

Simultaneous determination of wave speed and arrival time of reflected waves using the pressure–velocity loop

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Abstract In a previous paper we demonstrated that the linear portion of the pressure–velocity loop (PU-loop) corresponding to early systole could be used to calculate the local wave speed. In this paper we extend this work to show that determination of the time at which the PU-loop first deviates from linearity provides a convenient way to determine the arrival time of reflected waves (T_r). We also present a new technique using the PU-loop that allows for the determination of wave speed and T_r simultaneously. We measured pressure and flow in elastic tubes of different diameters, where a strong reflection site existed at known distances away from the measurement site. We also measured pressure and flow in the ascending aorta of 11 anaesthetised dogs where a strong reflection site was produced through total arterial occlusion at four different sites. Wave speed was determined from the initial slope of the PU-loop and T_r was determined using a new algorithm that detects the sampling point at which the initial linear part of the PU-loop deviates from linearity. The results of the new technique for detecting T_r were comparable to those determined using the foot-to-foot and wave intensity analysis methods. In elastic tubes T_r detected using the new algorithm was almost identical to that detected using wave intensity analysis and foot-to-foot methods with a

maximum difference of 2%. T_r detected using the PU-loop in vivo highly correlated with that detected using wave intensity analysis ($r^2 = 0.83$, $P < 0.001$). We conclude that the new technique described in this paper offers a convenient and objective method for detecting T_r , and allows for the dynamic determination of wave speed and T_r , simultaneously.

Keywords Wave speed · Reflected waves · Wave intensity analysis · PU-loop

1 Introduction

The arrival time of reflected waves to the root of the aorta is of physiological importance [27]. If the reflected waves arrive before the aortic valve is closed, the left ventricle will be required to produce extra work to overcome the increase in pressure associated with those reflected waves [8].

Several methods have been proposed to identify the arrival time of reflected waves. Westerhof et al. [29] used the input impedance to calculate the distance to the apparent reflection site, from which, they determined the arrival time of reflected waves. Van Den Bos et al. [28] introduced a method for determining the arrival time of reflected waves based on the time delay between the forward and backward components of the pressure waveform. Murgu et al. [20] suggested that the temporal difference from the initial pressure upstroke to the pressure inflection point is the time that it takes the wave to run forward, be reflected and arrive back. With knowledge of the wave speed, the distance to the reflection site can be determined. More recently, Pythoud et al. [25] proposed the “reflection profile” method to determine the distances of the most

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important reflection sites by deconvoluting the backward pressure wave. Parker et al. [23] introduced wave intensity analysis (WIA) for studying travelling waves in arteries. The method allows for the separation of waves into their forward and backward directions [24] and because WIA is a time-domain analysis, the arrival of the reflected waves to the measurement site is readily available in the results of this analysis as the onset of the backward wave. The accuracy of WIA has been tested *in vitro* [11], used *in vivo* in animal models [12, 26] and has also been used for detecting the arrival time of reflected waves in patients [10, 13]. The determination of the arrival time of the reflected waves using any of the above methods requires knowledge of the wave speed, which can be measured using any of the methods summarised in the following paragraphs.

Wave speed measurements can generally be grouped into two main categories, spatial and local techniques. Spatial wave speed in the arterial system has been predominantly obtained using the foot-to-foot method. This method has been used extensively and the results confirm that the wave speed along the aorta is not uniform; a significant increase is observed distally [14, 18, 21]. Although this method is being used clinically and in a number of epidemiological studies [1, 6, 19] the non-invasive results are somewhat controversial and subjective [7].

Local wave speed refers to the determination of wave speed at the measurement site. Westerhof et al. used the characteristic impedance to determine the local wave speed [28] and Davies et al. [4] introduced a new technique for determining local wave speed also based on the measurements of pressure and flow at the same site. In a previous paper we introduced the PU-loop method for determining local wave speed [9]. During the early part of systole, it is most probable that only forward waves are present in the ascending aorta, the relationship between pressure and velocity is linear and the initial slope of the PU-loop is directly related to wave speed.

We therefore hypothesise that the end of the initial linear part of the PU-loop during early systole marks the arrival time of reflected waves. Hence, the main objectives of this paper are: (1) to present a new technique to test this hypothesis, and (2) to demonstrate the simultaneous determination of the initial linear slope of the PU-loop indicating wave speed, and detection of the point of deflection at the end of this linear part indicating the arrival time of reflected waves.

2 Materials and methods

The pulse wave speed and the arrival time of the reflected waves were determined in two sets of data; *in vitro* and *in vivo*.

