A Cloud-Based Assessment of Arterial Stiffness Through Contour Analysis of A Photoplethysmography

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Abstract

Cardiovascular diseases (CVDs) are the leading cause of mortality globally. To effectively prevent CVDs, a variety of techniques have been employed to evaluate the mechanical properties of arteries, among which, aortic stiffness measured by aortic pulse wave velocity (PWV) has been proven to be an independent predictor of CVDs. However, the traditional way to measure PWV is complex and time consuming. Recent studies suggest the digital volume pulse (DVP) waveform to be an effective non-invasive method to obtain PWV. In this study, we present a cloud computing system that analyzes and calculates the relevant indices of arterial stiffness after receiving the measured DVP signals. The result of the analysis can be retrieved online for the user to view or download for further analysis. With this technique, arterial Stiffness Index (SI) for population can be obtained easily and inexpensively. This will help health authorities to do mass screening at population level and, hence, establish references of arterial SI for different cohorts by age, gender, ethnicity, and diseases.

Keywords: Cardiovascular, Photoplethysmography, Pulse wave velocity, Arterial stiffness, Digital volume pulse

1 Introduction

Cardiovascular diseases (CVDs) are the leading cause of death globally. An estimated 32% of all global deaths are from CVDs in 2019 and 85% were due to heart attack and stroke [1]. Many factors attribute to the disease including aging, diabetes, hyperlipidemia, hypertension, hereditary disease, smoking, lack of sleep, and poor lifestyle habits. But an important direct indicator of the severity of plaques in the carotid artery and severity of plaques in the aorta is the arterial stiffness, which is found to have a strong positive association with common carotid intima-media thickness, and in turn, association with CVDs [2-3]. In general, arteries stiffen gradually with age. Premature stiffness may be caused by the combination of arteriosclerosis and atherosclerosis. Studies have reported an association between arterial function indices and cardiovascular risk factors, as well as the risk of incident cardiovascular events, including coronary heart disease and stroke. Technically, measuring arterial stiffness directly by measuring changes in arterial pressure and diameter simultaneously is challenging. Usually, arterial stiffness is diagnosed in clinical settings by imaging techniques such as ultrasound, computed tomography, and magnetic resonance imaging [4-6]. However, these approaches require professional intervention and are costly and time-consuming. Developing a portable way in non-clinical setting to obtain an objective measure of arterial stiffness is critically needed to screen CVDs at the general population level. To date, pulse wave velocity (PWV), the velocity of arterial pulses moving from the aortic valve to the periphery, is the most widely used non-invasive method for determining arterial stiffness. The technique is based on the fact that blood flows faster when blood vessels are stiffened to a higher degree. It has been developed and proven to be a powerful, highly reproducible, and independent predictor for detecting arteriosclerosis and aortic stiffness [7-10]. The extant research results are overwhelmingly in favour of an independent role for aortic PWV in predicting fatal and non-fatal cardiovascular events in healthy and diseased populations and in evaluating cardiovascular risk [11-12]. PWV has been recognized by the European Society of Hypertension as an early indicator of large arterial stiffening [10]. This method shows high performance but has poor usability since the traditional way of measurement requires skilled technicians to operate the specialized equipment. Recently, the newly algorithm allows PWV to be obtained by noninvasive photoplethysmography (PPG), with which PWV can be retrieved by contour analysis of the digital volume pulse (DVP) wave. This pulsation is propagated from heart through the arterial tree and is affected by reflected waves from the arterial branching sites [13]. Due to the COVID-19 epidemic, using a portable pulse oximeter that implements PPG is becoming popular. The non-invasive principle of the device is to measure infrared light transmitted through the finger pup. Adopting this technique and promoting it to the general population is naturally the next step in preventing cardiovascular diseases. Thus, we utilize PPG in this research to provide a portable way for the general population to assess the healthiness of their arteries.

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Using the DVP wave obtained through PPG, we determine the time it takes for pulse waves to travel through the arteries. The speed by which the pulse travels through the arteries is reflected to the heart is directly related to arterial stiffness. This measurement makes PWV an effective, noninvasive tool for assessing vascular changes [13]. The advantages of this technique include simplicity, portability, easy to set up, low cost, and independence in operation. PPG has been widely applied for various indices such as blood oxygen saturation, heart rate, and cardiac output. However, the existing research on portable devices to calculate arterial stiffness only has capacity for small patient groups. To effectively prevent CVDs, quantifying and monitoring the degree of arterial stiffness with a comprehensive model for general population at a large capacity is in an urgent need

For this reason, we developed a cloud-based computing system that detect arterial stiffness in two steps. First, the DVP signals are uploaded after measurement. Secondly, the system automatically analyzes and calculates the relevant indices of arterial stiffness, with which the subject can compare the current indices with the previous measures and better monitor their cardiovascular health condition. With these easy steps that can be done in a non-clinical setting, mass screening for arterial stiffness for the general population can be achieved, and vast amounts of data would be gathered for establishing the references of arterial stiffness across age groups, ethnicity, disease groups, or other relevant categories.

