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 aim to introduce 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 a measure of arterial stiffness. The user can over-ride and correct the automatically determined parameters to ensure the results are physiologically representative.

Results: cfPWV is 36% higher than the local PWV in the ascending aorta from ultrasound images (5.9±0.6 vs. 4.3±1.0m/s). This difference is due to the smaller arteries with different mechanical properties in the carotid-femoral pathway.

Conclusions: The software described here can be used to assess, local arterial 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]. Hypertension can be caused by stiffened arteries, especially the ascending aorta. 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, compliance and mechanical properties.

Another technique based on non-invasive measurement of diameter and velocity have shown that local PWV can be determined non-invasively. Recently, the feasibility of this technique was shown in the adult ascending aorta and compared to carotid-femoral measurements [4].

The aim of this 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 minimum 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

Ultrasound images of diameter and blood flow in the ascending aorta were recorded in 12 healthy volunteers (4 females) aged 22-32, using GE Vivid E95 ultrasound system and 1.5-4.5 MHz transducer. The study was approved by the local ethics committee and written informed consent was obtained prior to measurements.

2.2. Data acquisition

Ultrasound images from each participant were obtained sequentially. Parasternal long axis (PLAX) view was used for diameter measurements and apical 5 chamber (A5CH) view was used for blood velocity measurements.

Diameter was recorded in M-mode to achieve a highly accurate tracking (as opposed to B-mode (2D) which would make the tracking highly dependent on acquisition frame rate [5]) by placing the cursor downstream the sino-tubular junction. 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 for each diameter then velocity the 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.

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, ECG is extracted based on color. The peak of the ECG R-waves is detected as the peaks in the ECG signal, higher than a threshold (0.8) of the maximum signal amplitude. The time-location of the R-wave is further used to separate each heartbeat.

Next step, the code is checking for the frame rate of the acquisition. Our machine capabilities limit the frame rate to maximum 15fps in the case of Doppler acquisition. This makes possible the automatic selection of 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 two points on the amplitude scale, minimum and maximum visible. Then, the distance between the two points is inserted in a pop-up box. This is used further for calibrating the diameter and converting the pixel measurements from images into centimeters. By default, the code assumes a distance of 12cm as this is the default for the parasternal scan on the ultrasound machine.

The time axis is preserved in pixels to have a higher resolution as conversion to milliseconds would diminish the resolution by ~ 30% (2.88 pixels correspond to 1 ms). Then, the code asks to delimit the areas where the upper and bottom walls are, 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 location. The end lines up to which the thresholding occurs are also user-input to limit the amount of time spent on the analysis.

Further, the first heartbeat is selected based on ECG. The ultrasound image is displayed with an initial tracing of the luminal diameter based on a default threshold. The initial thresholds, 45 and 40 units on the gray scale for the upper and bottom walls, were chosen based on the optimal values for most data analyzed. 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 the same for both walls. A smoothing spline is applied to the initial points detected by thresholding to smooth the wall tracing and to fill the gaps where no data points are found based on 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 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 final step in diameter extraction is to ask the user, again in a pop-up window, whether the tracing is appropriate and the diameter displayed is reasonable in shape and it will be kept for further analysis. The user then can type “yes” or “no” which will be recorded as a flag in the saved results of the analysis.

Velocity waveform extraction: Extraction of the velocity waveform has a similar code based on thresholding was used. First, the code asks the user to define the zero line (baseline on 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 (user manual input). The default scale is 1.2 m/s as it is the default setting on the ultrasound machine.

Then, the user is asked to select the line from which the thresholding will start and it will always go to the zero line selected previously. The default threshold is set to be 50 units on gray scale. 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 are overlapped the points from the tracing and the smoothing spline trace. Next to it the velocity waveform is displayed 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 analysis, thus having in the end one group of

