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The Use of Ultrasound Imaging in Continuous Blood Vessel Area and Velocity Data Acquisition for Determining the Local Pulse Wave Velocity

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The Use of Ultrasound Imaging in Continuous Blood Vessel Area and Velocity Data Acquisition for Determining the Local Pulse Wave Velocity

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Abstract

Pulse Wave Velocity (PWV) is a useful biomarker in the monitoring and risk stratification of various cardiovascular diseases including hypertension. The current gold standard for non-invasive is carotid-femoral PWV (cfPWV) measurement via direct tonometry. However, cfPWV is limited as it can only provide global and not local PWV measurement, hence an alternative local PWV measure is needed. One alternative is ultrasound whose good penetration depth, accessibility, low-cost nature makes it an ideal measurement mode for non-invasive, real-time acquisition of hemodynamic parameters to determine PWV. This paper will discuss the use of ultrasound imaging in vessel data acquisition, cover the different ultrasound-based imaging modalities for acquiring area and velocity data, and compare between simultaneous and non-simultaneous data acquisition for PWV estimation.

Keywords: ultrasound imaging; doppler measurement; continuous blood vessel measurements; pulse wave velocity

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1. Introduction

The Pulse Wave Velocity (PWV) is the rate at which pressure waves propagate through the arterial system [1]. Clinically, PWV has been established as a reliable, non-invasive measure of arterial stiffness [2] and an independent risk predictor of adverse cardiovascular events including hypertension [3,4]. Further explorations into PWV utility have led to the study of PWV as a possible parameter in the non-invasive monitoring of key cardiovascular measurements such as arterial blood pressure (ABP) [5]. In particular, the use of PWV in ABP measurement presents as a possible improvement to the current non-invasive clinical method of sphygmomanometry in allowing for more continuous monitoring of ABP and therefore facilitating investigations into the dynamic behaviour of the arterial system.

The current gold standard for non-invasive PWV measurement is the carotid-femoral PWV (cfPWV) measurement via direct tonometry [6,7] which involves measuring the transit time of the arterial waveform from one point on the carotid to a second point on the femoral artery [7,8]. However, the global nature of cfPWV in measurement over a long arterial segment limits the effectiveness of the method. Firstly, the distance measurement in cfPWV does not account for the path of blood from the aortic arch to the carotid artery, hence assumptions are made to appropriately adjust the measured time taken which limits the accuracy of the method [8,9]. Secondly, global cfPWV measurement conceals variations in arterial stiffness and mechanical properties of vessels [7,10] that may cause differences in local PWV. Additionally, previous studies have concluded that global PWV is less useful in providing significant clinical information than local PWV, taken in a specific arterial segment, in assessing arterial properties [11,12,13]. Hence, the utility of cfPWV method is limited.

Considering the value of PWV measurements in the monitoring of cardiovascular health and the limitations of global cfPWV, further research has investigated non-invasive alternatives for local PWV determination including magnetic resonance imaging (MRI) [14,15], plethysmography [4,16], and ultrasound [16]. Of particular interest among these methods is ultrasound which leverages on presence of and frequency shifts [17] in reflected high frequency sound waves for measurements at specific locations on the arterial tree. Ultrasound-based local PWV methods are indirect and require intermediate measurands for calculation and determination of PWV. These measurands include the diameter or lumen area of the artery and the velocity of blood flow in the measured region [5,16,18,19,20,21,22,23].

This review will discuss use of ultrasound imaging in vessel data acquisition, cover the different ultrasound-based imaging modalities for acquiring area and velocity data, and compare between simultaneous and non-simultaneous data acquisition for PWV estimation.

2. Background of Ultrasound Measurement for PWV Estimation

2.1. Loop-Based Estimation for PW

Imaging-based methods determine the pulsatile wave from haemodynamic variables including blood velocity, flow, wall velocity or acceleration [5,16,18,19,20,21,22,23,24], and vessel lumen diameter or cross-sectional area. In many imaging-based methods, the waveforms for a pair of haemodynamic variables are acquired over the cardiac cycle and plotted together to give a haemodynamic loop such as the lnDiameter-velocity (lnDU) loop (Figure 1) [20,21] or the flow rate-area (QA) loop (Figure 2) [19]. From the loops, the PWV is determined based on the gradient of the linear portion of the curve.