2.1 *In vitro* experiments

A schematic diagram of the experimental setup is shown in Fig. 1 and a description of the individual elements follows.

2.1.1 *The pump*

A positive displacement syringe pump was used to generate a single approximately half-sinusoidal pulse wave. The pump consists of a cylinder and a piston that is driven by an electric motor (Maxon, Sachseln, Switzerland). The cylinder of the pump is 5 cm in diameter and the linear movement of the piston is 2 cm, giving a displaced volume of approximately 40 ml. In all of the experiments we generated and analysed a single half-sinusoidal pulse, in which the piston moved forward from its bottom to top dead centre positions.

2.1.2 *Tubes*

We used flexible tubes made of latex (3S Health Care, London, UK). Tubes were uniform along their lengths with a circular cross sectional area and were obtained with a standard length of 100 cm. We used tubes with 4, 8 and 16 mm unstressed diameter with wall thickness approximately 0.25 mm.

To eliminate gravitational and contact stresses between the elastic tubes and any hard surfaces during the experiments, the tube was immersed in an open tank containing tap water. The tubes were able to extend and distend freely

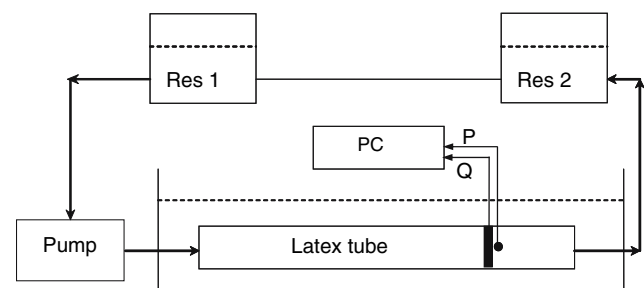


Fig. 1 Schematic diagram showing the experimental set up. The latex tube is connected to the pump at its inlet through a polyurethane tube, and its exit is connected to the downstream reservoir through a hard plastic (Portex) connector and a polyurethane tube. The pump generates a single half sinusoidal waveform in the forward direction. Pressure (P) and flow rate (Q) are measured simultaneously at different sites along the elastic tube. The measured signals are collected digitally into a personal computer. Reservoir 1 provides the pump with water and ensures the system is free from bubbles, and reservoir 2 collects the fluid volume displaced by the pump. The dashed lines indicate the level of water in the tank and reservoirs

and were fully immersed, where the level of water above the surface of the tube was approximately 1 cm. We note that the transmural pressure will vary for the different sized tubes, however, this variation is ignored as the difference is insignificant. We also note that there will be a hydrostatic pressure difference between the top and bottom surfaces of the latex tube, however, its value is considerably smaller than mean pressure in the tube. We expect its effect to be minimal, and so ignored it.

The outlet of each tube was attached to a hard plastic connector (Portex) of a matching size. The Portex connector was attached to a relatively rigid, thick-walled polyurethane tube that was connected to the downstream reservoir, which is made of hard plastic. The outlet of each tube was considered a strong reflection site because of the hard connector and rigid tubing. An upstream reservoir was connected to prevent pump cavitations and air bubbles entering the system.

2.1.3 Measurements

Pressure and flow-rate were recorded simultaneously at different locations along each tube, which are detailed as shown in Table 1. Pressure was measured using a 6F catheter with a strain gauge pressure transducer (Gaeltec, Scotland, UK), which was advanced to the measurement site through a Y connector at the inlet of the tube. Flow-rate was measured using an ultrasound flow meter and an ultrasound flow probe (Transonic, Ithaca, NY, USA), which fits snugly to each tube. The pressure catheter was calibrated against a column of water with a variable height, and the ultrasound flow probes were calibrated against the preset calibration signals of the flow meter. Data were sampled at a frequency of 500 Hz using Labview (National Instruments, TX, USA), and were subsequently analysed using programs prepared in Matlab (The Mathworks Inc, Ithaca, NY, USA).

