA estimation scheme utilizing these two parameters with additional parameter S_{bd} associated with the APG waveform is proposed. The improvement of the error standard deviation with this additional parameter turned out to be not very significant. However, the index S_{bd} will contribute to a specific case where the APG peaks take similar values but S_{bd}. An example is shown in Fig. 4. In this case, all parameter values *b/a-e/a* are the same and only the timing is different. S_{bd} gives the timing information. Without the parameter S_{bd} both APG waveforms give the same estimated vascular age. The presence of S_{bd} resulted in giving a reasonable VA difference of 5 years.

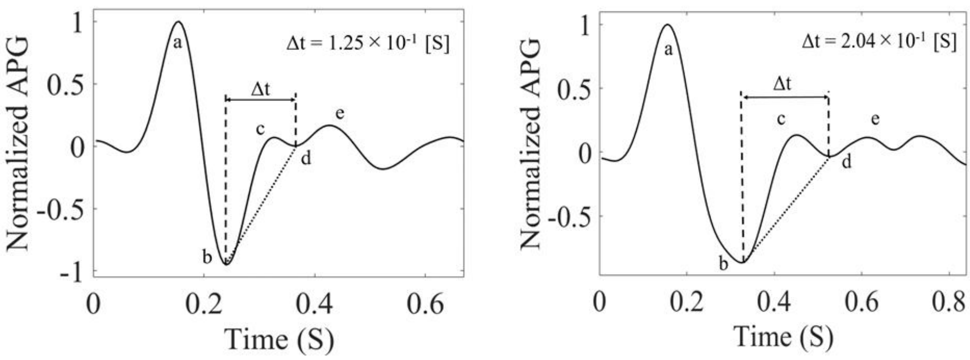

Fig. 4 An example of the APG waveforms showing the usefulness of the parameter S_{bd} .

It is noted that the parameter *c/a* shows the largest correlation value with subjects' age and is the major age-dependent index. Parameters *d/a* and S_{bd} relate to the amplitude and the propagating velocity of the blood reflection. Such interpretability of parameters may help to get some insights into the VA change.

For the reliable estimation of vascular aging, repeated observations over several days may be necessary to confirm the consistency of the estimation. A largescale validation with such repeating sampling for each subject must be planned to standardize the proposed formula.

5. Conclusions

Effective APG parameters are identified for the accurate VA estimation under the multi regression model. Since PPG signals, the source of APG, can be monitored by a simple device, the proposed VA estimation method may be effectively utilized for regular healthcare monitoring at home. A trend in the field of healthcare is to combine IoT technology with a cloud data system to monitor health-related indices continuously in a daily basis [9]. Regular APG monitoring could be key to the development of such a ubiquitous healthcare system. Regular APG monitoring could be key to the development of such a ubiquitous healthcare system. Toward this end, the data of cardiovascular patients need to be collected to clarify the effectiveness of the proposed method for the risk screening.

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References

[1] Word Health Organization, (2018). Global Health Estimates 2016: Deaths by cause, age, sex, by country, and by region, 2000-2016, Geneva, World Health Organization.

[2] Imanaga, I., Hara, H., Koyanagi, S., & Tanaka, K. (1998). Correlation between wave components of the second derivative of plethysmogram and arterial distensibility. Japanese Heart Journal, 39(6): 775-784.

[3] Otsuka, T., Kawada, T., Katsumata, M., & Ibuki, C. (2006). Utility of second derivative of the finger photoplethysmogram for the estimation of the risk of coronary heart disease in the general population. Circulation Journal, 70(3) : 304-310.

[4] Bortolotto, A., Jacques, B., Takeshi, K., Kenji, T., & Michel, S. (2000). Assessment of vascular aging and atherosclerosis in hypertensive subjects: second derivative of photoplethysmogram versus pulse wave velocity. American Journal of Hypertension, 13(2): 165-171.

[5] Takazawa, K., Tanaka, N., Fujita, M., Matsuoka, O., Saiki, T., Aikawa, M., Tamura, S., & Ibukiyama, C. (1998). Assessment of vasoacative agents and vascular aging by the second derivative of photoplethysmogram waveform. Hypertension, 32(2): 365-370.

[6] Baek, H., Kim, J., Kim, Y., Lee, H., & Park, K. (2007). Second derivative of photoplethysmography for estimating vascular aging. The 6th International Special Topic Conference on Information Technology Applications in Biomedicine: 70-72.

[7] Millasseaum, S., Kelly, R., Ritter, J., & Chowienczyk, P. (2002). Determination of age-related increases in large artery stiffness by digital pulse contour analysis. Clinical Science. 103(4): 371-377.

[8] Elgendi, M. (2012). On the analysis of fingertip photoplethysmogram signals. Current Cardiology Reviews, 8: 14-25.

[9] Yana, K., (ed.). (2016). Computational Electrocardiography: Revisiting Holter ECG monitoring *with editorial and discussion*. Methods of Information in Medicine, Vol. 55(4), 303-321.