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Digital pulse contour analysis: investigating age-dependent indices of arterial compliance

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Abstract

The resting peripheral volume pulse wave of 44 subjects within three age categories (30–39, 40–49, ⩾50) has been characterized using a novel algorithm for the automated determination of a mean pulse function. The contour of this resting mean pulse has been analyzed with regard to its systolic and diastolic characteristics. Previously described indices of arterial stiffness and viscoelasticity have been investigated for age-dependent variations associated with arterial mechanical properties. Measures of the minimum rise time (MRT) and the stiffness index (SI) demonstrated strong correlations with age and each other, although their derivations are unrelated. While significant correlations existed ($|r| = 0.50$–0.78, $p \leqslant 0.002$), pairwise comparisons between the right and left hands did not demonstrate significant differences for the minimum rise time parameter; however, the stiffness index was significantly lower in the left hand versus the right ($p = 0.009$). With regard to age, the youngest age group had significantly lower MRT and SI values than the two older groups. For these data, this was only demonstrated in parameters calculated for the right hand because of higher variability within age groups for the left hand. A normalized average mean pulse for each age group was determined which visually illustrated the contour changes associated with the MRT and SI parameters that occur in both the systolic and diastolic portions of the pulse. The finding that differences between the age groups were significantly more evident for the right hand suggests that the physical site for such testing may be an important consideration. This study provides further evidence regarding the merit of using contour analysis when assessing the peripheral volume pulse and the importance of establishing ageing indices for such analysis.

Keywords: pulse volume, photoplethysmography, arterial stiffness, peripheral pulse wave

Introduction

Photoplethysmography provides an estimation of cutaneous blood flow by measuring the dynamic attenuation of infrared light by the blood volume present in tissue. The signal's oscillating component provides a pulsatile wave, whose contour may include content descriptive of vascular health (Challoner 1979, Millasseau *et al* 2002).

Although the study of the peripheral pulse wave using the photoplethysmograph has been sporadic in the past, it has supported the usefulness of this noninvasive measurement with regard to vascular variations with age and disease. Frequency analysis has demonstrated the diminution of power in the harmonics of the pulse wave with increasing age and in the instance of arteriosclerosis (Sherebrin and Sherebrin 1990, Oliva *et al* 1976). Evaluation of pulse wave contour has historically been effective in the investigation of vasoactive drugs and has been used extensively in patient monitoring (Chowienczyk *et al* 1999, Bass *et al* 1989). Assessments of pulse transit time, using photoplethsmography in conjunction with the ECG R wave, have demonstrated declining values with increasing age attributed to the diminution of arterial compliance (Nitzan *et al* 2002).

Derivations of quantitative measures characterizing pulse shape have proven useful. One such parameter, the minimum rise time (MRT), has been derived from pulse height and characteristics of the ascending systolic slope. Significantly correlated with age, the MRT parameter was one of the first measures purporting a relationship to the mechanical properties of the vascular wall (Gavish 1987). Another age-related parameter, the stiffness index (SI), has recently been derived from contour analysis of the peripheral pulse wave and has been shown to correlate significantly with measurements of pulse wave velocity (PWV) generated using applanation tonometry (Millasseau *et al* 2002). PWV is a function of vascular compliance, which decreases with age, and is recognized as a strong predictor of cardiovascular events (Davies and Struthers 2003). The demonstration of correlations between parameters of peripheral pulse wave analysis and pulse wave velocity, measured both invasively and noninvasively, supports the revival of photoplethysmosgraphy as a simple and inexpensive technique for the assessment of vascular health (Loukogeorgakis *et al* 2002).

This paper reports the usefulness of contour analysis following the automated derivation of a mean pulse function. Several previously applied methods of contour analysis were evaluated simultaneously to investigate their overall concurrence, particularly with regard to the effects of ageing. Normalization and filtering of the data, as well as the importance of differences between the left and right hands, were also examined.