Thus far, there is no well-defined standard for a limit of arterial stiffness index [14]. Styczynski et al. suggest that the PWV is averaged 5.05 m/s for a healthy population. The value increased with age, and the average PWV is 6.77 m/s for health elder aged from 61 to 70. The high index has been shown to be with prognostic significance for arterial stiffening [14-15]. According to the current research results, if the PWV is greater than 14 m/s, there will be higher arteriosclerosis and risk of cardiovascular disease [16]. Specifically, SI elevates for patients with hypertension and CVDs. However, further reference values are yet to be established for more detailed disease category group [15].

Moreover, the raw data from each device for measuring the DVP signal are not shared since the device has a dedicated program. Gathering vast amounts of data across cohorts is essential for mass screening for arterial stiffness in the general population. To our knowledge, no SI calculation system is performed on a cloud-based environment. The existing algorithm is executed by dedicated software provided by the manufacturers. With this cloud-based computing system developed in this research, the goal of forming an extensive database and implementing data sharing will be achieved in the near future.

This study was approved by the research ethics committee of Nation Taiwan University (NTU-REC No.: 202002ES017). Informed consent was obtained from all subjects before the experiment began. This paper is organized as follows. Section 2 provides computational methods and the architecture of the web-based system proposed in this study. Section 3 explains the web service for the estimation arterial stiffness through contour analysis of a DVP wave. The conclusions are drawn in the final section.

2 Materials and Methods

The DVP is an optically obtained circulatory signal related to pulsatile volumes of blood in the microvascular bed of tissues. It can be acquired rapidly and simply by measuring the transmission of infrared light through the finger pulp [13]. Fingertip DVP indicates that changes in the blood volume are as pulse waves, providing information on beats of aortic origin, attributes of the vascular system, properties of the peripheral vessels and the blood flow status [17]. The contour of the DVP is determined primarily by features of the systemic circulation, including pressure wave reflection and PWV of pressure waves in the aorta and large arteries [18-19]. Hence, the timing of discrete components of the DVP can be used to formulate an index that relates to artery stiffness [20]. The descriptions of the estimation of the relevant indices are as flows.

2.1 Computational Methods

The contour of DVP measureed by PPG at fingertips exhibits an early systolic peak and a latter peak followed by a diastolic peak of reflection that occurs shortly after the first peak in early diastole, as shown in Figure 1. The systolic peak is a forward-going pressure wave moving along a direct path from the left ventricle to the finger. The diastolic peak arises from pressure waves transmitted along the aorta to small arteries in the lower body where they reflect back along the aorta and travel to the finger. The time for the waves traveling between the systolic and diastolic peaks can be used to infer the transit time taken for pressure wave that propagates along the aorta and large arteries to the major sites of reflection in the lower body back to the root of the subclavian artery [17]. The passage of time is assumed to be proportional to subject height, as a measure of the path length, based on which, a so-called stiffness index (SI) would be derived, as shown in equation (1) [20-23].

$$\textit{Stiffness Index}\ \ SI = \frac{h}{\Delta T_{DVP}}, \tag{1}$$

where h represents the body height and ΔT_{DVP} is the time between the systolic and diastolic peaks, as given in Figure 1.

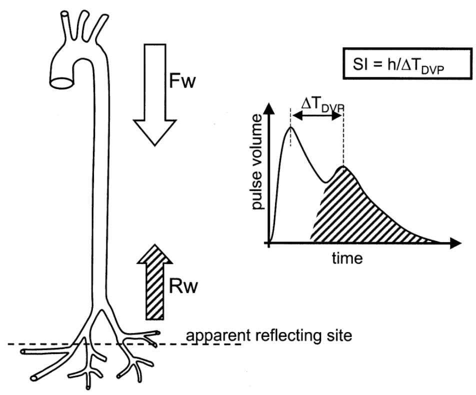


Figure 1. Stiffness index is related to the time delay between the systolic and diastolic components of the waveform and the subject's height (h) (from [20])

In addition, reflection index (RI) can be applied to the measurement for arterial compliance. RI is derived as a ratio of pulse inflection peak amplitude (diastolic peak) to the pulse max amplitude (systolic peak). RI provides a window to vascular age and arterial compliance and is defined as follows.

$$RI = \frac{Peak_{Diastolic}}{Peak_{Systolic}}. \tag{2}$$

The original DVP waveforms are coarse with noises caused by respiratory rhythm and other higher frequency disturbances. The de-trending and low-pass filtering techniques are adopted in our system in the pre-processing stage to delineate the waveforms accurately. The peak detection algorithm is applied to the filtered signal.