2.2 In vivo experiment

2.2.1 Animal preparations

This study, which conformed to the ‘‘Guiding Principles of Research Involving Animals and Human Beings’’ of the American Physiological Society, was performed in 11 mongrel dogs (average weight 22 ± 3 kg, 7 males). Animals were anaesthetised with sodium pentobarbital, 30 mg/kg-body weight intravenously, and a maintenance dose of 75 mg/h was given intravenously for the duration of the experiment. Each dog was endotracheally intubated and

Table 1 The arrival time of reflected waves in tubes with different diameters

Tube Diameter (mm)	Wave speed (m/s)	Distance to reflection site (m)	Arrival time of reflected waves (s)		
			f-t-f 2L/c	PU-loop R	WIA M
4.00	6.77	0.30	0.091	0.096	0.092
		0.40	0.118	0.114	0.118
		0.50	0.142	0.140	0.136
		Mean	0.117	0.116	0.115
		SD	0.025	0.022	0.022
		% Change	1		-1
8.00	5.66	0.30	0.106	0.116	0.110
		0.40	0.141	0.124	0.128
		0.50	0.176	0.178	0.176
		Mean	0.141	0.139	0.138
		SD	0.035	0.033	0.034
		% Change	1		-1
16.00	3.80	0.30	0.147	0.136	0.138
		0.40	0.216	0.216	0.214
		0.50	0.274	0.288	0.276
		Mean	0.212	0.213	0.209
		SD	0.063	0.076	0.069
		% Change	0.3		2

Values of mean \pm SD and the percentage change of the arrival time of reflected waves as determined using three methods; the new technique using the PU-loop method (point R, Fig. 3), Foot-to-Foot method (f-t-f) and wave intensity analysis (WIA) using Eq. 1 (point M, Fig. 3). The % change is calculated as the difference of the f-t-f, wave intensity methods, and the PU-loop method, compared to the PU-loop method

mechanically ventilated using a constant-volume ventilator (Model 607, Harvard Apparatus Company, Millis, MA, USA). After a median sternotomy, an ultrasonic flow probe (Transonic Systems Inc., Ithaca, NY, USA) was mounted around the ascending aorta approximately 1 cm distal to the aortic valve. ECG leads were connected to both fore-legs and the left back leg. A high-fidelity pressure catheter (Millar Instruments Inc., Houston, TX, USA) was used to measure the pressure in the aortic root as near as possible to the site of the flow probe without creating interference (a few millimetres away from the flow probe, proximal to the aortic valve). The pressure catheter was advanced from either the right or the left brachial artery. Snares were placed at four different sites during the preparation of each dog: the upper descending thoracic aorta at the level of the aortic valve (thoracic); the lower thoracic aorta at the level of the diaphragm (diaphragm); the abdominal aorta between the renal arteries (abdominal) and the left iliac artery, 2 cm downstream from the aorta-iliac bifurcation (iliac).

2.2.2 Protocol

At each occlusion site, data were collected for 30 s before the occlusion (control), during the occlusion; 3 min after the snare was applied [12], and after the snare was removed. At each site, total occlusion was confirmed by observing no flow distal to the occlusion site, and another Millar high-fidelity pressure catheter was advanced from either the right or left iliac artery to measure pressure at the occlusion site. A time interval of 10–15 min was allowed between occlusions to return to control conditions. In order to eliminate effects due to the cumulative time of the procedure, the sequence of occlusions was varied from dog to dog using a 4 by 4 Latin-square. The circumference of the post-mortem ascending aorta was measured to convert the measured flow rate into velocity. We note that the circumference of the ascending aorta of each dog was measured at zero transmural pressure and hence the calculated diameter may be less than the actual diameter in vivo. However, in order to account for that difference, we did not take into consideration the wall thickness and assumed that the measured external radius is the correct value to be used in calculating the velocities [12]. To eliminate the effect of the possible time lag attributable to the filter in the ultrasonic flow meter, the foot of the pressure and velocity waveforms were aligned at the onset of ejection, as previously described [9], and the lag was accounted for prior to carrying out the analysis.

The pressure catheters were calibrated prior to each experiment against a mercury manometer. All in vivo data were recorded at a sampling rate of 200 Hz, stored digitally and were analysed using Matlab software (The MathWorks Inc., Natick, MA, USA).

For each data set, the analysis was performed on three beats, whose average is represented in the results. Regression and paired *t* test analyses were performed to identify the correlation factor and its significance. Values of $P < 0.05$ were considered significant. The Bland–Altman [2] technique was used to establish whether there was a significant difference between the results of the new technique and those of WIA. The acceptable range for the mean difference was taken as $\pm 2SD$.

3 Analysis

Three methods to determine the arrival time of the reflected waves have been used: the foot-to-foot, WIA and the PU-loop.

3.1 Foot-to-foot

As discussed above, the foot-to-foot method is traditionally used for calculating wave speed. The method involves the

measurements of either pressure or velocity waveform at two sites that are at a known distance (L) apart and wave speed, c , is simply calculated as $c = L/\Delta t$, where Δt is the time it takes the wave to run from one site to the other. In our analysis we used the same principle but with measurements of the pressure waveform at one site. If c and the distance between the measurement and reflected sites (L) are known, the relative arrival time of the reflected waves can be determined as $\Delta t = 2L/c$, which is the time it takes the wave to run from one site to the other, be reflected and run back to the measurement site. This method has been used in the in vitro study only.