Study population

Peripheral pulse measurements were collected from the right and left middle fingers of 53 participants with ages ranging from 31 to 59 years and median age 44 years. Participant data come from an IRB-approved study enabled through the City of Cincinnati (OH) Sewers, Water Works & Public Services. The data were taken from a larger study initially undertaken for the assessment of occupational vibration exposure. Eight subjects were excluded due to missing information (age or height) and/or unacceptable pulse volume data. An interview was conducted to identify any workers who may have experienced the symptomatic color changes and/or discomfort associated with Raynaud's phenomenon or vibration white finger (Maricq and Weinrich 1988). This resulted in the exclusion of one female subject who presented with a borderline response. The characteristics of the resulting 44 subjects included in the analysis are presented in table 1.

Table 1. Study population.

Clinical parameter	30–39 years	40–49 years	⩾50 years	Significance p
Subjects (male/female)	14 (11/3)	22 (19/3)	9 (9/0)	NA
Handedness (right/left)	12/2	21/1	7/2	NA
Age distribution (years)	34 ± 2.7	45.3 ± 2.7	52.2 ± 2.8	NA
Height (m)	1.78 ± 0.11	1.77 ± 0.07	1.78 ± 0.08	0.95
Systolic blood pressure (mm Hg)	130 ± 6	125 ± 10	126 ± 12	0.34
Body mass index (kg m^{-2})	31.8 ± 5.4	32.3 ± 5.7	31.1 ± 6.2	0.91
Weight (kg)	99.9 ± 19.1	99.9 ± 17.7	94.0 ± 11.4	0.76
Heart rate (min^{-1})	70.9 ± 12.1	71.3 ± 10	70.7 ± 7.2	0.98

The results are presented as mean ±SD (NA, not applicable).

Methods

Subjects were asked to avoid caffeine and smoking for 2 h prior to testing. The procedure was explained during acclaimation to the testing environment, which was a quiet room maintained at 23 ± 0.8 °C. Measurements were made using customized instrumentation to eliminate the need for, and remove variations due to, physical attachment of the sensor. A commercial grade photoplethysmograph transducer (Biopac Systems, Inc., CA, USA) was embedded into a wooden platform. A cold mirror (Edmund Industrial Optics, NJ, USA) overlay eliminated potential sensor deformation that could affect signal integrity. Peripheral pulse measurements were recorded for 1 min with the subject's arm positioned at heart level and the finger resting in contact with the mirror over the sensor. Approximately 60 s of resting data were acquired (1024 Hz) from each hand using a 16-bit data acquisition card (National Instruments, TX, USA). The signal was amplified using a photoplethysmogram amplifier module (Biopac Systems, Inc., CA, USA) with a bandwidth of dc to 10 Hz. A digital filter (Butterworth, highpass, 0.5 Hz) was applied to the data prior to analysis to eliminate low frequency baseline fluctuations. All processing and post-processing programs were written in LabVIEW (National Instruments, TX, USA).

Derivation of the mean pulse function

A computer algorithm was implemented to determine a mean pulse from the window of resting photoplethysmograph data. This algorithm involves an automated iterative correlation procedure which selects a set of measured pulses with which to estimate a mean pulse function. The set of measured pulses is optimized for contour similarity in order to minimize the presence of movement and damping artifacts normally present in such data. The validity of the method has been demonstrated previously in this laboratory (data not shown), in which the computer-derived mean pulse was compared to those derived independently by each member of a 'gold standard' panel (two clinicians and two physiologists). The overall correlation between computer and raters for 25 windows of data had a mean of 0.994 ± 0.005. The intraclass correlations (ICC) for rater agreement were as follows: ICC = 0.98 for pulse area, and ICC = 0.97 for pulse width (Shrout and Fleiss 1979). Correlations between the automated algorithm and each rater varied from 0.98 to 0.99 for average pulse area and 0.96 to 0.98 for average pulse width. Additionally, normalization of the mean pulse function was performed for overall shape assessment and to eliminate variability due to heart rate differences. This was achieved, as previously described (Allen and Murray 2003), by normalizing the amplitude (0,1) and dividing the width of the pulse into 100 equal divisions of time. The normalized mean pulses within each age group were averaged to yield a group pulse shape.