2.2 System Architecture

The existing researches on portable device to calculate arterial stiffness mainly focus on the indicators identification based on a small number of population. For example, Wu et al. had 80 subjects in the pulse wave and DVP study [21], and Millasseau et al. used 87 subjects [20]. To quantify and monitor the degree of arterial stiffness, a comprehensive model should be developed based on a large number of diverse cohorts. Thus, this study utilizes the existing network technology to design a cloud-based computing system to assist in sharing clinical trial data and establish physiological information across cohorts. In the time of COVID-19 pandemic and the social distance that must be maintained, it is more difficult than ever to obtain the measurements of DVP for the diverse cohorts in the community. To acquire the measurement data and, at the same time, to comply with the pandemic restrictions, it is crucial to design a system to that allows subjects to upload their measurement data by themselves. By doing so, the artery stiffness database can be established and the degree of stiffness across different age groups can also be explored.

The proposed cloud computing system in our study has several advantages, such as:

(1) The system fits all computer operating systems. No extra effor is needed to build an additional application for the different operating system. Users just need a web browser to access it through the internet.

(2) The system is updating itself in the central server; thus, users do not need to update the system.

(3) Since the system is running in a central server, end users do not need to install the application in each of users' devices.

(4) All the data are centralized since the software is centralized. Thus, uploaded data are analyzed and compared in the pooled central server, which provides convenience and instantly up to date results to all the end users.

The proposed cloud computing consists of three main modules: signal browsing module, signal processing module, and pdf result module. The system architecture is given in Figure 2. When the proposed system is running, an application that coded by C# automatically detect the presence of uploaded data. Then it calls python interpreter to run the codes for analyzing the contour of DVP signal. Once the analysis is finished, the report in pdf format will be built automatically. The details of the three modules are as follows.

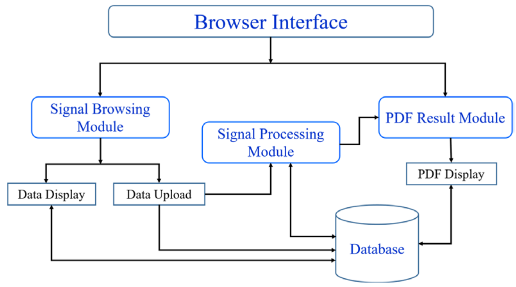


Figure 2. Three main modules and its functionalities of the proposed system

2.2.1 Signal Browsing Module

For users to conveniently browse the assessment results, the system automatically calls the signal processing module for data analysis after the DVP signals uploaded. In addition, the system could process signals that are generated by devices from various manufactures. The processed data are stored in a standardized format for retrieving and viewing online any time.

2.2.2 Signal Processing Module

Our cloud-based computing system aims to estimate the relevant indices of artery stiffness using DVP with appropriate computing method. After the DVP signals are uploaded, the system will pro-actively call for signal processing module. De-trending, filtering, peak detection, and estimation of indices are to be performed in this module. In the processes of de-trending, filtering, and peak detection, the pan-tompkins algorithm is adopted in the proposed system [24]. Among the methods for calculating stiffness index and reflection index [21, 25-27], we estimate the two indices based on basic derivative [20].

2.2.3 Report Module

One of the most exciting features of the system is the automatic generating of reports that summarize the information about arterial stiffness. The report design is easy to read and straightforward, thus guaranteeing a fast and direct overview of the input data and the derived indices. The report includes personal information such as age, gender and height, and statistics for SpO2, heartbeat, SI, and RI in our system. In addition, the system provides the waveforms of original and filtered signal and the location for each peak used to validate the signal processing module.

2.3 System Implementation

The proposed system was developed using Python, C#, APS.NET, jQuery and Bootstrap. jQuery and Bootstrap are popular programming frameworks for building responsive user interfaces. In the signal processing module, the algorithms of filtering and detection are developed using Python for its number of features such as easiness to code, object-oriented language, free and open source, extensibility, and portability. The signal browsing module is constructed by C# and APS.NET. The key features of using ASP.NET include the follows aspects:

(1) ASP.NET drastically reduces the amount of coding requirement when building large applications.

(2) ASP.NET and HTML together generate dynamic web pages smoothly.

