Semi-automatic Vendor-Independent Software for Assessment of Local Arterial Stiffness

Madalina Negoita[1], Shima Abdullateef[1], Alun D Hughes[2], Kim H Parker[3], Ashraf W Khir[1]

[1]Brunel Institute of Bioengineering, Brunel University London, UK
[2]Institute of Cardiovascular Science, University College London, UK
[3]Department of Bioengineering, Imperial College, London, UK

Abstract

Background: Stiffened arteries represent a major cardiovascular risk.

Aim: We describe a vendor independent software for the non-invasive determination of arterial stiffness using ultrasound images.

Methods: We have developed an intensity-based semi-automatic software for determining the edges of the luminal arterial walls (M-mode) and blood velocity (PW Doppler) to extract diameter and velocity waveform from ultrasound images. The upstroke of the two waveforms is automatically determined as well as the fit of the initial linear portion of the ln(D)U-loop. Pulse wave velocity (PWV), which is proportional to the slope of ln(D)U-loop during early systole is calculated as a measure of arterial stiffness. The user can over-ride and correct the automatically determined parameters if necessary.

Results: A semi-automatic code was developed for tracing the luminal diameter and blood velocity in the human ascending aorta. D and U waveforms were extracted and used in ln(D)U-loops to calculate PWV.

Conclusions: The software described here can be used to assess, local aortic stiffness non-invasively, by using ultrasound measurements/images of the diameter and velocity waveforms.

1. Introduction

Cardiovascular diseases represent a major cause of death worldwide [1]. Arterial stiffening is a risk factor for hypertension. Currently, arterial stiffness is clinically assessed by measuring PWV [2].

The most common technique for the non-invasive measurement of PWV is the foot-to-foot method [3], which gives an estimate of PWV between two measurement locations, usually the carotid and femoral arteries. This average PWV, cannot account for local variations in the PWV due to the different arterial dimensions and mechanical properties.

Local PWV can be determined non-invasively using measurements of diameter and velocity. Recently, the feasibility of this technique was shown in the adult ascending aorta and compared to carotid-femoral foot-to-foot measurements [4].

The aim of the current study was to develop a semi-automatic vendor independent software which can estimate PWV in human ascending aorta, based on diameter and velocity recorded by ultrasound, with minimal user input.

2. Methods

A semi-automatic vendor-independent software developed in-house was used to analyze ultrasound images and estimate PWV in the human ascending aorta.

2.1. Study population

12 healthy volunteers (4 females) aged 22-32 were recruited. The study was approved by the local ethics committee and written informed consent was obtained prior to measurements.

2.2. Data acquisition

Ultrasound images of diameter and blood flow in the ascending aorta were recorded using a GE Vivid E95 ultrasound system with a 1.5-4.5 MHz transducer. Ultrasound images from each participant were obtained sequentially. A parasternal long axis (PLAX) view was used for diameter measurements and an apical 5 chamber (A5CH) view was used for blood velocity measurements.

Diameter was recorded in 2D M-mode to achieve tracking with a high temporal resolution (as opposed to B-mode (2D) which would make the tracking highly dependent on acquisition frame rate [5]) by placing the cursor downstream of the sino-tubular junction with the M-mode line as perpendicular as possible to the aortic wall. Blood velocity was measured with pulsed wave Doppler

and the sample volume was placed in the ascending aorta, as close as possible to the measurement location for diameter.

Throughout all measurements the volunteers were connected to ECG. Each recording lasted 20s and both diameter and velocity measurements were repeated 3 times, allowing the operator to rest their hand between acquisitions. The cine-loops were saved in Dicom format and images were used for semi-automatic off-line analysis.

Ultrasound image acquisition	
PLAX M-mode	A5CH PW Doppler

Concatenate images

Extract ECG

If FR > 15 fps	If FR <= 15 fps
Diameter	Velocity

Analysis per heart beat

User-defined thresholding independent for the two walls	User-defined thresholding