3.2 Wave intensity analysis

The theoretical basis of WIA is the solution of the classical 1-D conservation of mass and momentum equations and the derivation of the following equations is found in earlier papers [22, 23]. The net wave intensity, dI , is calculated as $dI = dP dU$, where dP and dU are respectively, the pressure and velocity differences over one sampling period. The pressure and velocity differences across the measured wavefronts are assumed to be the addition of the differences across the forward (+) and backward (–) pressure and velocity wavefronts; $dP = dP_+ + dP_-$ and $dU = dU_+ + dU_-$. This assumption enables us to write the intensities of the forward and backward waves

$$dI_{\pm} = \pm \frac{1}{4\rho c} (dP \pm \rho c dU)^2 \quad (1)$$

Where ρ is density and c is wave speed, which was determined using the PU-loop method [8]. We note that wave intensity has the useful characteristics that it is positive for forward waves and negative for backward waves. Therefore, the relative arrival time of reflected waves was determined as the time of the first sampling points when dI_- (the backward intensity) was substantially bigger than the noise level determined from the initial part of the dI_- curve. This method has been used in both the in vitro and in vivo studies.

3.3 PU-loop

The theoretical basis of the PU-loop method for determining wave speed is the water hammer equation, which can be written for the forward and backward waves as

$$dP_{\pm} = \pm \rho c dU_{\pm} \quad (2)$$

Equation (2) describes the relationship between changes in the pressure and velocity, and plotting the measured

pressure against the measured velocity over the cycle we obtain a PU-loop. During the very early part of the cycle when only forward waves are expected to be present, the slope of the PU-loop should be linear. On arrival of the reflected waves, the linear relationship between pressure and velocity will no longer hold and there will be a deflection point, after which the loop becomes non-linear. The slope of the PU-loop, S , during any time interval is $S = dP/dU$. We define $t = 0$ as the time of the foot of the initial pressure waveform, and $t = Tr$ as the time at which the reflected wave returns to the site of measurement.

When $t < Tr$ and only forward waves are present, the slope of the initial linear part of the loop is

$$S_0 = \frac{dP_+}{dU_+} = \rho c \tag{3}$$

when the reflected wave arrives back to the measurement site, and both forward and backward waves are present, the slope at $t = Tr$ can be written

$$S_r = \frac{dP}{dU} = \rho c \frac{dP_+ + dP_-}{dP_+ - dP_-} \tag{4}$$

Calculating the relative change in slope, ΔS , at $t = Tr$ gives

$$\Delta S = \frac{S_r - S_0}{S_0} = \frac{2dP_-}{dP_+ - dP_-} \tag{5}$$

when ΔS was greater than a threshold, ε , the initial part of the PU-loop was deemed no longer linear and the time of that interval is considered to be the arrival time of the reflected wave. The optimal value of ε was determined by trial-and-error and found to be $\varepsilon = 0.35$.

A program was written in MatLab (MathWorks Inc, Natick, MA, USA) to automate the determination of the linear part in the PU-loop and to detect the sampling point at which the loop deviates from linearity, which we hypothesise to be the arrival time of reflected waves. The program calculates the local slope, S_i , at each sampling time $S_i = \frac{P_{i+1} - P_i}{U_{i+1} - U_i}$, where P_i and U_i are the pressure and velocity at time t_i . To find the end of the initial linear part of the PU-loop, denoted by point R in Fig. 2, the program calculates the relative difference between the current slope and the average of all the previous slopes starting from the beginning of the linear part, point K.

$$\Delta S_i = \frac{S_i}{\left(\frac{1}{i-K} \sum_{j=K}^{i-1} S_j\right)} - 1 \tag{6}$$

when $\Delta S_i \geq \varepsilon$, the time of that interval is considered the arrival time of the reflected wave.

This algorithm is a point-to-point technique and the program analyses one interval at a time. The program starts

the analysis at the foot of the pressure waveform, which is the beginning of the linear part, proceeds to find the end of the linear part indicating the arrival time of reflected waves, and simultaneously determines the slope of the initial linear part indicating wave speed, then it stops. This method has been used in both the in vitro and in vivo studies.