(3) ASP.NET framework is language independent, meaning that there is great flexibility in choosing programming language. Anyone would suit the application well.

(4) With the built-in configuration information, ASP.NET is easy to deploy.

(5) The features of ASP.NET such as early binding, JIT compilation, caching services and native optimization supports give the application the high level of performance.

(6) With built-in Windows authentication and per-application configuration, the applications are safe and secured.

The result module adopts a PDF library of iTextSharp that allows document creation in a portable format [28].

The data was stored in MS-SQL Server database running on the ASP.NET web server. The database consisted of four primary data stores; the schema for which was as follows: raw DVP signals, relevant processing information for each DVP signal, the report for each uploaded DVP signal and account administration. The database resided on an online server and was password protected to ensure privacy of information. By doing so, no identifiable information was collected. Containing a program coded by C#, the server allows the data to be available for various functions. It handled the flow of data collected from the users, processing the wave signals and PDF result compiling.

3 Results and Discussion

In this section, we demo the user interface, main software frameworks and technologies for the realization of the proposed system (http://120.125.78.221). The system is deployed on a virtual machine of HP 360G workstation (CPU: Intel X5690*2; RAM: 32 GB; OS: Windows Server 2016; hard disk: 300 GB) at the Medical Information Laboratory, Ming Chuan University. The server is connected to the Internet via a gigabit router. The information about adopted technologies is descripted as shown in Table 1. The presented user interfaces correspond to the modules are as aforementioned.

To validate the proposed system, we obtain DVP signal at fingertip by using the device AT101B with a sampling rate of 250 samples/s produced by Leadtek [29], a certified medical device by the Taiwan Food and Drug Administration (with certification No. 005876). Following the protocol provided by the manufacture, we program an application to receive the DVP signal by USB port, which will then be saved data in CSV format, as shown in Figure 3. In this study, DVP signal measurements are collected concurrently from both left and right index fingers for studying and analyzing arterial conditions. All subjects are requested to rest five minutes before the DVP recording to ensure the stability of cardiovascular performance. Each recording lasts for a durations of thirty seconds. During the measurements, subjects remain calm and breathe normally in a sitting position.

Table 1. Development tools and operating environment of system

Environment	Software
OS	MS Windows Server 2016 Standard Edition
Web platform	ASP.NET on IIS
Development tool	Microsoft Visual Studio 2019, Anaconda (Ver. 4.10.1)
Programming language	C#, Python (Ver. 3.8.3 64-bit)
Database	Microsoft SQL Server 2017 Standard Edition

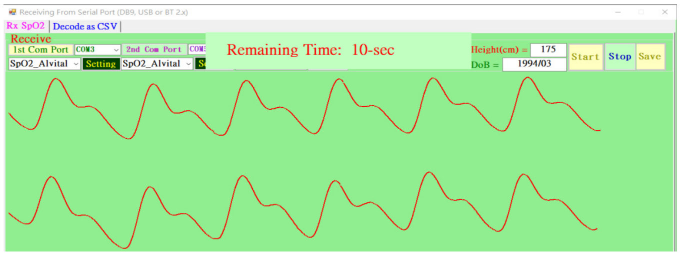


Figure 3. The application that receive DVP signal by USB port

3.1 The Interface of Signal Browsing Module

The signal browsing module provides two functions. The first function is for users to login into the system (or to register an account for the first-time users), as shown in Figure 4 and Figure 5, respectively. For new users, after submitting the application during registration, the information of the user will be reviewed by the authorized personnel and then stored in the central database. The second function is the uploading and analyzing of the DVP signals of registered users. After the uploading is completed, analyses of the signals are performed sequentially, then the results would be compiled in PDF format for viewing online or download. For non-registered users, the proposed system provides a temporary account, i.e. “Test”, to analyze the measurement. This temporary account is not kept in the database. Its password is just a date format of “MMddyyyy”. If the date of login is “2023/01/15”, then the password is “01152023”.

Figure 4. The login form in the proposed system

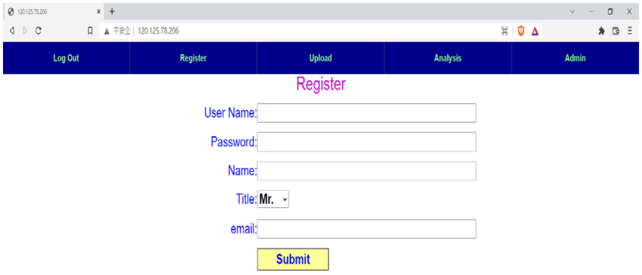


Figure 5. The register form in the proposed system

For the registered users, after logining successfully, the system would switch to the main menu, in which three functions were built: Upload, Analysis and Admin. The user utilizes the Upload function to transmit the DVP signal to the system. However, to cope with the DVP signal of instruments of different brands, we define the data format to include DVP signal, gender, height, age, and sampling rate, as shown in Figure 6. The data for each row of signal has IR signal, Red signal, SpO2 value and heart rate value. The extension of the uploaded file must be CSV.