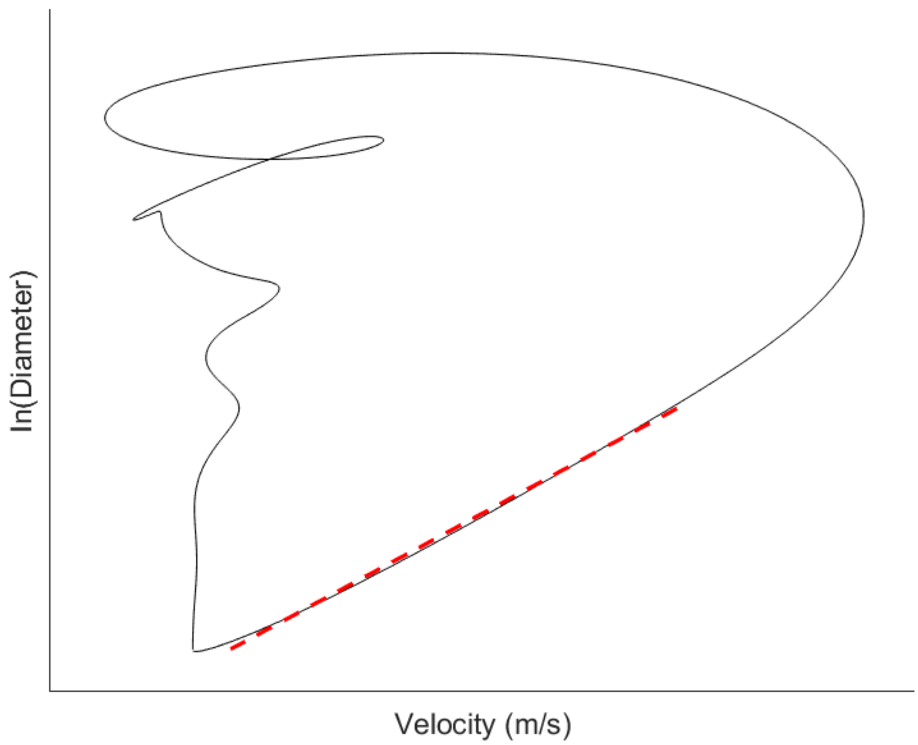

Figure 1. lnDiameter-Velocity (lnDU) loop where PWV is determined from the gradient of the loop at the linear portion of the loop (---) [21].

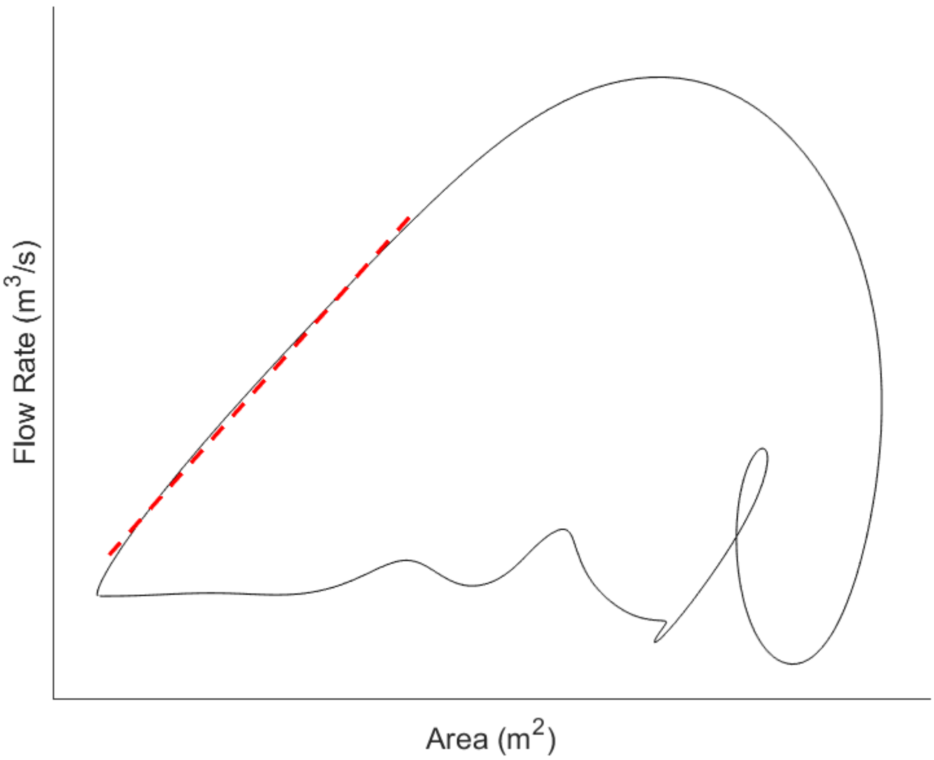

Figure 2. Flow-Area (QA) loop where PWV is determined from the gradient of the loop at the linear portion of the loop (---) [19].