Minimum rise time

The minimum rise time (MRT) parameter has previously been defined (Gavish 1987) as

$$\mathrm{MRT} = \mathrm{d}t/\mathrm{d}y \times \text{Maximum Pulse Height}$$

representing the inverse of the normalized maximum rate of rise of the digital pulse volume. These calculations were determined automatically from the derived mean pulse function of each subject. The high sampling rate (1024 Hz) necessitated the resampling of the data at a lower rate following the application of a moving average filter (window of 11) in order to accurately determine dy. Care was taken such that the integrity of the pulse contour was maintained (shape and slope were not altered by the resampling procedure).

Stiffness index

The peripheral pulse wave at the finger characteristically exhibits a systolic peak resulting from the direct pressure wave traveling from the left ventricle to the digit, and a diastolic peak or inflection resulting from reflections of the pressure wave by arteries of the lower body back to the finger. The time between these two peaks (ΔT) is a coarse measure of transit-time between the subclavian artery and such reflection sites and has been used to define a noninvasive measure of large artery stiffness. Assuming this path length to be proportional to a person's height, the stiffness index has been defined as

$$\mathrm{SI(m/s)} = \text{Body Length}/\Delta T.$$

Determinations of ΔT and SI were made as previously detailed by Millasseau *et al* (2002. Briefly, peaks were resolved programmatically using the derivative of the mean pulse function. The systolic peak was defined by the first zero crossing and the subsequent negative zero crossing, or positive inflection nearest to zero determined the time of the diastolic peak or inflection occurrence.

Frequency analysis

The power spectrum of each subject's resting photplethysmograph data was generated utilizing the fast Fourier transform (FFT) written using Labview graphical programming language. The power of each harmonic from the second to the ninth was normalized by dividing by the power of the fundamental frequency as previously described (Sherebrin and Sherebrin 1990).

Statistical analysis methods

All categorical variables were summarized by frequencies and percentages; while quantitative variables were summarized by means and standard deviations. Relationships between continuous variables were characterized with the Pearson correlation coefficient and accompanying t statistic for testing the null hypothesis of zero correlation. Comparisons for simple group means across independent populations were performed with ordinary analysis of variance (ANOVA) methods using SAS PROC GLM (SAS STAT 1999). Since measures for right and left hands are correlated, all analyses for hand by age group interactions were performed by means of repeated measures ANOVA using SAS PROC MIXED (SAS STAT 1999, Little *et al* 1996). Mixed models extend ordinary ANOVA to include correlated error

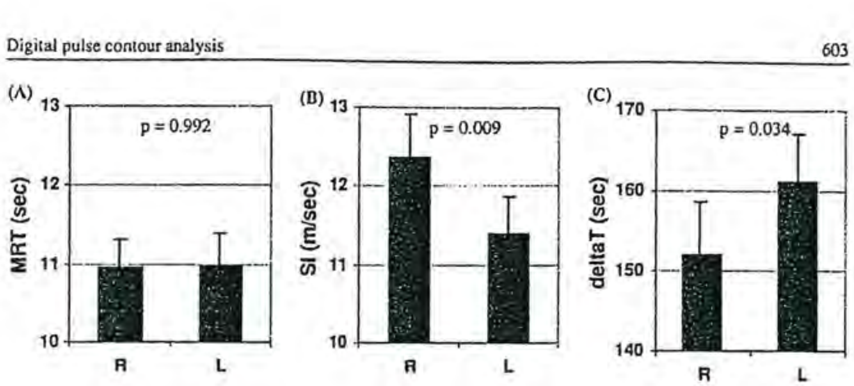

Figure 1. Overall mean values (±SEM) for right- and left-hand parameters.

