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A Linear Regression Model for Assessment of Interdependent Parameters of Central Pressure Determined from the Peripheral Pulse

F. Camacho, A.P. Avolio, N.H. Lovell
[1]Graduate School of Biomedical Engineering, University of New South Wales, Sydney, Australia

Abstract—**The central aortic pressure waveform (CW) is determined by cardiac and vascular parameters. In the intact circulatory system, the influence of individual parameters on CW cannot be readily assessed because of parameter interdependence. This study presents a linear regression model for estimating CW from a range of measurements of heart rate (HR), brachial systolic pressure (BSP) and frequency components of previous CWs for an individual subject. The model was constructed using data from 34 subjects (age 20-76 years) in whom multiple CWs were determined from the radial pulse waveform over a given range of HR (42-77 bpm) and BSP (90-172 mmHg). For each subject a model was created to estimate the particular CW for any given heart rate and BSP. All models were validated independently using a cross validation technique. The model was able to estimate CW to within a mean error of <1 mmHg. The models were used to compare the influence of BSP on the late systolic pressure augmentation (Augmentation Index (AIx)) for a fixed HR.**

This study suggests that a linear regression model that estimates the CW can be used to assess the effect of individual parameters on specific waveform features. This allows the characterization of the effect of individual parameters on CW features, such that the response can be quantified independently of other parameters as a family of CWs over a specified range.

Keywords— **aortic pressure waveform, linear regression model**

I. Introduction

There has been increasing interest in the use the central aortic pressure wave (CW) as an improved representation of left ventricular load and its estimation from non-invasive measurement of the radial pulse [1, 2]. Pulse waveform features related to the amount of late systolic augmentation pressure (Augmentation Index (AIx)) [3], ejection duration (ED), arterial wave transmission [4] and other parameters have been proposed for characterization of cardiovascular status, including degree of arterial stiffness, wave reflection and cardiovascular risk. The CW characteristics are influenced by many interdependent physiological factors, such as heart rate (HR), mean blood pressure (MP), subject's height, gender, peripheral resistance [5]. It may be also affected by external factors such as patient posture [6]. Many of the physiological parameters affecting CW are interrelated, making it difficult to separate the influence of one single parameter from another, as is the case for the interdependent association of HR and brachial systolic pressure (BSP) and their effect on AIx [7].

This paper presents a modeling technique for generating CWs for specified HRs and BSPs for individual subjects. This technique allows the comparison of variation of CW characteristics for controlled conditions identical for each subject as well as the individual analysis of CW characteristics.

The analysis of the influence of BSP on AIx is presented as an example of the use of this technique.

II. Methodology

This study consists of three separate parts. Initially a database was created to collect the data and select the study population. Second, models of CW for each subject were created and finally the influence of BSP on the variation of a specific CW parameter (AIx) was analyzed.

1) Population: A centralized and integrated database (DB) was created. Data were collected from seven different studies of central pressure in Australia. These data included subject's gender, HR, age, BSP, and CW, along with other parameters not used in this study. For each subject the CWs were estimated from the tonometric measurements of the radial waveform and sphygmomanometric blood pressure readings, using the SphygmoCor device (AtCor Medical, Sydney, Australia). Subjects with less then 28 separate CW measurements, BSP variation (ΔBSP) less then 8 mmHg or HR variation (ΔHR) less then 9 bpm were not included. A total of 34 subjects was selected. Table 1 summarizes the studied population.

TABLE I
SUMMARY OF POPULATION STUDIED (n=34)

	mean	sd	min	max
Number of CW per patient	59	16	28	118
Age (yrs)	51.0	15.7	20	76
Minimum average BSP (mmHg)	115.0	13.9	90	145
Maximum average BSP (mmHg)	137.2	17.1	110	172
Average ΔBSP (mmHg)	22.1	9.1	8	43
Average HR (bpm)	57.1	7.2	42	77
Minimum average HR (bpm)	50.0	6.4	36	67
Maximum average HR (bpm)	66.3	9.1	51	95
Average ΔHR (bpm)	16.3	5.3	9	34

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2) MODEL: CW modeling was performed in the frequency domain. All CWs were converted into frequency components by Fast Fourier Transform (FFT) and estimated FFT components were transformed back to time by inverse FFT. Only the first 8 components where used. It has been shown that 8 harmonic components are sufficient for accurate representation of the pulse wave [5]. The predictor parameters were HR and BSP and the predicted parameters were the first 8 FFT components used to generate the CW.