To ensure high accuracy of measurement and owing to precise measurement needed over each cardiac cycle, the techniques used in imaging-based PWV measurement require high framerates to provide adequately high temporal resolution [16].

2.2. Functioning Principles Behind Ultrasound Measurement

Non-invasive ultrasound-based PWV measurement has continued to be of great interest in PWV research given the various advantages of ultrasound such as its good penetration depth [25], the ability to conduct real-time imaging [26,27], and existing use in cardiovascular monitoring [28]. In ultrasound measurement, transducers containing piezoelectric elements emit and receive high frequency sounds typically in the diagnostic range of 2 – 15 MHz [29] for measurement with different modes available in the ultrasound system to capture different variables.

Area or diameter measurement using ultrasound takes advantage of the phenomenon wherein the naturally differing acoustic impedances of tissues cause partial reflections and hence variations in the return time of ultrasound echoes [30]. Meanwhile, velocity or acceleration measurement, utilises the Doppler effect to perform measurement [31].

One area of development in using ultrasound to obtain PWV is in the methodology used. The exact methodology of ultrasound-based PWV measurement varies from using incremental lumen area displacements across an arterial segment [24] to measurement of velocity and area at one point on the arterial segment [5,19,21]. Variations in methodology also involve simultaneous or non-simultaneous data acquisition, number of transducers used [32], and data processing techniques of measured variables such as the use of the QA [5,19] or ln-DU loop [21,33,34]. Advances in ultrasound measurement have also focused on upgrades in the electronics and computation of the ultrasound system. These improvements involve better scanning capabilities such as plane wave insonification, coherent spatial compounding, multiline transmission, and motion matching technique that serve to improve framerates and therefore temporal resolution [16].

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2.3. *Advantages of Ultrasound Imaging*

As an imaging modality, ultrasound is relatively low-cost compared to the other imaging methods used clinically such as computed tomography (CT) and MRI [35]. Additionally, current ultrasound machines allow not only for real-time imaging of the arterial segment of interest but the variety of transducers available also allow for imaging and data acquisition from both shallower arteries like the common carotid arteries [36,37] and deeper central arteries like the abdominal aorta [38].

There are also several factors that make ultrasound more favourable than MRI, which is considered as another non-invasive alternative in routine PWV measurement. Apart from the cost, a limiting factor of MRI utility compared to ultrasound is the long duration [39,40,41] and the need for breath-hold to minimise noise during acquisition [15]. Breath-hold usually occurs over a period of 10-20s and may not be possible in some patients including individuals with shortness of breath or cardiac failure [15]. Moreover, in comparison to the large, generally immovable machinery used in MRI, ultrasound machines are more compact and portable [42] with ultrasound being used regularly in hospitals and clinics for in cardiology and obstetrics [43]. Furthermore, improvements in ultrasound transducer technology have also led to the creation of handheld transducers that can be connected directly to smartphones [44], thereby further increasing accessibility of ultrasound.

These advantages make ultrasound favourable for clinical applications in routine measurement of PWV and monitoring of cardiovascular health.–

3. Key Challenges and Considerations in Ultrasound Imaging for PWV Measurement

Given the advantages ultrasound imaging has over other methods, the use of ultrasound imaging in PWV measurement warrants continued research and development. This thereby involves the management of challenges and awareness of key considerations in the ultrasound imaging measurement process.

3.1. *Challenges in Ultrasound Imaging*

3.1.1. Wave Reflections

A key challenge faced by all imaging-based methods, particularly in the use of the haemodynamic loops is the presence of reflected waves. Wave reflections occur due to impedance mismatches in the arterial tree such as at sites of bifurcation and tapering as vessel size decreases in the periphery [45,46]. The presence of backward reflected waves complicates PWV calculations based on forward blood flow and cause an undesired divergence in the pressure and flow waveforms [46,47]. To circumvent the issue, the gradient of most linear portion of the loop is used which corresponds to the reflection-free period of the cardiac cycle. However, this solution is not foolproof as while this period is typically found during early systole [5], the presence and duration of the reflection free period may vary depending on the imaged vessel [48,49]. Moreover, this may put a further limitation on the measurement location as peripheral vessels have significantly shorter reflection-free periods than more central arteries [5]. Yet while wave reflection may still cause wrong estimates for PWV [50], it is argued that high sampling rate and knowledge of wave speed can help to separate forward from backward flow [5].