Table 2. Paired samples correlations.

Parameter	Correlation	Significance p
MRT right & MRT left	0.500	0.002
SI right & SI left	0.779	0.001
ΔT right & ΔT left	0.781	0.001
MRT right & SI right	0.689	0.001
MRT right & ΔT right	−0.667	0.001
MRT left & SI left	0.723	0.001
MRT left & ΔT left	−0.693	0.001

structures. Several repeated measures ANOVAs were then performed with hand and age as independent variables and the parameters of interest as the dependent variables in order to test for an interaction between age group and hand.

Results

The SI, MRT and ΔT data for the right and left hand were significantly correlated (table 2). For each hand, the MRT calculations also strongly correlated with corresponding SI and ΔT values. Figure 1 indicates that the overall means for the right and left hands for the MRT parameter were not significantly different ($p = 0.992$); however, for the right hand, the stiffness index was significantly higher ($p = 0.009$) and the related parameter, ΔT, was significantly lower ($p = 0.034$). Approximately 13% of the subjects tested were left-hand dominant (table 1). Omitting these five subjects and repeating the analyses did not demonstrate any significant change in the above results.

All three parameters (MRT, SI and ΔT) were found to be affected by age as noted in figure 2. We also analyzed these data using two-way repeated measures ANOVA, with age group as a between-subjects factor (30–39 years, 40–49 years, $\geqslant$50 years) and hand as a within-subjects factor. This analysis was performed to explore the relationship between left- and right-hand measurements, age group and the pulse parameters of interest. The test for hand by age group interaction was not significant for any of the three parameters ($p = 0.33$ for MRT: $p = 0.36$ for SI and $p = 0.27$ for ΔT). This result can be interpreted to mean that there is no evidence of a difference in the relationship between age and pulse between right and left hands. It is interesting to note that there appears to be higher variability for the left hand so that even though the age trends appear similar, the left-hand measurements do not have