4 Results

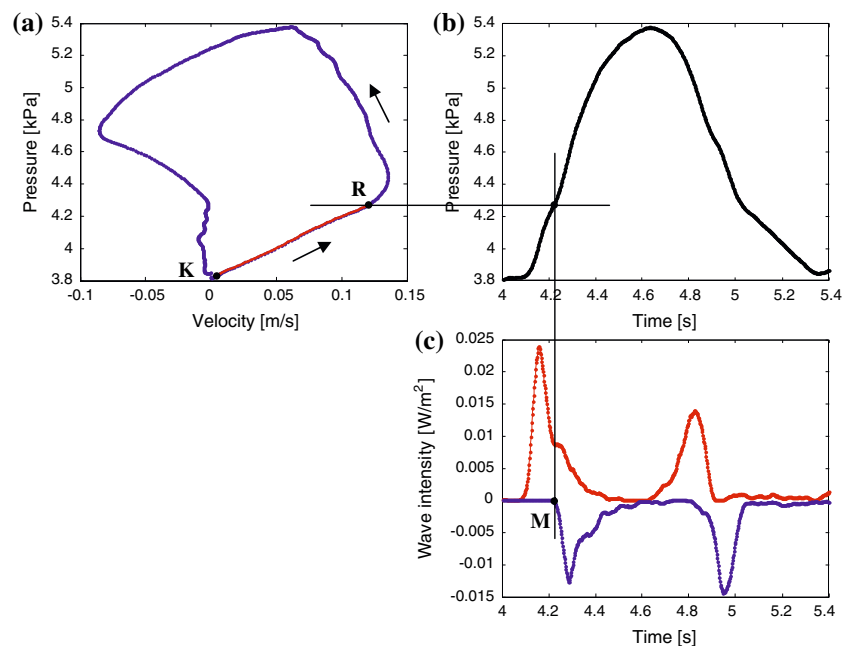
4.1 In vitro experiment

For each of the three tubes, three measurements were taken at three distances; 30, 40 and 50 cm away from the reflection site. The time of arrival of the first reflected wave was determined for each case, using three methods: the new technique utilising the PU-loop, WIA and the foot-to-foot method. The arrival time of reflected waves detected using the PU-loop method in vitro, point R, highly correlated with that detected using the foot-to-foot-method ($r^2 = 0.97$, $P < 0.001$) and the WIA, point M, ($r^2 = 0.95$, $P < 0.001$). Figure 2 shows that the time of the sampling point at the end of the linear part of the PU-loop as determined by the new algorithm, and the onset of reflection as determined by wave intensity, occur almost simultaneously. This was found to be true in all of the cases that we tested. Times of arrival of the reflected wave to the different measurement sites in the different size tubes using the three methods are given in Table 1. The maximum difference between the arrival time of reflected waves determined by the new algorithm and both other methods was approximately 2%, which occurred in the 16 mm diameter tube.

4.2 In vivo experiment

Figures 3 and 4 show the time of the sampling point at the end of the linear part of the PU-loop as determined by the new algorithm, point R, and the onset of reflection as determined by wave intensity, point M, during control and during thoracic occlusion, respectively. During occlusion the strong reflection site results in a strong reflected wave that is marked by a clear deflection point on the PU-loop, point R, as shown in Fig. 4. Although the end of the initial linear part of the PU-loop during control is less obvious than that during occlusion, the new technique accurately detects the time of arrival of reflected waves as detected by WIA in both cases. The arrival time of reflected waves determined by the PU-loop during all measurements correlated well with those determined by the WIA ($r^2 = 0.83$, $P < 0.001$), as shown in Fig. 5a. Results of the paired t test

Fig. 2 The determination of the initial linear part of the PU-loop is shown in (a) and the *arrows* indicate the direction of the loop. The pressure measured in a latex tube of 1 m length and 12 mm diameter at 0.30 m away from the reflection site is shown in (b). Wave intensity analysis is shown in (c). End of linear part, point R, corresponds well with the onset of reflected wave from wave intensity analysis, point M. Note that wave speed is determined by the average of all the slopes of each of the sampling intervals over the period between points K and R



show that the PU-loop using the new algorithm systematically calculates a higher value for T_r than that determined by WIA (0.056 vs. 0.053, s).

We used Bland–Altman plot to compare the results of the WIA and the PU-loop methods for determining the arrival time of reflected waves. The mean value of the difference between the results of the two methods was 0.003 and the standard deviation of that mean was ± 0.004 . As shown in Fig. 5b most of the data points, as well as the zero line fell within the acceptable confidence range of the average, double the standard deviation ($\pm 2SD$) of the

difference, indicating no statistical difference between the results of the two methods.