Removing artefacts in the image

Flagging the waveform

Accepted diameter waveform	Accepted velocity waveform

Upstroke determination and user correction

ln(D)U - loop

Fit determination and user correction

PWV
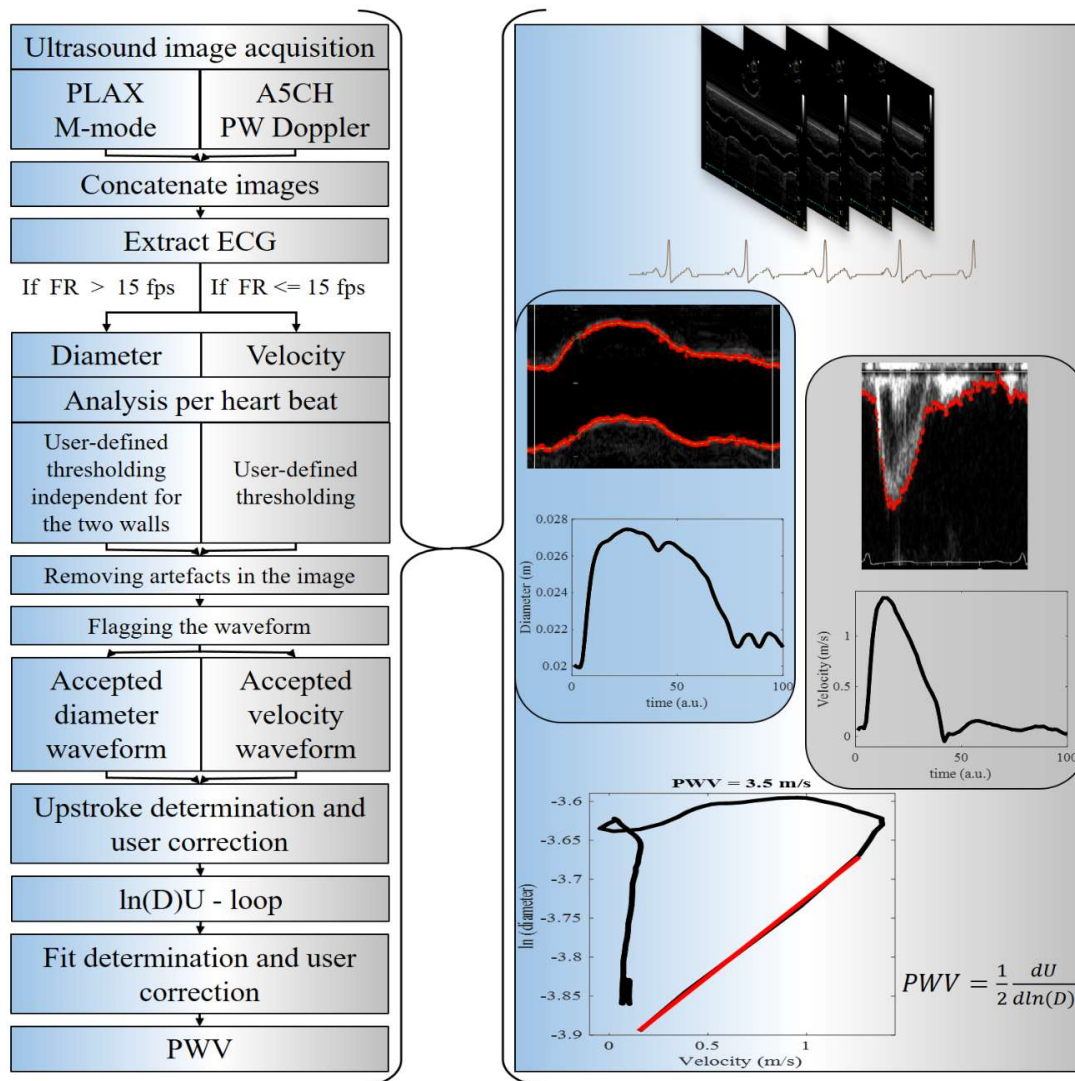
$$PWV = \frac{1}{2}\frac{dU}{dln(D)}$$

Fig. 1. Left: A schematic description of the steps used in the code to extract PWV from ultrasound images of diameter and velocity in the adult ascending aorta. Right: An example of ultrasound images analysed and the resulting waveforms extracted from them and used to calculate PWV. The ln(D)U-loop derived from the D and U waveforms is shown at the bottom of the figure. The upstroke of the two waveforms determines the start of the loop and the linear portion of the loop, denoted in red, is determined by linear regression

2.3.   Image analysis

A Matlab algorithm was developed in-house to extract the continuous waveforms of diameter and velocity in the ascending aorta from cine-loops stored in Dicom files.

The code first reads the Dicom images and the information on cine-loops to account for the total number of frames. Then, the frames are concatenated as the images are renewed on the machine during acquisition to ensure a continuous display of all the heart-beats.

From the entire concatenated image, the ECG is extracted based on its color. The peaks of the ECG R-waves are detected as the peaks in the ECG signal, higher than a threshold (0.8) of the maximum signal amplitude. The time of the R-wave is used to separate each heartbeat.

