

Evaluation of Arterial Diameter by Mathematical Transformation of APG for Ambulatory Stiffness

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Abstract

Background and Objective: Non-invasive, continuous measurement of arterial stiffness indices has established utility in cardiovascular risk stratification. This study aims to develop a subject-specific model of soft tissue sandwich from the common carotid artery wall to the skin surface layer using acceleration plethysmograph (APG) waveforms. It was then used to estimate the lumen arterial diameter waveform using APG for stiffness evaluation.

Methods: The carotid APG waveforms were collected using the developed accelerometer probe and its associated measurement system. Our clinically validated ARTSENS[®] device, performing diameter measurement and stiffness evaluation with a single-element ultrasound transducer was used as the reference system. The relationship between carotid diameter and APG from the neck was evaluated via mathematical models using system identification performed in MATLAB. The viscoelastic characteristics were considered for modeling the skin-tissue layer above the carotid artery. The performance of the developed model for non-invasive assessment of carotid lumen diameter waveform and stiffness indices using APG was validated on 15 subjects.

Main results: The developed model was implemented in real time and continuously evaluated carotid diameter waveform using APG captured from the neck of all the subjects. An RMSE of less than 0.14 mm was observed between the constructed carotid diameter waveform (using APG) when compared with a true diameter measured using the ultrasound-based system. A beat-to-beat variation of less than 8 % was observed for the estimated end-diastolic and arterial distension. Various carotid stiffness indices (evaluated using the estimated diameter parameters and measured blood pressure) demonstrated acceptable accuracy when compared with the reference system.

Conclusion: The study results demonstrated the feasibility of using a subject-specific skin-tissue model with APG waveforms for arterial diameter measurement and estimation of the vessel stiffness indices.

1. Introduction

Arterial wall mechanics plays a crucial role in blood circulation throughout the arterial tree. It has been researched for its clinical implications of cardiovascular and vascular diseases. Arterial wall radial motion has been investigated for the estimation of the wall stiffness, neglecting the longitudinal motion [1]. The arterial wall stiffness evaluation helps in the early diagnosis of atherosclerotic or arteriosclerotic changes in the arterial tree for preventing the development of vascular diseases. Indirect measures of arterial stiffness includes the assessment of arterial compliance, arterial distensibility, Young's modulus, and pulse wave velocity [2]. Ultrasound imaging is a well-known non-invasive technique for direct visualisation and motion estimation of the arterial vessels. But these state-of-art devices demands complex instrumentation and trained operators. Hence are not suitable for long term monitoring [2].

We present a method and an instrumentation for measuring the arterial stiffness. The study initially presents a theoretical viscoelastic model of soft tissue sandwiched from the carotid arterial wall to the skin surface layer. Further, a black box model was derived, simulations were performed based on the acquired set of single APG waveform input and diameter waveform output data and processed using MATLAB System Identification toolbox. This identified model along with the input surface APG waveform can be used to obtain the true carotid lumen diameter waveform for arterial stiffness evaluation.

2. Theoretical modeling

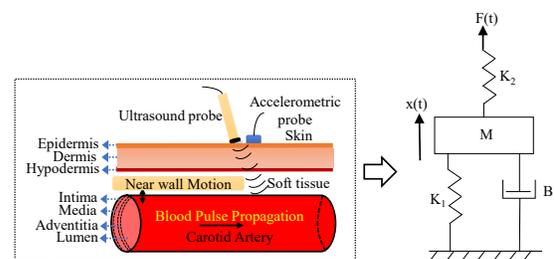


Figure 1. (a) Schematic representation of probe placement above the carotid arterial wall and its surrounding soft tissue layers. (b) Equivalent dynamic system model

Carotid arterial wall is found to be viscoelastic in nature [3]. The wall elasticity is related to the elastin content, whereas the viscosity is related to the collagen and smooth muscle content. The arterial wall anatomy is composed of three layers namely intima, media, and adventitia separated by elastic membranes. The arterial luminal surface which are in contact with the blood is lined with a layer of endothelial cells. The shear stress developed by the blood flow is applied to the endothelial cells. Among the above mentioned three layers of arterial wall, the media supports the load induced by the blood pressure and hence its mechanical properties represents the properties of arterial wall [3]. Carotid arterial wall surface is surrounded by geometrically and mechanically nonlinear biological soft tissues such as muscle, and skin [4-6]. Skin consist of three layers epidermis, dermis, and hypodermis. But the contribution of the fat layer and epidermis to the mechanical response of the skin are negligible. It is assumed that the dermis is the unique element responsible for the skin mechanic [7].