A. Model description

The model consisted of a set of linear regression equations between the predictor and predicted parameters in which all parameters are orthogonal to each other. This is similar to the Gram-Schmidt orthogonalization process [8], but linear regressions are made explicit from one parameter to another. This process is carried out in a specific order, as a linear regression is done on one parameter with respect to another. The selected parameter order was: HR, BSP, FFT mean pressure, real part of first harmonic, imaginary part of first harmonic, real part of second harmonic and so forth up to the 8th harmonic. In this process the first parameter (HR) did not change, and all other parameters have a mean value of 0 corresponding to the mean value in the orthogonal space. The set of linear regressions can then be used to recreate the process backwards and regenerate a set of parameters in the non-orthogonal space.

B. Model generation

The set of linear regressions was generated in a sequential process. Initially all parameters were made independent (orthogonal) from HR, the first parameter. Then, all parameters were made independent from the already transformed BSP (the second parameter). The process was repeated for all but the last parameter, as it will be already independent from all other parameters. All linear regressions utilized for this orthogonalization process constitute the model.

The model for each subject was generated using the complete dataset for that specific subject. A cross validation process was subsequently utilized to ensure the quality of the technique.

C. CW reconstruction

The reconstruction process consists of three steps: *(i)* BSP is transformed using the regression equation obtained for the orthogonalization of BSP from HR, *(ii)* a value of 0 is assigned to all FFT parameters, which correspond to the mean value of each parameter in the orthogonal space, *(iii)* the inverse orthogonalization process is performed. The final CW is reconstructed by transforming the FFT parameters back to the time space. This is effectively the "average" wave corresponding to the predictor variables.

D. Model validation

The model was validated using cross validation [9], dividing each subject data set into 10 equally sized sets. A testing model was generated using 9 of the 10 sets and validated against the last one. The process was repeated for each of the 10 sets for each subject. For each estimated waveform the error was calculated as the average difference point by point from the original wave. The variance was calculated as the average square difference point by point from the original wave. The final error by subject was calculated as the average of the errors for each waveform. The same was done for calculating the variance for each subject.

3) EXAMPLE OF TECHNIQUE IN USE. As an example of the use of CW modeling presented in this paper we studied the variation in AIx due to changes in BSP at constant HR. A set of 5 CWs estimated for specified characteristics (HR = 60 bpm, BSP = {100, 115, 130, 145, 160} mmHg) were generated for each of the 34 subjects. For each of the generated waves, AIx was calculated. The population was divided into two groups of equal size (high and low AIx at BSP = 100 mmHg). The variation of AIx for the two groups was compared.

III. RESULTS

A. Model

Fig. 1 shows a typical CW generated using the estimation model. Absolute pressure values and waveform characteristics compare closely between the original and the generated waves. The oscillation at the end of the wave is due to the limited amount of harmonics used for modeling and reconstruction.

The total error and variance obtained from cross validation for all subjects' models are shown in Table 2. The minimum and maximum error and variance by subject are also shown. The standard deviation corresponding to the total variance (averaging variance across 34 subjects) and to the variance for the minimum and maximum error values are also presented.

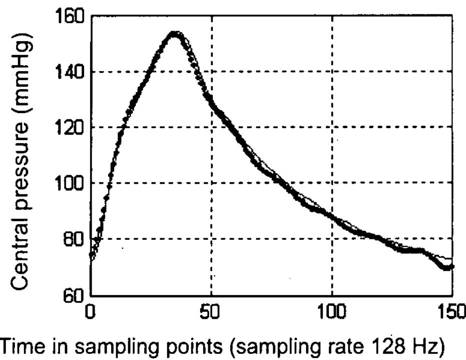

Fig. 1. Typical generated CW. Continuous line (thin) is the original CW. Line with asterisks (thick) is estimated CW.

TABLE II
MODEL ESTIMATION ERRORS AND VARIANCE

	mean	sd	min	max
Total error	-0.01	0.05	-0.18	0.07
Total variance	2.57	1.65	0.58	8.77
sd	1.60		0.76	2.96

B. CW generation

Figure 2 shows four sets of CW generated with the model for constant HR (60 bpm) and specified BSPs {100, 115, 130, 145, 160 mmHg} for four different subjects. It is clear from the waveforms that CW characteristics change differently for each subject for identical variations in BSP only, although parameters to fully characterize these changes are not yet established.