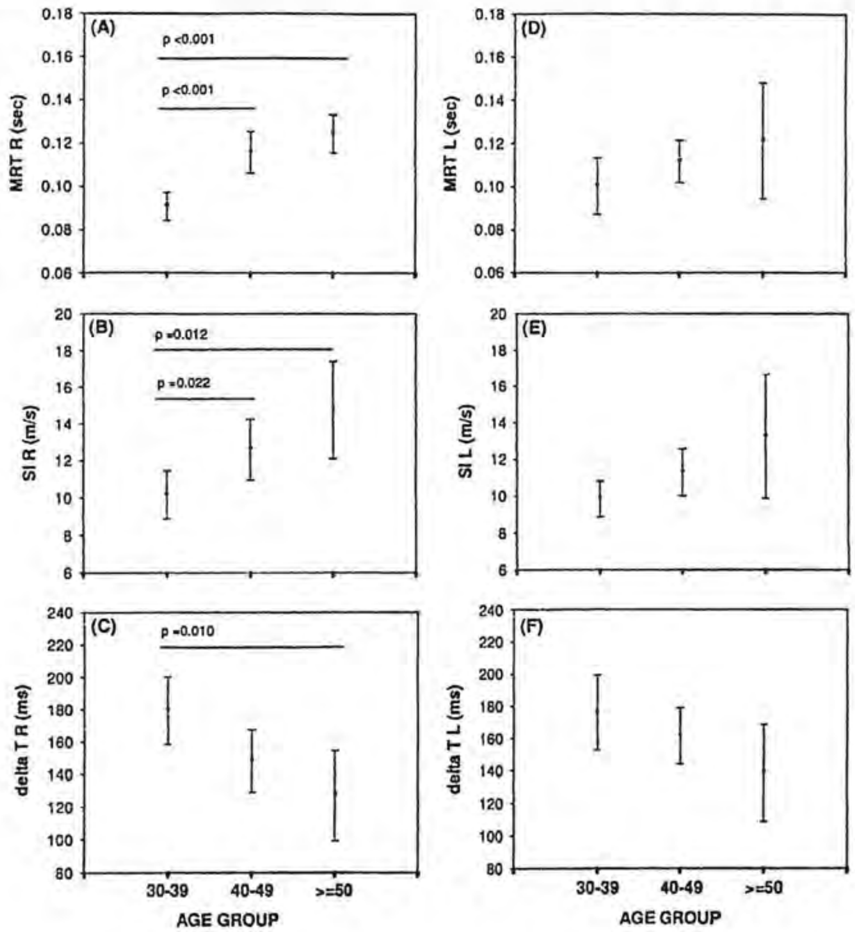

Figure 2. Right-hand (A)–(C) and left-hand (D)–(F) mean parameter values for the three age groups. Error bars represent 95% confidence interval.

statistically significant trends while the right-hand measurements do result in significance for this sample size.

Characteristics of the pulse shape for each age group are shown in figures 3(A) and (B). The mean group pulse of the oldest group was subtracted from those of the 30–39 and 40–49 age groups; the results are depicted in figures 3(C) and (D), respectively. Consistent with the parameters under study, the group pulse contours confirm that changes with age predominantly reside in the ascending systolic slope and the dicrotic notch demarcation, as evidenced in the difference plots. One should note that the averaging of individual pulse functions for group contour analysis can obscure the actual features related to parameters such as ΔT. This is evidenced by the observation that the monotonic decrease in ΔT found in figure 2(C) is not necessarily seen in figure 3(A).

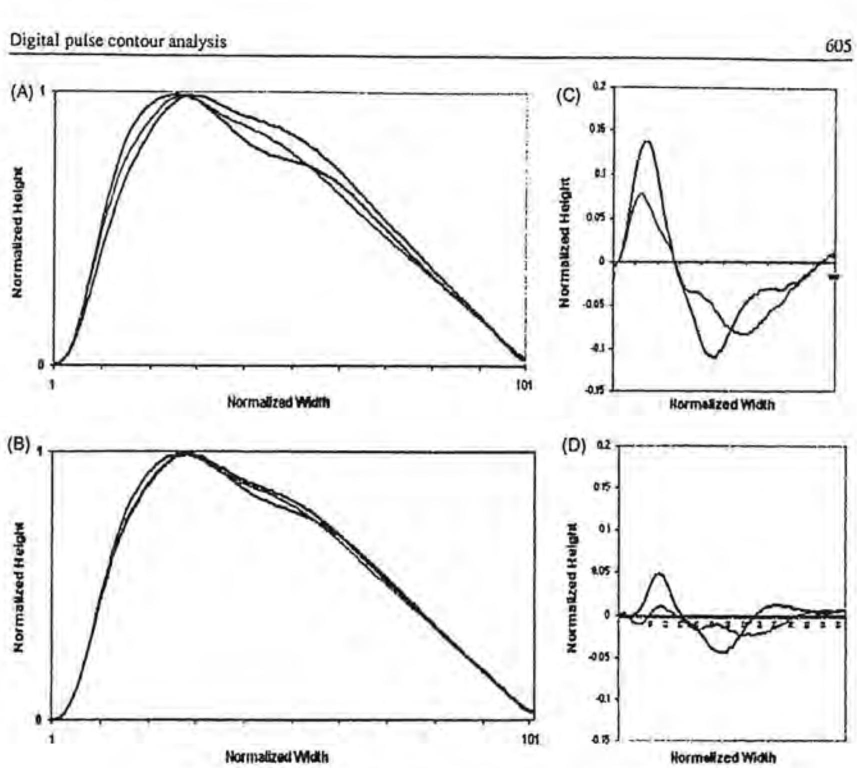

Figure 3. Normalized mean pulse functions for the right (A) and left hands (B) for age groups: 30–39 (———), 40–49 (———), and ≥ 50 (———). Right- (C) and left-hand (D) difference plots subtracting the oldest group from the 30–39 (———) and 40–49 (———) age groups.