Considering the above properties of the different layers, and due to the time-harmonic nature of the radial motion of the arterial wall, the wall and its surrounding soft tissues are modelled as a linear system with displacement $x(t)$ and axial blood flow force $F(t)$. It is impossible to propose a perfect mathematical model for the real carotid arterial wall and soft tissues. But as in initial attempt, a linear model was assumed that can approximate linear dynamic behaviour neglecting the nonlinear properties. The proposed theoretical model (Fig. 1) consist of the arterial wall and soft tissue system in series. The arterial wall can be modelled as a spring (K_1) and dashpot (B) in parallel as in Fig. 1. The skin and the other soft tissues system respond in a different way under applied pressure as compared with the load cell [7]. These soft tissues reaction can be represented as a linear spring mass system with spring constant (K_2) as in Fig. 1. The transfer function for this proposed system is:

$$\frac{X(s)}{F(s)} = \frac{1}{[Ms^2 + Bs + (K_1 + K_2)]} \quad (1)$$

With mass $M=1$, the driving force $F(s)$, the damping coefficient B , the spring stiffness K_1 , and K_2 . Previous studies [2] have shown that the carotid surface APG waveform displays a great similarity with the axial blood flow force pattern through the carotid artery. Also, it was found that this axial blood flow is responsible for the radial motion of the arterial wall. Due to these two results, the APG waveform from the carotid surface can be used to approximate the driving force $F(t)$. Therefore in the present in-vivo study APG waveform is taken as the input to the system to estimate the carotid lumen diameter waveform.

3. Materials and methods

3.1. In-vivo experimental setup

The overall instrumentation setup developed for the experimental validation of the proposed accelerometric system for continuous carotid lumen diameter measurement and stiffness estimation is depicted in Fig. 2. The carotid APG waveform was collected using an accelerometric patch probe (LIS344ALH, STMicroelectronics) and its associated measurement system with a sampling frequency of 1 kHz [8]. This designed patch probe derives the APG waveforms associated with the displacement of the carotid vessel due to the influx of blood pulse wave through the carotid artery. Also, as shown in Fig. 2, our clinically validated image-free ultrasound technology ARTSENS® device [9] was integrated with the accelerometric system for developing a subject-specific mathematical modeling using the real-time acquired APG and diameter waveform. This model is used for reconstructing the lumen diameter waveform using accelerometer system alone and the ARTSENS® is used as the reference for validation study. The reference device consist of a probe with a single element ultrasound transducer (center-frequency = 5 MHz) to acquire A-scan ultrasound frames for continuous measurement of lumen diameter. The device analog front-end consists of a pulser-receiver circuitry for operating the ultrasound transducer in pulse-echo mode and procuring A-scan at high frame rates