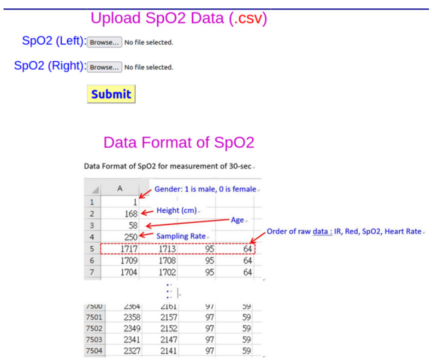


Figure 6. The upload form in the proposed system and the data format of CSV for DVP signal

The proposed system provides simultaneous upload of two measurements for two fingers, with which appropriate analysis would be performed based on the relevant information. Once the data is uploaded successfully, the user can browse the DVP signal, as shown in Figure 7(a). The information about the locations of systolic and diastolic peaks can be viewed when the data is analyzed by the signal processing module, as illustrated in Figure 7(b).

(a) Raw signal

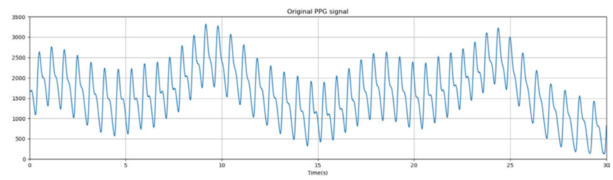
(b) Analyzed signal

Figure 7. The browsing function in the proposed system

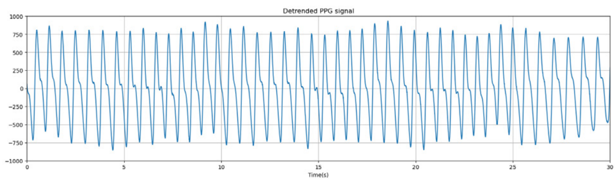
3.2 The Signal Processing Module

To estimat the stiffness index of the DVP signal at the fingertips, the locations about the first systolic peak and the early diastolic peak (or inflection point) must be detected. Since baseline wandering usually occurs in measuring the DVP signal at the fingertips, it must be removed in order to calculate the reflection index accurately. This calculation needs the correct magnitude of the first systolic peak and the early diastolic peak/inflection point. Hence, the signal processing module provides baseline wandering removing, low-pass filtering and peak detection.

To implement the algorithms, we adopt Python as the programming tool to build the signal processing module. The advantage of adopting Python is its easiness to debug and analyze in the development of the algorithm. Once done, the proposed system would automatically integrate the code. A recorded DVP signal with baseline wandering is filtered is given in Figure 8. The peak detection of the filtered DVP signal is shown in Figure 9. To carefully observe the relationship between the detected peak location and the first derivation, information between 5 and 10 seconds is extracted for review. As shown in Figure 10, the systolic peak and diastolic peak or inflection point can be detected successfully.