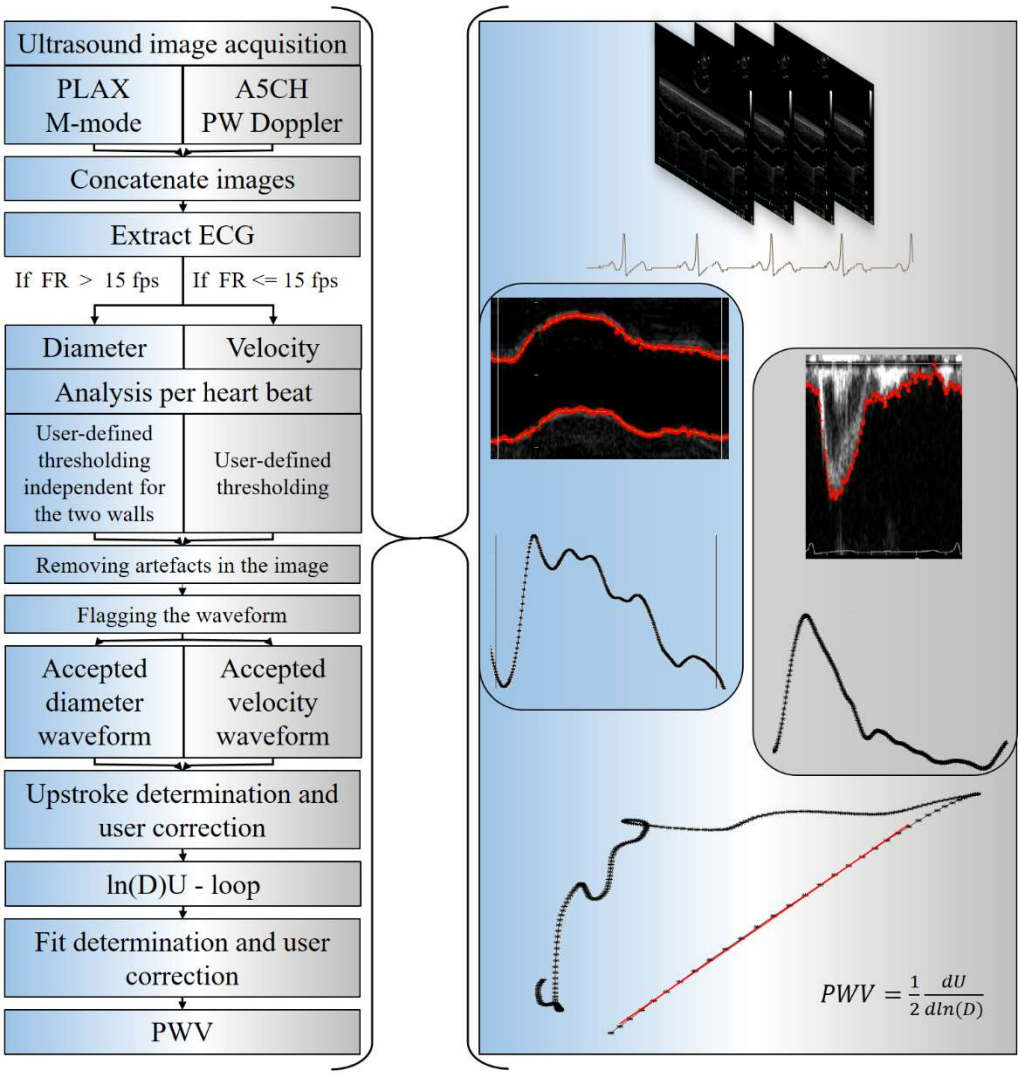

Fig. 1. Left: A schematic description of the steps used in the code to extract PWV from ultrasound images of diameter and velocity in the adult ascending aorta. Right: An example of ultrasound images analysed and the resulting waveforms extracted from them and used to calculate PWV

6 consecutive heartbeats representative for each run.

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 selected as above are "matched" with each other in ln(D)U-loops and a PWV is extracted from each match.

Because of the impossibility of acquiring simultaneous measurements of diameter and velocity due to the physics of the probe and the human body shape, 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. Another issue is the upstroke of the two waveforms which will occur at different moments in time in the case of sequential measurements, thus requiring the determination of these points.

Determining the upstroke: First, the foot of the waveforms was determined. The foot of the waves was determined by fitting a line and imposing a deviation from linearity threshold of 0.985, which was chosen small enough to ensure noise in the signal is not interpreted as nonlinearity.

To plot the ln(D)U-loop, the D and U waveforms have start from previously determined upstroke. End of the initial linear portion is determined automatically based on the deviation from linearity using a threshold of r^2=0.98.

User-corrections are allowed on these points (upstroke of the two waveforms, D and U and linear fit) 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 per person is calculated as 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. Minimum 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 or to make the corrections when the software fails to pick the right parameters used for calculating PWV.

4. Discussions

Arterial stiffness is an important parameter in assessing cardiovascular risk and is measured through PWV which was recently shown to be measured locally using non-invasive ultrasound measurements of D and U in adults ascending aorta [4].

The algorithm presented here uses images acquired in a routine clinical setting and export them in dicom format to extract PWV off-line. Minimum user-input is required to extract the waveforms and to verify and adjust, the correct estimation of PWV.

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 lower number of runs to be analyzed provided that 6 consecutive heartbeats will be extracted after thresholding.

The software is vendor-independent, i.e. can analyze ultrasound images of diameter and velocity recorded on any ultrasound machine and estimate PWV in adults ascending aorta.

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 ultrasound images which are the parameters used to calculate local PWV and evaluate arterial stiffness.

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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. Journal 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 Computing in Cardiology. 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 Journal 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. Journal of Biomechanics. 2010;43;455-462

Address for correspondence.
Name: Prof Ashraf W Khir
Full postal address: Brunel University London, Kingston Lane, Uxbridge, Middlesex, UB8 3PH
E-mail address: Ashraf.Khir@brunel.ac.uk