The magnitudes of the shape changes in figure 3 are clearly more distinctive in the right hand. To further demonstrate these distinctions, two parameters used to derive the minimum rise time (dy) and the stiffness index (ΔT) have been calculated from the normalized mean pulses within each age group. These parameters were analyzed using two-way repeated measures ANOVA. The age by hand interaction terms were not statistically significant ($p = 0.28$ for dy and $p = 0.07$ for normalized ΔT). The trends with age for dy and ΔT are presented in figure 4.

It is noteworthy that traditional frequency analysis corroborated the overall findings (table 3). The attenuation of power in the harmonics with increasing age has previously been demonstrated (Sherebrin and Sherebrin 1990). Using similar methods which normalized the power at each harmonic by that of the fundamental, t-tests assuming unequal variances were performed. Analogous results were demonstrated, concurring also with the finding that age-related differences are more evident in measurements of the right hand.

Discussion

The parameters of contour analysis under investigation, MRT and SI, are derived from measures of distinctive portions of the digital pulse, the systolic and diastolic regions, respectively. Our results indicate that these parameters significantly correlate with one another (and to the related

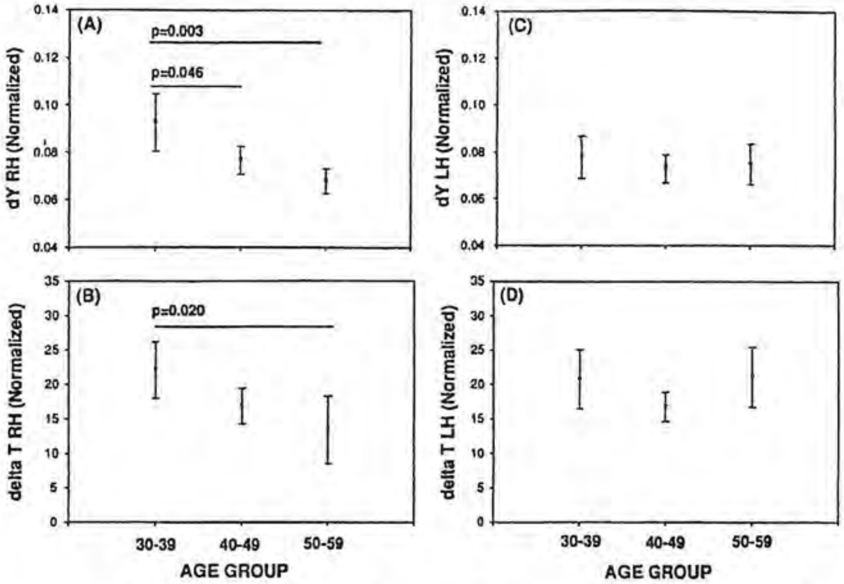

Figure 4. Right- (A)–(B) and left-hand (C)–(D) mean parameter values of dy and ΔT from normalized pulses for the three age groups. Error bars represent 95% confidence interval.

Table 3. Frequency analysis: power attenuation with age.

Hand	Harmonic	p value		
		Group I versus II	Group I versus III	Group II versus III
R	2	0.031*	0.003*	0.183
R	3	0.064	0.006*	0.197
R	4	0.150	0.004*	0.034*
R	5	0.181	0.041*	0.453
R	6	0.839	0.267	0.148
L	2	0.335	0.185	0.481
L	3	0.996	0.455	0.408
L	4	0.929	0.398	0.414
L	5	0.571	0.883	0.666
L	6	0.766	0.289	0.329

The power at each harmonic was normalized by that of the fundamental.
*p values representing significant differences. Group I: 30–39 years, group II: 40–49 years, group III: 50–59 years.

parameter, ΔT). As well, measurement of both of these parameters has demonstrated an ability to significantly differentiate between the 30–39 age group and the two older groups (40–49 and $\geqslant$50), indicating increasing MRT and SI values with age. These findings are in agreement with the previously published results of Gavish and Millasseau (Gavish 1987, Millasseau *et al* 2002), lending credence to the validity and the methodologies applied in their derivations.