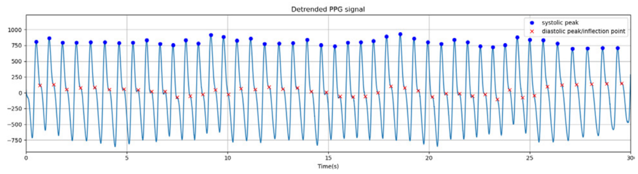


(a) Original DVP signal with baseline wandering

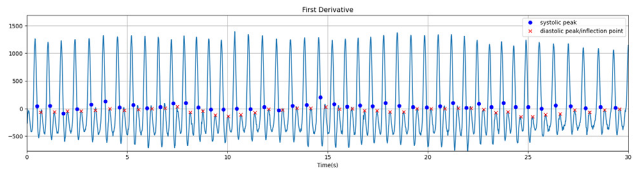


(b) Filtered DVP signal

Figure 8. A recorded DVP signal



(a) The peak detection of Filtered DVP signal



(b) The first derivative of Filtered DVP signal

Figure 9. The filtered DVP signal

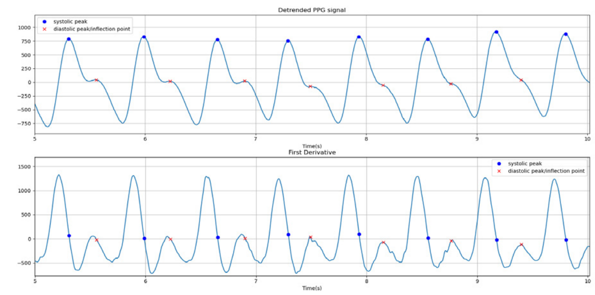
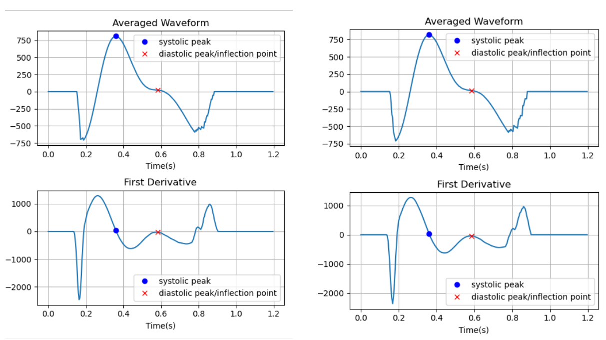
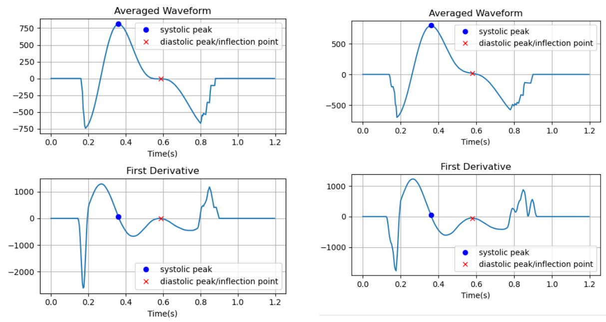


Figure 10. The peak detection of Filtered DVP signal between 5 and 10 seconds

When the relevant peaks are detected, we take a segment consisted of the initial 30% samples and the last 70% samples referenced at the peak point and sampling rate. For every ten seconds, the average segment waveform is obtained. DVP signals were recorded over a total 30s duration; in which we obtain a single waveform by ensemble-averaging over a ten-second period, and the rolling sequential waveforms were recorded every 5-second interval. Thus, over the 30-second duration, five waveforms were obtained with 5-second overlaps with the subsequent waveforms. The results are shown in Figure 11. SI and RI indices would then be calculated based on these averaged waveforms.





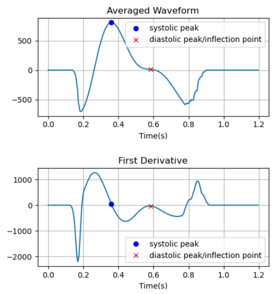


Figure 11. The averaged waveform from a recorded DVP signal

3.3 The Interface of pdf Report Module

The relevant data is generated after analyzed of specify DVP signal, the report in pdf format will be built automatically for users to view online and download, as shown in Figure 12.

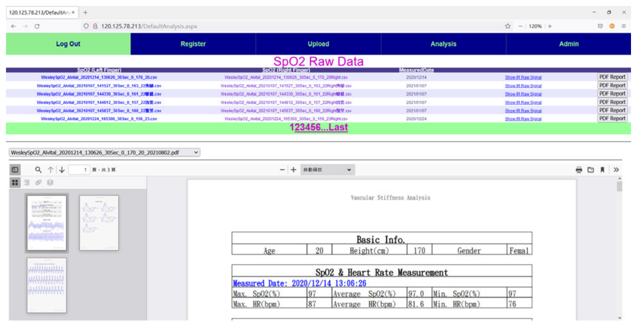
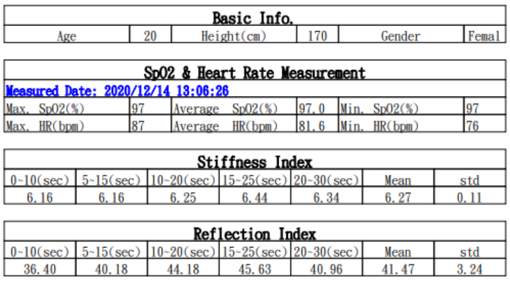


Figure 12. The report sample for a specific DVP signal

Several parts constitute the pdf report, as exhibited in Figure 13. The section of Basic Info. contains subject's age, height, gender; section of SpO2 and Heart Rate measurement present the maximum, mean and minimum values; the sections of SI and RI indices presents the five DVP signals, means and standard deviations of RI and SI; lastly, in the graph section, original DVP signal, filtered DVP signal, five average waveforms, and detected peaks of filtered DVP signal are presented. The steps of the waveforms processing and computation are shown in panels (b) through (d) in the graph section. By so doing, the reliability of the proposed system could be validated. Furthermore, if the measurements are collected concurrently from the left and right index fingers, the reports can be viewed, as illustrated in Figure 13(e).