3.1.2. Operator Skill Issue

A challenge that is more specific to ultrasound measurement is operator skill as this measurement modality is highly operator dependent during both image acquisition and data interpretation [51]. This operator dependence presents a risk in accuracy reduction and in impacting the intra- and inter-operator repeatability of measurements [52]. Given the prevalence of ultrasound in clinical use [53], several studies have examined methods to tackle reliance on operator skill.

For vessel image acquisition, automatic wall tracking methods assist in attaining more accurate, precise and consistent measurements of vessel diameter changes over the cardiac cycle [54,55,56,57]. In Doppler ultrasound for velocity or volumetric flow measurements, a study suggested that greater operator independence may be achieved using 3D Doppler ultrasound that captures volumetric data rather than the velocity data in a specific plane, thereby reducing the need precisely transducer alignment [58]. However, despite these purported improvements, the method still relies on doppler angle correction by the operator wherein inaccuracies in angle estimation can introduce velocity measurement errors [59]. Moreover, 3D Doppler reduces but does not eliminate precise probe alignment as a poorly positioned transducer relative to vessel can cause signal degradation and measurement errors. While these methods help to assist in reducing issues due to operator skill, they do not yet sufficiently mitigate possible issues arising from poor positioning and angling of transducers or sub-optimal selection of the region of interest in ultrasound technology.

A future approach to tackling operator skill reliance is the use of machine learning to assist in data acquisition. Machine learning systems may be able to provide real-time feedback or guidance to operators during image acquisition itself along with image quality control and automatic rather than manual selection of the vessel region of interest [27].

3.2. Considerations in Ultrasound Imaging

Considerations in the use of ultrasound for PWV measurement involve accounting for limitations in current ultrasound technology to optimise data acquisition.

3.2.1. Key Software-Based Imaging Parameters in Ultrasound Data Acquisition

In ultrasound measurement, there are several key parameters that need to be considered and, where needed, adjusted for optimal measurement. These are summarised in Table 1. Several of the key imaging parameters such as pulse repetition frequency, frame rate, gain, and sampling frequency can be adjusted for on the ultrasound machines and consideration of these parameters is crucial as it affects the choice of measurement location and choice of transducer. For instance, PWV measurement in the abdominal aorta may require a 3.5MHz transducer that provides sufficient tissue penetration (>15cm) for imaging at the cost of lower image resolution [29] whereas it is likely more appropriate to use a higher 7.5MHz frequency transducer [60] that provides a lower penetration depth but higher image resolution for measurement in the more superficial common carotid artery (CCA).

3.2.2. Other Relevant Considerations for Optimising Data Acquisition

An important consideration for ultrasound imaging that is not software-based is the use of gel or water mediums during imaging. For the signals to be optimally transmitted through the tissue layers to arrive at the organ of interest, the transducer head must be in full contact with the skin surface. Given that large differences in acoustic impedances cause reflection of the sound waves, the presence of air pockets between the transducer head and the skin surface will prevent transmission of sound for imaging. Hence, a medium is used to decrease the difference in acoustic impedance [61]. There are several medium options used. For clinical imaging, a liquid gel is typically spread over the measurement location which is fast and convenient. However, a limitation is that the gel spreads inconsistently, particularly for irregular surface anatomy and reapplication might be needed for wider area measurement.

An alternative to liquid gels is the gel pad which is more suited for irregular surfaces such as the neck. These pads are laid over the area of interest or attached to the transducer head and provide a consistent and wide region for scanning [62]. Water baths are another alternative to gel mediums and involves submersion of the whole patient or a body part of the patient into water [63,64]. The water bath method has been shown to provide superior imaging quality when compared to gel-based imaging, particularly in peripheral vessels, and removes the need for direct skin contact. However,

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water immersion for imaging may be less convenient for imaging central arteries such as the CCA and abdominal aorta whose measurement locations are at the neck and back respectively.

Another consideration is the significant differences in acoustic impedances within the human body. Given that reflections in ultrasound are generated at tissue boundaries where the acoustic impedances differ, significant differences in acoustic impedance such as between tissue, bone, and gas can cause unwanted artifacts [65] like shadowing that prevent imaging of deeper tissue structures. This has implications on the feasibility of ultrasound imaging at different arteries. For instance, the thoracic aorta, which is surrounded by the rib bones, and gas in the lungs is typically not imaged by non-invasive ultrasound methods [66,67]. Meanwhile, while ultrasound imaging of the abdominal aorta is feasible, bowel gas may cause undesired artifacts that affect imaging [38,68]. The effect of bowel gas on abdominal aorta imaging may be mitigated with fasting prior to imaging [69].