5 Discussion

In our earlier work we established that the linear portion of the PU-loop corresponding to early systole could be used to calculate the local wave speed [9]. In this paper we extended this work and demonstrated that the time at which the initial part of the PU-loop first deviates from linearity

Fig. 3 Pressure and velocity measured in the ascending aorta during control conditions. In a the PU-loop is constructed, the initial linear part of the loop is determined using the new technique and the *arrows* indicate the direction of the loop. The pressure is plotted against time in b to translate the end of the linear part, point R, to time. Wave intensity analysis is shown in (c). Although the end of the initial linear part in the PU-loop is not very obvious, it was detected by the new method, point R, which corresponds well with the onset of the reflected waves as determined using wave intensity analysis, point M

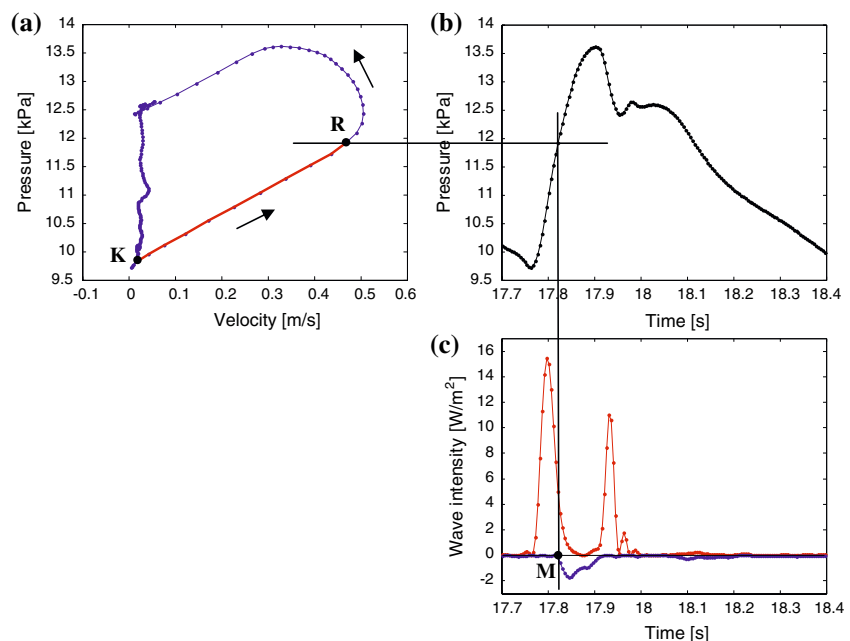
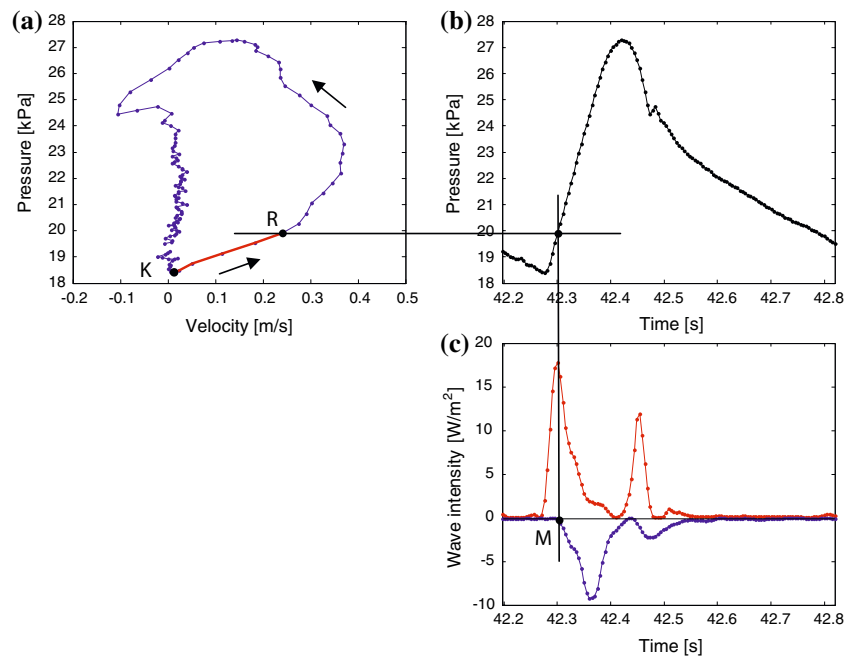


Fig. 4 Pressure and velocity measured in the ascending aorta during thoracic occlusion. In **a** the PU-loop is constructed, the initial linear part of the loop is determined using the new technique and the arrows indicate the direction of the loop. The pressure is plotted against time in **b** to translate the end of linear part, point R, to time. Wave intensity analysis is shown in **(c)**. The end of the initial linear part in the PU-loop is more obvious in this example than in the example of Fig. 3 due to the earlier arrival of the reflected wave. Similar to Fig. 3, the end of the initial linear part of the loop, point R, corresponds well with the onset of the reflected waves as determined using wave intensity analysis, point M



provides a convenient way to determine the time of arrival of the reflected wave. Using the technique described in this paper allowed for the simultaneous determination of wave speed and the arrival time of reflected waves.