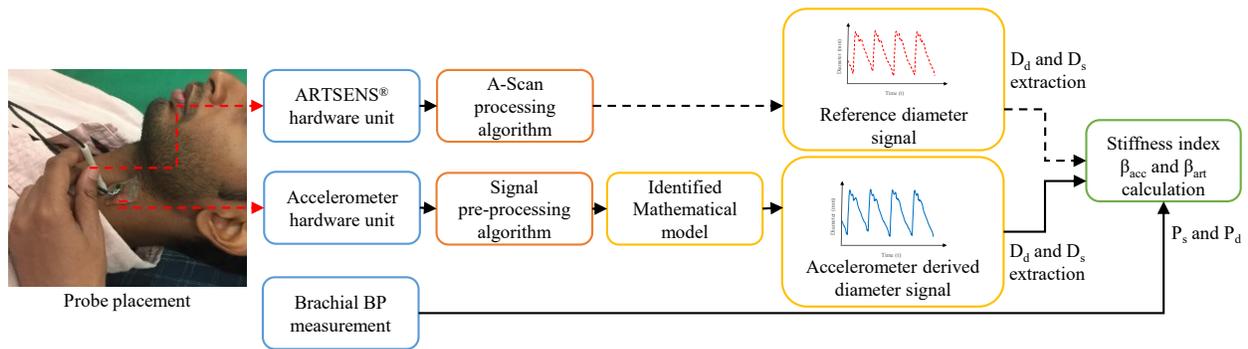


Figure 2. Developed measurement system for carotid lumen diameter and arterial stiffness estimation.

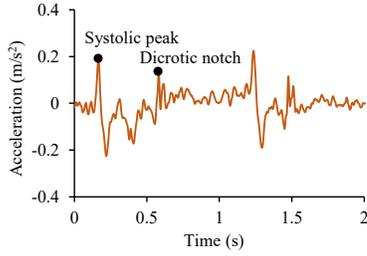


Figure 3. Continuous carotid skin surface APG waveform from a volunteer.

using ARTSENS[®] technology and its automated software architecture for continuous evaluation of diameter [9].

The separation distance between the accelerometric probe and the single element ultrasound transducer is confirmed to be very minimal for single site measurement of both the waveforms as illustrated in Fig. 2. The simultaneous acquisition of these waveforms with a sampling rate of 1 kHz was achieved by synchronizing the analog front-end of the accelerometric system with ARTSENS[®] device hardware. Further, the systolic (P_s) and diastolic BP's (P_d) are measured using an upper arm clinical-grade sphygmomanometer (SunTech[®]247[™]) to obtain the related carotid P_s and P_d values [9]. The relationship between the carotid lumen diameter and surface APG from the neck was evaluated via the mathematical model estimated and validated using the System Identification performed in MATLAB software. This carotid arterial wall and surrounding soft tissues system model along with real-time acquired APG waveform results in carotid lumen diameter. Hence by the continuous acquisition of carotid arterial diameter and deriving the diastolic diameter (D_d), and systolic diameter (D_s) for each cardiac cycle with corresponding P_s , and P_d measures, arterial stiffness index β can be evaluated in a beat-by-beat manner as:

$$\beta = \frac{\ln\left(\frac{P_s}{P_d}\right)}{\left(\frac{D_s - 1}{D_d - 1}\right)} \quad (2)$$

3.2. Data collection

An in-vivo experimental study was conducted on a study population of 15 healthy subjects (mean age = 30 ± 5 years, 10 males, and 5 females). The study protocol confirmed the Helsinki Declaration and informed consent was obtained from all the recruited participants. The main objective of the study was the evaluation of the carotid lumen diameter by mathematical transformation of the surface APG waveform for the estimation of stiffness and comparison with the reference method, to evaluate the accuracy of the proposed system.

All the experimental readings were performed by a

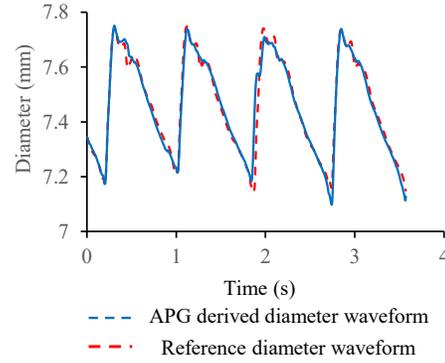


Figure 4. Overplot of lumen diameter measurement from accelerometric system with ARTSENS[®] reference.

single operator after asking the subjects to rest for 5 minutes in supine position. The accelerometric and ultrasound probes were placed on the left side of the neck above the carotid artery for the subjects after identifying the exact location with palpation as in Fig. 2. It should be noted that two datasets were taken for each subjects (D0, and D1), measuring approximately 15 sec for model estimation and later 25 sec for the validation study in MATLAB software. Each collected data set consist of a surface APG waveform, a carotid lumen diameter waveform, and brachial BP readings.