Table 1. Summary of key software-based imaging parameters in ultrasound data acquisition.

Parameter	Definition	Details on parameter	Ref.
Frequency of transducer	Number of sound wave oscillations per second emitted by transducer	• Higher frequency improves spatial resolution but compromises penetration depth. • Each transducer has different frequency ranges in MHz.	[25,29]
Axial resolution	Ability to distinguish between two structures parallel to the beam	• Higher axial resolution improves distinction between two objects. • Dependent on ultrasound frequency. • Minimum distance for objects to be distinct is more than or equal to half the wavelength.	[25]
Lateral resolution	Ability to distinguish between two structures perpendicular to beam direction	• Dependent on ultrasound frequency. • Affected by beam width which depends on transducer choice	[25]
Temporal resolution	Ability to capture fast-moving structures for analysis	• Sufficiently high temporal resolution needed to capture changes in arterial hemodynamic variables over time. • Affected by frame rate, sampling frequency. • Greater temporal resolution limits penetration depth.	[70]
Attenuation	Decrease in ultrasound intensity due to absorption, scattering, and reflection.	• Attenuation increases for higher frequencies and denser tissues. • Limiting factor for penetration depth of the ultrasound wave.	[71]
Depth of Focus	Depth where image remains sufficiently focused	• Higher frequencies increase the depth of focus.	[29]
Beam width	Physical width of the ultrasound beam	• Narrower beams improve lateral resolution and focusing. • Higher frequencies and transducers with more piezoelectric elements reduce beam width	[29]
Sampling frequency	The rate at which the ultrasound system digitizes returning echo signals.	• Higher sampling rates enhance image resolution. • Sampling frequency varies with different imaging modes. • Should comply with the Nyquist-Shannon sampling theorem. • Aliasing occurs if the sampling rate is too low. • Lower sampling rates may still work when using advanced signal reconstruction techniques.	[72,73,74]
Pulse repetition frequency (PRF)	Number of ultrasound pulse emitted over time	• Higher PRF reduces artifacts due to aliasing but limits penetration depth • Adjusted directly on the ultrasound machine interface	[75]

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Frame rate	Number of image frames per second	• Main factor affecting temporal resolution. • Higher frame rates improve analysis accuracy of dynamic arterial behaviour.	[76,77]
Gain/ Time Gain Compensation (TGC)	Controls brightness of image	• Gain function amplifies echoes to overcome attenuation and increase image brightness. Excessive gain increases noise and decreases the signal-to-noise ratio. • Time gain compensation allows for selective amplification of signals at greater depths without affecting noise in more superficial layers.	[29]

4. Ultrasound Imaging Modes for Vessel Area Acquisition

4.1. Imaging Modalities

In area or diameter measurement, sound waves emitted by the transducer are partially reflected and transmitted at tissue boundaries with different acoustic impedances in the beam path which cause differences in echo return time and facilitates detection of different tissues at different depths [29]. There are three main imaging modes available on ultrasound machines, namely Amplitude (A-mode), Brightness (B-mode), and Motion (M-mode). However, owing to the lack of use of A-mode for vessel are acquisition and in clinical practice, only B-mode and M-mode (Figure 3) ultrasound will be discussed and are summarised in Table 2.