5.1 Wave speed

Wave speed is an important property of an arterial segment and directly related to its compliance. Wave speed has been long used as a surrogate marker for aortic stiffness, which has recently been thought of as an independent predictor of stroke [16] and cardiovascular mortality [15] in hypertensive patients. Aortic stiffness has also been associated with the reduction of coronary flow [17]. Thus, automating the determination of wave speed is of clinical relevance and the results of this paper are encouraging towards achieving this aim. The PU-loop method is easy to use but requires the simultaneous measurements of pressure and flow velocity at the same site. We note that Dujardin and Stone used a similar loop (the flow-pressure loop) to determine the characteristic impedance [3].

The wave speed determined using the PU-loop is traditionally made by establishing the slope of the initial part of the loop by eye. The new algorithm allows for automating this process, making the determination of wave speed by the PU-loop more objective. The average difference between the results of wave speed determined by the slope of the PU-loop as established by the new algorithm and by eye in the *in vivo* experiments, is in the order of 3% as shown in Table 2.

Because of the difficulty in obtaining accurate measurements of pressure non-invasively, other researchers have used a wall tracking system, which allows for substituting pressure with vessel diameter [5]. Harada et al. used an online technique for determining wave speed, and suggested that towards end of systole there may be another period where waves in the ascending aorta are also unidirectional, similar to the period at early systole. We anticipate the relationship between pressure and velocity at that time to also be linear, and if desired, the computer program implementing the algorithm in this paper could be adapted to detect other linear parts in the PU-loop. To do so, another search procedure is applied after the first linear part has been detected and this algorithm can simply be used to detect other linear parts if needed.

5.2 Arrival time of reflected wave

Theoretically the end of the initial linear part of the PU-loop should occur at the same time as the onset of the first reflected wave determined using WIA. The comparison between the two methods is made to verify how well the new algorithm is able to detect the onset of nonlinearity between the pressure and velocity in the loop, which is regarded as the onset of reflected waves. As shown, the results of the new algorithm for the detection of the arrival time of the reflected waves are in agreement with those determined by both WIA and foot-to-foot methods, indicating the viability of the new technique. It is worth noting, however, that one of the limitations of this technique is that