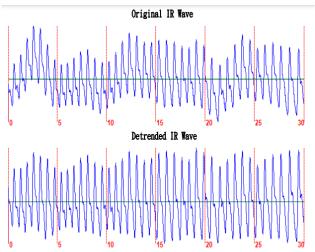
Basic Info.					
Age	20	Height(cm)	170	Gender	Femal

SpO2 & Heart Rate Measurement					
Measured Date: 2020/12/14 13:06:26					
Max. SpO2(%)	97	Average SpO2(%)	97.0	Min. SpO2(%)	97
Max. HR(bpm)	87	Average HR(bpm)	81.6	Min. HR(bpm)	76

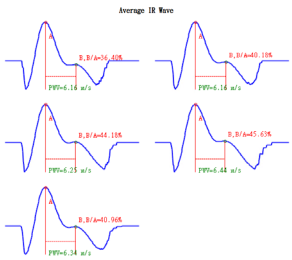
Stiffness Index						
0~10(sec)	5~15(sec)	10~20(sec)	15~25(sec)	20~30(sec)	Mean	std
6.16	6.16	6.25	6.44	6.34	6.27	0.11

Reflection Index						
0~10(sec)	5~15(sec)	10~20(sec)	15~25(sec)	20~30(sec)	Mean	std
36.40	40.18	44.18	45.63	40.96	41.47	3.24

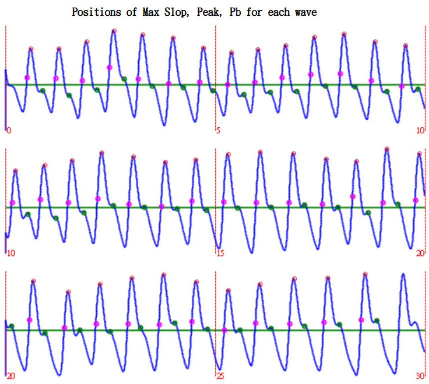
(a) The relevant information



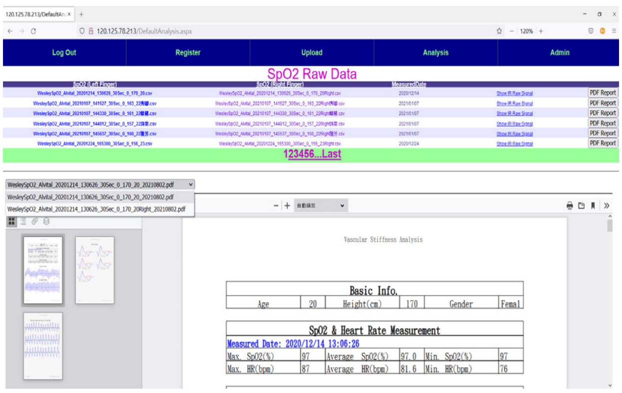
(b) Original and filtered DVP signal



(c) The averaged waveform



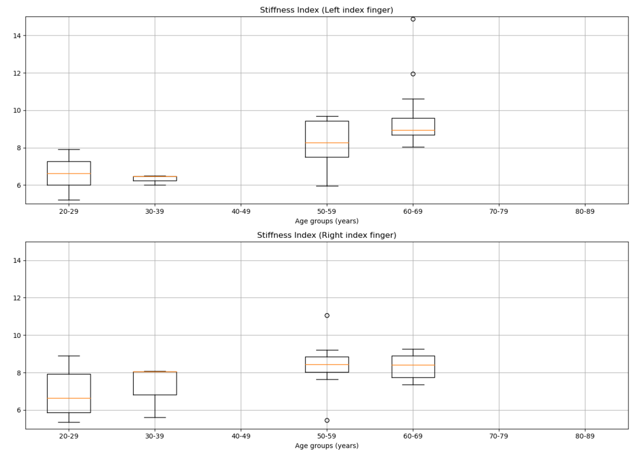
(d) The detected peaks



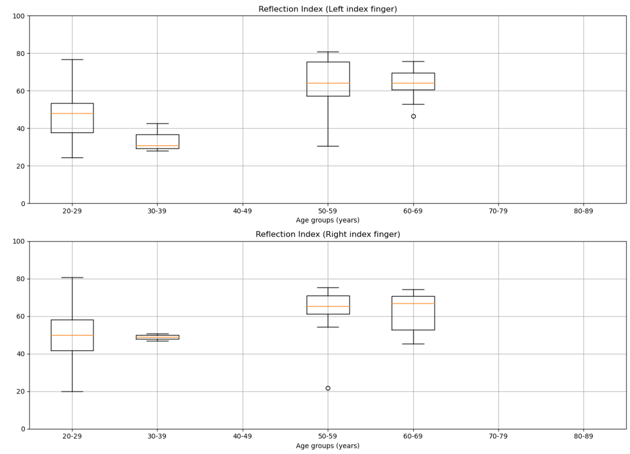
(e) Multiple reports for simultaneous measurements