3.3. System identification and validation

The mathematical model was developed using black-box modeling approach. Initially from the experimental data's, the APG waveform which is related to the axial blood flow force was regarded as the input ($u(t)$) to this unknown model. The carotid diameter waveform was considered as the corresponding output ($y(t)$) from the unknown model. Afterwards, multiple linear and nonlinear model structures are generated and chosen based on previous knowledge along with trial and error method. These selected models are then identified and validated on other data sets to see whether they meet the model requirements

4. Experimental results and discussion

The proposed accelerometric system yielded highly reliable continuous non-invasive APG waveform from all the subjects as shown in Fig 3. Also, high fidelity lumen diameter waveform was simultaneously acquired with the above signals with ARTSENS[®] device for estimating the mathematical model in real-time and later as a reference for diameter and stiffness measurement validation. These recorded waveforms was found to hold relatively less phase delays due its time synchronized hardware acquisition, the matched frequency responses of the

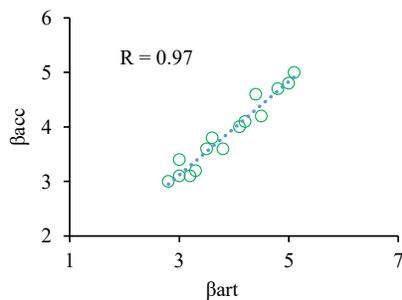


Figure 5. Regression plot of β_{acc} versus β_{art} .

designed systems and very close separation distance between the two probes.

These real-time collected APG input and carotid diameter data were tested with linear models, and later with nonlinear models. In order to validate the authenticity of the model, the best fitting between the simulation response of the identified model and the true diameter was recognized. Essentially, model with best fit percentage signifies how much that model is able to represent the actual carotid arterial wall and surrounding soft tissues system. Among this, nonlinear autoregressive (ARX) model with exogeneous variable provided the best performance with (1,2,1) model structure when compared with other models including linear models. The accuracy of the model was examined by comparing the model simulated output with the reference device output in MATLAB. The fit percentage was more than 90% for all the subjects. Fig. 4. illustrates the fitting result of the model output with the reference diameter at the same time instant.. Similar results were obtained for all the recruited subjects with good accuracy. The solid lines is the APG derived diameter waveform using the model and the dashed line is the reference device diameter waveform. Apart from the best fit, autocorrelation of residuals and cross correlation analysis were examined as well. The confidence level for both correlations was set at 95% (p-value of 0.05) and were within the range.

A linear dynamic model was assumed in the theoretical modeling to describe the layers of the carotid arterial wall and its surrounding soft tissues for its computational efficiency. This model, however, does not consider the effect of the nonlinear properties. But human biological soft tissues shows the nonlinear properties and composed of inhomogeneous structures. Hence this black box modeling for real tissue yielding a nonlinear model provides a better model with good agreement. The root-mean-square-error less than 0.14 mm was observed between the simulated diameter waveform when compared with the true diameter measured using the reference system at that time instant. Also, a beat-to-beat variation of less than 8 % was observed for the estimated end-diastolic diameter (D_d) and distension (ΔD). The correlation plot for the arterial stiffness index between the accelerometric

system and reference was found to have $R = 0.97$ (as Fig.5). The carotid stiffness index demonstrated acceptable accuracy when compared with the reference system.

5. Conclusion

This work has proposed a method for mathematical transformation of the carotid surface APG waveform for the determination of the changes in lumen diameter of the carotid artery. The theoretical model-based analysis considered a linear system model of the arterial wall and its surrounding soft tissues so as to explain the dependency of the carotid APG waveform and the lumen diameter. A nonlinear ARX system model was obtained using system identification toolbox in MATLAB with the real-time acquired data. The feasibility and accuracy of the developed model was further validated using a new sets of data for all the subjects. The study results demonstrated the feasibility of using a subject-specific carotid arterial wall and surrounding soft tissues model with APG waveform as the input for arterial diameter measurement and hence for vessel stiffness evaluation.

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