In the next step, the code checks for the frame rate of the acquisition. Machine capabilities limit the Doppler acquisition to a much lower frame rate. This makes it possible to automatically select the function that will be used to analyze the images, i.e. diameter or velocity.

Diameter waveform extraction: The code displays a frame as acquired from the machine and asks the user to select the minimum and maximum of the amplitude scale. This distance is displayed and used to convert measurements from image pixels into centimeters.

Since time is used only parametrically in the loop method for determining wave speed, it is not necessary to calibrate the time axis of the waveforms. Then, the code asks the user to delimit the areas, regions of interest (ROI), where the upper and bottom walls are, i.e. the areas where the thresholding will take place. To limit the number of artefacts interfering in the thresholding process, the starting lines for the top and bottom walls are chosen at different locations. The end lines up to which the thresholding occurs are also inputted by the user to limit the amount of time spent on the analysis.

The first heartbeat is selected based on the ECG. The ultrasound image is displayed with an initial tracing of the luminal diameter based on a default threshold. Due to an optimized gain during acquisition as well as time gain compensation (TGC) change, the user can change the thresholds independently for the two walls to ensure an appropriate tracing. The code will redo the tracing each time a new value is inserted for either wall until the values are kept the same as the previous iteration. A spline is applied to the points detected by thresholding to smooth the wall tracing and to fill the gaps where no data points are found based on the threshold or they are identified as artefacts and removed in the second step.

The code displays the diameter waveforms resulting from the subtraction of the two walls, using the smoothing spline fit next to the wall tracing in the ultrasound image. This allows the user to visualize the resulting waveform and to allow for dismissing diameters that might seem right in shape but do not follow the contour described by the measured wall movement.

The code then asks the user, in a pop-up box, if there are any points that need to be removed; the default setting is "no". If artefact removing is required, the user types "yes" in the box and the code will allow placing a rectangle around the points that need to be excluded. The process repeats until all outliers are excluded. The code moves to the next step, when "no" is typed in the pop-up box.

The diameter waveform is displayed next to the ultrasound image on which the tracing is overlapped and the user is asked if the tracing is appropriate and the waveform should be considered for further analysis.

Velocity waveform extraction: Extraction of the velocity waveform has a similar code based on thresholding. First, the code asks the user to define the zero line (baseline on the ultrasound image) by displaying a frame as acquired. Then the scale is selected for the conversion from pixels to m/s using a pop-up window.

The user is then asked to select the line from which the thresholding will start and it will always go to the zero line selected previously, to determine the ROI. The threshold can be changed and artefacts can be excluded by selecting an area around them. Then, the code displays the ultrasound image between two consecutive R-wave peaks on which the points from the tracing and the smoothing spline trace are superimposed. The velocity waveform is displayed next to the image and the user is asked if the tracing is appropriate and the waveform should be considered for further analysis.

Selecting 6 consecutive waveforms: From all the accepted diameters and velocities, groups of 6 consecutive waveforms are selected with a moving window of 1 heartbeat. The groups in each run that are most similar in length to the groups of velocities in each run are selected and used for further analysis. The analysis of the local wave speed is carried out using 3 sets of 6 consecutive heartbeats for both diameter and velocity.

ln(D)U-loop and Pulse Wave Velocity: The extracted waveforms from the above analysis represent the input into ln(D)U-loops and PWV analysis. Each group of diameters and velocities are "matched" with each other and a ln(D)U-loop and a PWV is extracted from each match.

Because of the impossibility of acquiring simultaneous measurements of diameter and velocity due to the design of the available probe, the measurements are acquired sequentially. This raises the issue of "matching" beats with similar duration in the ln(D)U-loop by truncating the waveforms in diastole. The ln(D)U-loop method relies upon determining the slope of the loop during the initial part of systole. We do this by determining the 'upstroke' in both the D and U waveforms.

Determining the upstroke: First, the foot of the waveforms was determined. It is observed that both the D and U waveforms increase rapidly and nearly linearly during the initial part of systole. The foot of the waves was determined by fitting a linear regression to this part of the waveform and finding the time at the start of the line where the data deviates from linearity using a threshold of 0.985. This threshold was chosen by trial and error in our experiments and may depend on noise levels in the data acquisition and analysis.

The ln(D)U-loop is plotted for each pair of D and U waveforms starting at the determined upstrokes. The linearity of the loop during the initial part of systole, guaranteed by the linearity of the individual waveforms during this period, is determined by least squares. The end of the initial linear portion of the loop is determined automatically based on a deviation from linearity using a threshold of r^2-0.98.