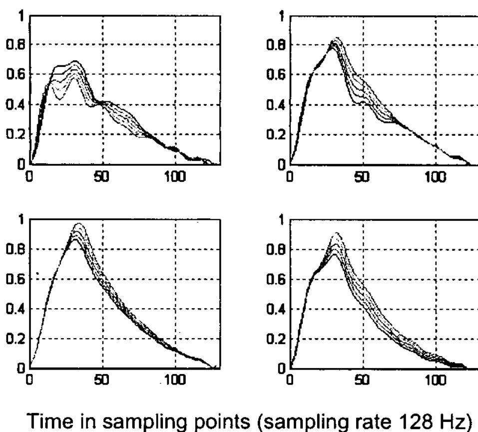

Fig. 2. Generated CW for four different subjects. Each of the 5 waves shown in each graph correspond to the estimated CW for a fixed HR (60 bpm) and BSP of 100, 115, 130, 145, 160 mmHg. Graphs are normalized with respect to measured brachial pressures.

C. Influence of BSP in AIx

Figure 3 shows the influence of BSP on AIx for a fixed HR (60bpm). The variation of AIx is greater for subjects with a smaller AIx at 100mmHg but the reduced number of subjects and AIx variability does not allow for conclusive significant difference.

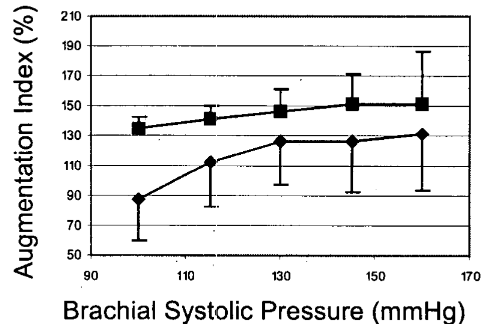

Fig. 3. AIx as a function of brachial systolic pressure. Lines represent mean values. Error bars indicate ± 1 sd. Lines represent two populations separated by AIx at 100mmHg (n=17 in each population.).

IV. DISCUSSION

The use of subject specific models to estimate CW derived from measured parameters such as HR and BSP enhances the scope for pulse wave analysis. It enables comparisons across subjects in terms of response to physiological changes for specified conditions. This is not always possible in the clinical or experimental setting due to parameter interdependence. The modelling technique can be extended to include other parameters, such as brachial diastolic pressure or pulse pressure, hours after medication, posture, and others. The model does not have any restriction for the number of predictor variables used.

Because this is a linear model, the physiological limits of the subject parameters do not restrict extrapolating the estimation of a waveform outside those limits, although this must be done with extreme caution. Furthermore, since the models for two different subjects have the same structure, it is possible to compare them. The actual meaning of each of the model parameters is not yet known, but the fact that the estimated CWs are very close to the measured CWs, suggests that characteristics (independent from HR and BSP) of the cardiovascular system are represented in the model.

A possible limitation of this technique is that it requires many measurements taken in different conditions for each subject. This could make it difficult to apply in certain

situations where a broad enough range of parameter variations could not be readily obtained. However, one possible solution is to obtain measurements during specific interventions, such as the Valsalva maneuver, where a range of heart rates and blood pressure and different pulse wave morphology can be elicited.

The analysis of the influence of BSP in AIx at fixed HR demonstrated the value of using CW modeling, making it possible to increase BSP while maintaining HR constant.

Due to the variability of AIx, much larger studies are required to characterize AIx variation with changes in BSP. The variability of that parameter and the small number of subjects in this particular study does not allow for a statistically significant variation of AIx with BSP changes.

The analysis of variability of AIx demonstrates the use of the technique presented in this paper for the study of one specific parameter. The technique can be used not only to analyze existing and predefined parameters, but also to investigate other parameters that can better describe the characteristics of the CW, subjects' parameters and cardiovascular risk.

V. CONCLUSION

This study has shown that multi-parameter models based on linear regression and orthogonal relationships that estimate the CW can be used to assess the effect of individual parameters on specific waveform features. This allows the characterization of the effect of individual parameters on CW features, such that the response can be quantified independently of other parameters as a family of CWs over a specified range.

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