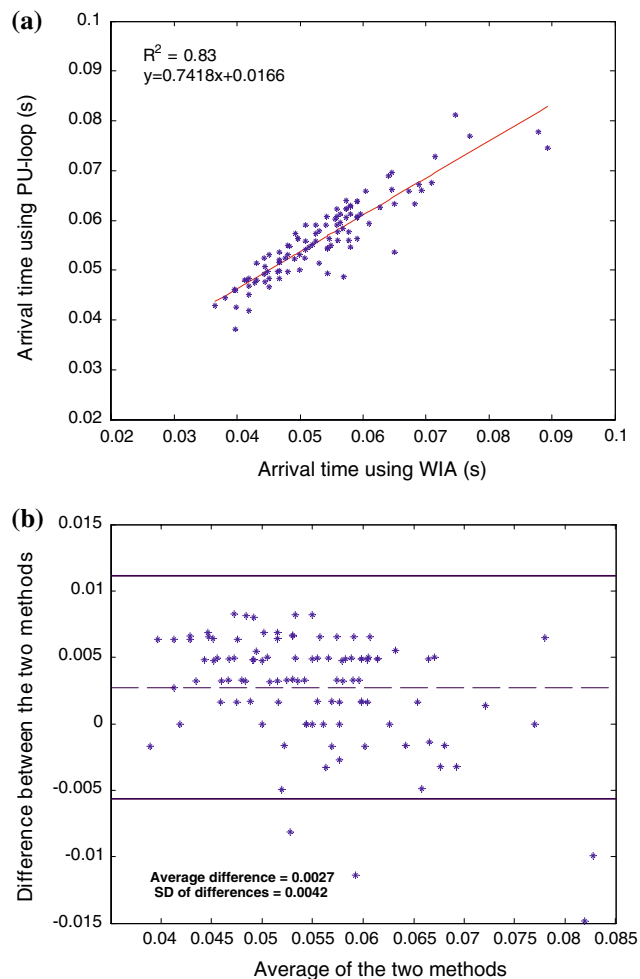


Fig. 5 **a** The relative arrival time to the aortic root determined using the PU-loop is compared with that determined using wave intensity analysis. The results of the new technique using the PU-loop correlates well with those of wave intensity analysis ($r^2 = 0.83$, $P < .001$). Paired t test shows that the PU-loop using the new algorithm systematically calculates a higher value for Tr than that calculated using WIA. **b** Bland–Altman plot showing the agreement between the two results. Dashed line is the mean difference between the two methods and the continuous lines indicate $\pm 2SD$ of the mean difference. Note that most of the data points fell within $\pm 2SD$ range, and the zero line fell within the acceptable confidence limits of the average, indicating no statistical significant difference between wave intensity analysis and the PU-loop methods for determining the arrival time of reflected waves

incorrect temporal alignment of pressure and velocity can influence the correct determination of the slope of the linear part, and thus the value of wave speed. Similarly, a time lag between the measurement of pressure and flow (or velocity) can introduce errors in the determination of the arrival time of the reflected wave.

The augmentation index (AIx) is used extensively clinically to quantify the magnitude of the reflected waves [22]. The determination of AIx depends principally on detecting a change in the shape of the pressure waveform

Table 2 A comparison between wave speeds measured using different techniques

Dog no.	Wave speed (m/s)		$(c_1 - c_2)/c_1$ (%)
	c_1	c_2	
1	4.67	4.60	1.6
2	8.70	8.18	6.4
3	4.25	4.22	0.8
4	4.83	4.82	0.1
5	4.38	4.23	3.4
6	9.65	9.20	4.9
7	8.03	7.79	3.0
8	5.52	5.42	2.0
9	5.87	5.91	-0.7
10	5.60	5.53	1.2
12	7.01	6.85	2.2
Average	6.23	6.07	2.6

Wave speeds determined by the slope of the PU-loop as established by the new algorithm, c_1 , and by eye, c_2 . For each method, the wave speed is the average of the entire wave speeds measured at control and all of the interventions. The global average of the percentage difference between the two techniques is 2.6%

upon the arrival of the reflected waves using some derivative of the waveform [20]; most authors used the fourth derivative. The accuracy of the technique depends upon the ability to detect an inflection point or shoulder on the pressure waveform. However, in our experiments an inflection point in the pressure waveform was not always obvious as shown in the pressure waveforms in Figs. 3, 4. Other researchers have also reported similar observations of the lack of an inflection point in vivo [30]. A comparison of the results of detecting the arrival time of the reflected wave between the method discussed in this paper and those used in establishing AIx has not been reported previously and it is a question for a separate study.

5.3 The program

As discussed in the analysis, the threshold ε , determines the accuracy of the linear part represents the minimum allowed relative difference between slopes. We initially tested the algorithm and found by trial-and-error that $\varepsilon = 0.35$ is the value that gave the best results with in vitro data. The same value of ε has also given the best results with in vivo data. Since the in vivo data was collected at 200 Hz and the in vitro data at 500 Hz, it seems that the threshold is most likely sample rate independent.

To make sure the initial linear part of the PU-loop is not detected within the noise level, the length of the linear part was calculated and had to be at least 20 ms long before it

was acceptable. The value of 20 ms has also been determined by trial and error and gave the best results in both the in vivo and in vitro data. If the length of the linear part is below this value, the program assumes the found linear part is within the noise level and continues searching for real linear part. Further, this technique has also been tested using these values of ε and the minimum length of the linear part with other data that are not presented here but was recorded at 1 kHz and also gave the best results. Therefore we found these values to be optimal in our experiments, and anticipate they could be suitable for analysing similar data that are recorded at sampling frequencies in the range of 200 Hz–1 kHz.

In Conclusion, the PU-loop method for determining local wave speed can also be used to detect the arrival time of reflected waves by identifying the end of the initial linear part of the loop. The proposed algorithm is most likely independent of sampling rate, and the results for calculating wave speed and determining the arrival time of reflected waves compare well with the results of wave intensity analysis and foot-to-foot methods. The new technique offers an objective method for determining the initial slope of the PU-loop indicating wave speed, and the end of the linear part of the loop indicating the arrival time of reflected wave. The new algorithm utilising the PU-loop provides a new technique for the dynamic determination of wave speed and the arrival time of reflected waves simultaneously.

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