Due to the noise in the extracted waveforms, the automatic determination of the upstroke and the linear fit in ln(D)U-loop might not be appropriate. User-corrections

are allowed on these points to ensure a proper alignment and fit and hence a correct determination of PWV.

Determining PWV: PWV, by definition [6], is determined as half the ratio of change in velocity to the change in natural logarithm diameter $PWV = \frac{1}{2}\frac{dU}{dln(D)}$. For all diameters and velocities selected in the groups of 6, PWV is determined and stored.

The final value for each person is calculated as the arithmetic mean of all PWV values obtained from matching all 6 waveforms representative for each run representing diameter or velocity acquisitions, in total 324 (6*6*9) values.

3.   Results

PWV was measured in the ascending aorta of 12 healthy adults through non-invasive measurements of diameter and velocity waveforms.

The code was successful in tracing the luminal diameter and blood velocity in the ascending aorta from the ultrasound images. Minimal user-input was needed for the extraction of D and U waveforms which are used in ln(D)U-loops to calculate PWV. The user input comes to limit the processing time by delimiting the ROI or to make the corrections when the software fails to pick the right parameters used for calculating PWV (due to the noise in extracted waveforms, the automatic detection of the upstroke fails and it's being detected in the linear part of the waveform; the user can manually point the foot of the wave by "correcting" the automatic determination).

4.   Discussions

Arterial stiffness is an important parameter in assessing cardiovascular risk and is usually measured through the PWV. We recently showed that local PWV can be measured using non-invasive ultrasound measurements of D and U in the ascending aorta of adults [4].

The algorithm presented here uses images acquired in a routine clinical setting and saved in DICOM format to extract PWV off-line. Minimal user-input is required to specify the ROI where the waveforms will be extracted.

Because the technique would be implemented in a clinical setting, 6 consecutive waveforms were selected as representative for a run. Although 6 runs were measured in our protocol (3 for diameter and 3 for velocity), the software can also allow a different number of runs to be analyzed provided that 6 consecutive heartbeats are extracted after thresholding.

The software is vendor-independent, i.e. can analyze ultrasound images of diameter and velocity recorded on any ultrasound machine as long as they are saved in DICOM format and estimates the PWV in the ascending aorta of adults.

5.   Conclusions

The present study describes a vendor-independent semi-automatic software for the extraction of diameter and velocity waveforms in the human ascending aorta from DICOM ultrasound images, the waveforms are then used to calculate local PWV and evaluate arterial stiffness.

Acknowledgements

References

[1]   Laurent S, Boutouyrie P, Asmar R, Gautier I, Laloux B, Guize L, Ducimetiere P, Benetos A. Aortic stiffness is an independent predictor of all-cause and cardiovascular mortality in hypertensive patients. Hypertension. 2001;37:1236-1241

[2]   Ben-Shlomo Y, Spears M, Boustred C, May , Anderson SG, Benjamin EJ, Boutouyrie P, Cameron J, Chen CH, Cruickshank JKC, Hwang SJ, Lakatta EG, Laurent S, Maldonado J, Mitchell GF, Najjar SS, Newman AB, Ohishi AB, Pannier B, Pereira T, Vasan RS, Shokawa T, Sutton-Tyrell K, Verbeke F, Wang KL, Webb DJ, Hansen TW, Zoungas S, McEniery CM, Cockcroft JR, Wilkinson IB. Aortic pulse wave velocity improves cardiovascular event prediction: an individual participant meta-analysis of prospective observational data from 17,635 subjects. J of the American College of Cardiology.2014;636-646

[3]   Millasseau SC, Stewart AD, Patel SJ, Redwood SR, Chowienczyk PJ. Evaluation of carotid-femoral pulse wave velocity influence of timing algorithm and heart rate. Hypertension. 2005;45;222-226

[4]   Negoita M, Hughes AD, Parker KH, Khir AW. Non-invasive technique for determining local pulse wave velocity in humans ascending aorta. IEEE CinC. 2017;44;1-4

[5]   Negoita M, Zolgharni M, Dadkho E, Pernigo M, Mielewczik M, Cole GD, Dhutia NM, Francis DP. Frame rate required for speckle tracking echocardiography: a quantitative clinical study with open-source, vendor-independent software. International J of Cardiology.2016;218;31-36

[6]   Feng J, Khir AW. Determination of wave speed and wave separation in the arteries using diameter and velocity. J of Biomechanics.2010;43;455-462

Address for correspondence.
Name: Prof Ashraf W Khir; Ashraf.Khir@brunel.ac.uk
Full postal address: Brunel University London, UB8 3PH