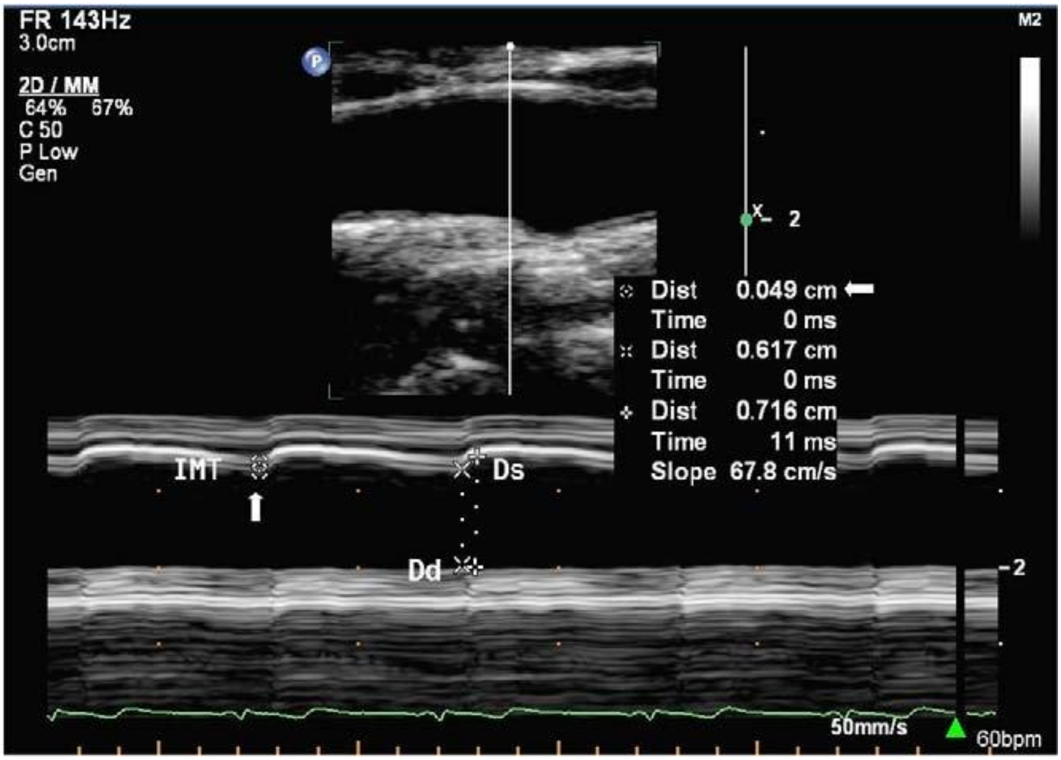

Figure 3. M-mode imaging of CCA with graphical trace of diameter changes below the B-mode image [78]. Reprinted from Perspectives in Medicine, Volume 1, Issues 1-12, Galinda Baltgaile, Arterial wall dynamics, Pages 146-151., Copyright (2012), with permission from Elsevier.

In both modes, transducer placement depends on the desired region of interest. In PWV measurement, the transducer is typically placed longitudinally, with the transducer head parallel to the vessel [5,33,34]. This is likely because subsequent velocity measurements need to be taken for calculations which requires longitudinal measurement either for Doppler ultrasound or flow profile analysis. Non-loop methods for PWV measurement such as pulse wave-based ultrasound manometry (PWUM) may also require longitudinal placement for observation of incremental vessel distension along the vessel [24].

4.2. Automatic Wall Distension Tracking Methods

In the measurement of vessel diameter, inbuilt digital callipers can be used to manually mark the desired region of interest for measurement. However, such manual tracking of wall distension in either B-mode or M-mode can be problematic due to its time-consuming and subjective manner, wherein, small deviations in placement from the measured region of interest due to visual identification can cause large errors in area measurement. Hence, developments of more objective and automatic wall tracking methods are crucial.

Owing to its necessity, wall tracking for ultrasound-based methods have been studied in detail from the use of threshold detectors to study echoes from the arterial wall [79] which is limited due to distance dependence to arterial wall that varies through the arterial cycle, to methods that use phase-locking devices which tracked a specific vessel wall echo [80,81]. Further developments also investigated combining the tracking system to B-mode imaging [82] and pressure recordings [83]. Alternatives to these phase-locking methods were also studied with the use of conventional autocorrelation, which is independent of radiofrequency (RF) centre frequency [84,85] but requires lower sampling rates, and subsequently RF cross-correlation [86,87]. Cross-correlation techniques, however, have an estimator bias that depends nonlinearly on actual displacement [54]. To address this, a modification was made to the autocorrelation method to estimate of mean Doppler frequency and RF centre frequency for wall tracking [88,89]. In this modified method, wall tracking is conducted by integrating wall velocities as estimated by Doppler techniques. This method was found to track wall vessel motion with lower bias and variance than previous cross-correlation methods which improves tissue tracking accuracy [54].

Another type of algorithm developed to measure vessel diameter using B-mode image utilises the differences in pixel intensity values or brightness within a user defined region of interest the determine wall location and hence measure diameter [55,57]. To accurately determine wall location, the transducer is placed longitudinally to the vessel. During acquisition, resolution of the images must be sufficiently high to observe the vessel wall layers. Additionally, electrocardiogram (ECG) gating may be employed to capture images over the cardiac cycle wherein the R signal is used as a reference point. An advantage of this algorithm is its purported simplicity that facilitates possible integration into current clinical machines while being robust to differences in image quality [55].