Measurements were made using both the right and left hands, hypothesizing that there would be little or no difference between the two. Although there was a suggestion of an age effect in measurements of the left hand, this result was not statistically significant. The results from the right hand, which appear to have less variability than those for the left at the higher age group, had statistically significant differences between the lowest and highest age groups for all parameters and between the lowest and middle age group for MRT and SI (figure 2). As this was the case also for the related parameters of the normalized pulses, the inference exists therein that the choice of testing location may indeed be relevant and suggests the need for further investigation. While one could speculate with regard to the differences between the right- and left-hand measurements, perhaps being due to anatomical differences in the vasculature, it is a novel finding from a small subject population and outside the scope of the present study.

It should be noted that none of the results were adjusted for smoking, hypertension or diabetes because there were so few individuals in the sample with these characteristics. Analyses were performed demonstrating that eliminating participants with these characteristics had negligible effect on the overall results (data not shown). While this does suggest that age exhibits an independent influence, it is not meant to minimize or suggest a lack of import of these other factors. Additional studies should be done to further characterize the effect of other factors on peripheral pulse contour.

Initial calculations of MRT, SI and ΔT were performed on data which had not been manipulated beyond the instrumentation's 10 Hz lowpass filter. This conservative approach was taken given the variations between individuals, and in an effort to maintain the integrity of the original signal, particularly with regard to shape. In order to process the data in a manner consistent with the previously published protocols, a highpass digital filter (Butterworth, 0.5 Hz) was employed prior to the implementation of the automated algorithm. While these procedures did eliminate some low frequency baseline fluctuations, it is noteworthy that when the statistical analyses were rerun, the overall results of the study remained unchanged (data not shown). The frequency content of peripheral pulse waveforms is complex, unique to each individual and measurement, which certainly confounds the selection of the most appropriate approach for analysis. The impact of applying other filtering approaches merits further investigation, particularly with regard to establishing standardized procedures for the treatment and subsequent analysis of physiologic data.

While there have been several methodologies for pulse wave analysis described in the literature, it is outside the scope of this paper to compare all of the approaches. Instead, the minimum rise time and stiffness index in particular were chosen as representative means of characterizing the pulse wave, of particular interest since each considers shape changes during a different portion of the volume pulse. The computations for determining each parameter demonstrated the need for careful consideration of issues such as sampling rate, filter implementation, normalization, mathematical methods and the maintenance of signal integrity. It became evident during data processing that measures which involve quantifying the dicrotic notch or incisura are confounded when the notch or inflection is not easily distinguishable, an apparent disadvantage for many of the methods to which this calculation is integral, including the stiffness index.

Further investigation of age-related changes to the peripheral pulse contour using a much larger and diverse population is necessary for the establishment of important ageing indices. The evaluation of overall vascular health using such methods will require such elaboration.

Conclusions

This study proposed to assess the pulse contour of a mean pulse function derived from resting photoplethysmograph data utilizing an automated, iterative correlation algorithm.

Previously described methods for evaluating two unique parameters, MRT and SI, as well as the characterization of the normalized pulse shape with regard to age, have been applied to the resultant mean pulse functions. The pulse shape assessment demonstrated a strong correlation between the unique parameters, MRT and SI, and verified their ability to significantly differentiate between the youngest and older age groups, although only in the case of measurements of the right hand. Similarly, calculations of related parameters for normalized pulses illustrated significant differences with age in measurements of the right hand. The results of frequency analysis of the resting data were consistent with the theory that the power in the harmonics of the pulse wave decrease with age, albeit these results were again significant for the right hand only. The agreement of the various methodologies for pulse contour analysis with regard to ageing has been demonstrated. The significant and coherent findings derived from measurements of the right hand advocate further evaluation regarding the importance of sensor placement with regard to anatomical location.

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