Figure 13. The PDF report

To test the proposed system, we collected DVP signals from 31 healthy individuals with ages ranging from 20 to 69 in the pilot analysis. The DVP signals at fingertip of both hands are obtained simultaneously. The estimated indices of SI and RI for all subjects are illustrated in Figure 14. From the results, the SI and RI of elderly are higher than younger subjects, consistent with expectation. Our results also show that the indices differ slightly between the measurements taken from left and right hands; but the two measures are highly correlated. The raw pulse waveforms measured from aged subjects (and also subjects with premature arterial stiffening or CVDs) may exhibit indistincinct pulse contours that lead the systolic and diastolic peaks become difficult to identify. Following the technique proposed by Millasseau [20], our system generates SI and RI to be a trustworthy estimate of arterial properties, as shown in the steps of Figure 8 to Figure 11, and Figure 13.



(a) The distribution of SI for left and right hand



(b) The distribution of RI for left and right hand

Figure 14. Box plot for SI and RI of different age groups

The result of this research shows that our proposed system analyzes DVP signals effectively, and accurately, and demonstrates the capacity for large-scale screening for CVDs. The future goal of this study is to collect the DVP signals from healthy people as well as patients from different CVD categories with diverse age groups to establish references of SI and RI for different cohorts. Our system features a platform that generates reports in PDF format with summary of the assessment results. The report is readily for viewing, downloading, and providing information for verifying the estimated indices. It can be important source of information for subjects to discuss with their cardiologists if abnormity is detected. The accuracy of SI calculation depends on the measured accuracy of ΔT_{DVP}, according to the definituin of SI formula. Wu et al. proposed an improved SI calculation utilizing Hilbert-Huang transformation to decompose the original DVP waveform for obtaining a certain intrinsic mode function (IMF5) that used to calculate ΔT_{DVP} [21, 26]. However, in this research, we only estimated SI in the manner of the original calculation of SI for two reasons. First, our study results show satisfactory preliminary accuracy after computing the 1st and 2nd-order derivatives of the waveforms, as shown in Figure 9 through Figure 11. Secondly, our primary goal in this study is to develop a cloud-based assessment tool. In future studies, we will incorporate the algorithm of Wu et al. [21] after collecting a large amount of data. By doing so, the comparison of the accuracy between different SI calculations using the abundant cohorts' information for cross-references of SI data among different age groups and disease groups will be possible.

4 Conclusion

This paper proposed a cloud computing system that is an online web framework designed for health monitoring for CVDs preventation. Integrating the web technology that adopts ASP.NET and high-level object-oriented language Python, the system automatically receives and analyzes uploaded DVP signals and then generated reports of arterial stiffness index (SI) and reflection index (RI). The process includes analysis of DVP wave, estimation of the relevant indices, and creation a PDF report file. The execution time took 5850 ms for two DVP signals (left and right index fingers).

The benefits of the proposed system are fourfold. First, it is done is a non-clinical setting. The measurement taken by a portable device can be performed anytime and anywhere with great accuracy. Secondly, the computing technology designed in the system can effectively reduce system construction time and improve data processing accuracy. Thirdly, a registered user can compare the analyzed results between repeated measurements over time. Lastly, the indices of SI and RI calculated from the uploaded DVP signals from each subject will allow for the construction of the cardiovascular indices' databank at a great population level. This will help health authorities to build standards and references of SI and RI for different cohorts by age, ethnicity, and disease groups. This is also suitable for comparative analysis for drugs efficacy applied before and after patients receiving vasoactive drugs [30].

The proposed system only requires DVP signals, it is suitable for ubiquitous home healthcare applications. With this cloud-based comprehensive computing module, a simple objective measure can be quickly obtained to understand how one's vascular system is functioning. Early prediction for future CVDs for patients will be achieved at individual level [31]. Applied at a greater scale, this system allows for screening for general population. Consequently, mass screening for high-risk patients to prevent CVDs at the population level will be accomplished.

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