In automatic wall tracking, algorithms also exist for diameter measurement using transducer placed transverse to the vessel [56]. However, as aforementioned, transverse transducer placement is not optimal for subsequent velocity measurement and movement of the transducer may cause changes in measured region, hence such wall tracking methods are less useful in PWV acquisition.

5. Doppler Ultrasound Imaging Modes for Velocity Acquisition

In velocity or acceleration measurement, the Doppler ultrasound mode used leverages on the change in frequency of sound wave, or Doppler shift, due to reflectors such as blood elements, moving towards or away from the transducer to perform measurement (Figure 4) [90]. This frequency shift is proportional to velocity [90]. In Doppler imaging, the magnitude and presence of the Doppler shift is affected by the Doppler angle which is the angle between the ultrasound beam and the direction of blood flow [90]. As mentioned in Table 1, the Nyquist limit is crucial in image for the accurate measurement of velocity via Doppler ultrasound. Beyond the Nyquist limit, undesirable aliasing occurs which can appear as incomplete peaks in the velocity curve trace for spectral Doppler or as a colourful mixture of colours in the imaged vessel under colour Doppler mode [91].

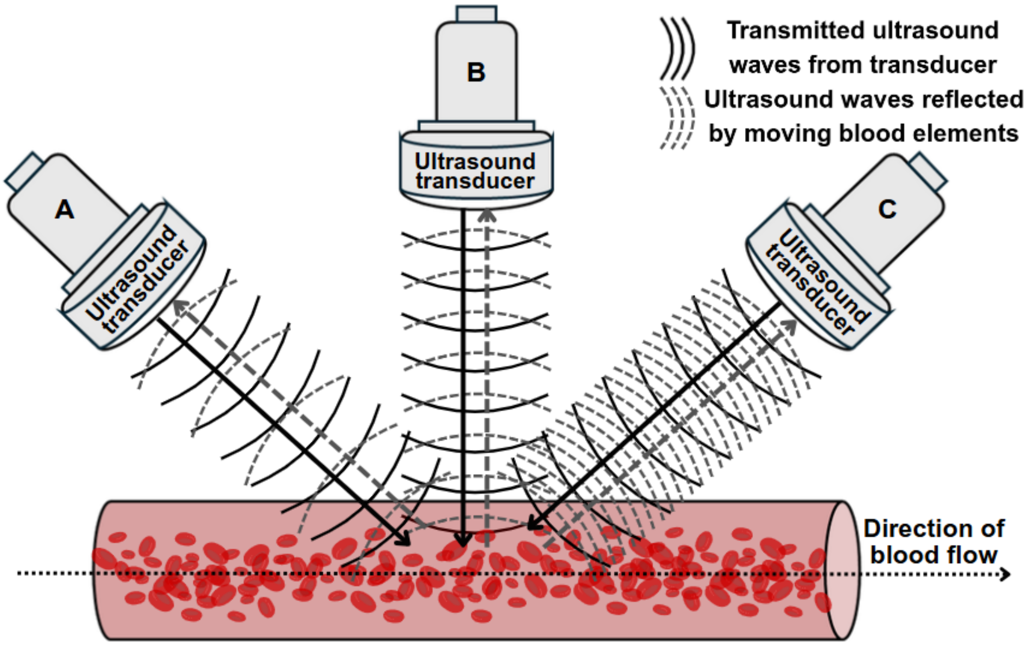

Figure 4. Doppler shifts with transducers at different angles. Frequency increases when blood flows toward transducer (A) and decreases with flow away from the transducer (C). There is no change in frequency when the transducer is perpendicular (B) to the vessel.

There are four main Doppler modes that can conduct velocity measurement which are summarised in Table 2.

Table 2. Summary of ultrasound imaging modes for data acquisition.

Ultrasound imaging mode for vessel area acquisition			
Imaging modality	**Functioning principle**	**Use of modality**	**Ref.**
B-mode (Brightness mode)	• Cross-sectional (two dimensional) image of body made of multiple scanlines. • Each scanline is made up of multiple points and corresponds to the relative position where transmitted echo returned from. • Image brightness is relative to echo strength returning from each point.	• The vessel area is determined from the measured diameter. • Diameter is measured in the longitudinal plane as distance between the anterior and posterior walls in B-mode. • Use digital callipers for manual diameter measurement or wall tracking algorithms for automated measurement	[55,92]
M-mode (Motion mode)	• One dimensional display of motion over time. • Relates ultrasound wave amplitude to imaging of moving structures. • Used for fine measurements.	• Focus in one dimension in M-mode allows for higher temporal and spatial resolution. • M-mode imaging displays the displacement of a detected tissue boundary graphically (Figure 3) for diameter measurement	[93]
Doppler ultrasound imaging modes for velocity acquisition			
Imaging modality	Functioning principle	Use of modality	Ref.
Spectral Doppler	• Doppler effect is used to analyse spectrum of frequencies in ultrasound echoes	• Used in vascular imaging • Graphical representations of velocity over time • Determine velocity at different timepoints	[94]
Colour Doppler	• Measurements of velocity and direction of blood flow are used to superimpose a colour pattern onto the B-mode image	• Two complementary colours represent flow toward and away from the transducer • Colour shades represent higher (lighter) or lower (darker) velocities	[93]

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		• An intermediate colour (green) indicates flow turbulence.	
Pulsed wave (PW) Doppler	• Allows for the measurement of velocity at a specific location at a specific tissue depth • Allows for precise blood flow measurement.	• Requires high PRF • Frequency of the transducer used should be compatible with the depth of tissue measured (i.e. higher frequencies for superficial structures) • Transducer angle should be less than 60°	[93,94]
Continuous wave (CW) Doppler	• Uses separate piezoelectric crystal elements to transmit and receive ultrasound	• Sensitive • measures velocity along entire ultrasound beam • Does not return specific information on depth, direction of flow or velocity.	[94]

6. Non-Simultaneous Versus Simultaneous Area and Velocity Acquisition

This section focuses on the comparison and evaluation of ultrasound-based data acquisition for PWV calculations via the haemodynamic loop methods. As aforementioned, the loop methods namely, QA and lnDU, both require the acquisition of velocity and diameter from the artery of interest. However, there are differences in how data is acquired, whether simultaneously or non-simultaneously. Hence, this section aims to describe, compare, and evaluate these acquisition methods.

6.1. Non-Simultaneous Acquisition Methods

Non-simultaneous acquisition methods involve the use of one ultrasound transducer for both velocity and area measurements. The transducer is adjusted perpendicularly for area measurements and subsequent tilting and angle corrections are done for Doppler velocity imaging.

One non-simultaneous acquisition method utilises B-mode imaging for diameter acquisition and PW Doppler for velocity acquisition before using the lnDU loop for PWV measurement [60]. The method involves obtaining B mode images with the region of interest in the focal zone and the images must clearly capture anterior and posterior walls for optimal diameter curve measurement with little noise. Subsequently, using the same scan projection, PW Doppler is conducted with as small an angle correction as possible to prevent shifts in the scan location [60]. Angle correction is needed as Doppler imaging requires the Doppler angle for frequency shifts and velocity measurement. To prevent a mismatch in features of both diameter and velocity curves over each cardiac cycle, high frame rate electrocardiogram (ECG) gating is used during acquisition [95].

Another non-simultaneous acquisition method utilised M-mode imaging to record ultrasound data over 3 to 5 cardiac cycles for diameter acquisition. Akin to the previous method, after diameter acquisition, PW Doppler was used to extract maximum velocities across the vessel before using the QA loop for PWV measurement. To ensure proper alignment, the intima layers for both anterior and posterior walls had to be clearly visible. With the non-simultaneous acquisition, the transducer could be adjusted for optimal data collection and the diameter distension measurements were shown to be of high accuracy and precision [19].

6.2. Simultaneous Acquisition Methods

Simultaneous acquisition of diameter and velocity data is generally more complex than non-simultaneous acquisition owing to the need for acquisition of both velocity and diameter at the same transducer angle.

One simultaneous acquisition method tested on the CCA utilised M-mode for diameter measurement and PW Doppler for velocity measurement. Prior to data acquisition, the transducer was positioned longitudinally in B-mode, ensuring that the vessel walls were clearly delineated. The Doppler angle used was near optimal at 58 to 60 degrees and the Doppler gating was adjusted in B-mode as well. Subsequently, during measurement, a split screen was used to obtain both diameter and velocity data at a sampling frequency of 1000Hz. While PWV could be obtained in this method with simultaneous measurement of diameter and velocity, the gates and angles still needed to be adjusted manually which may affect the signals, particularly in the derivative calculations to obtain PWV from the lnDU loop [33,34]. This method was also used in separate research for testing on a position near the aortic arch wherein 10-beat cine loops were used in M-mode and PW Doppler imaging. A particular addition of note to the methodology is the use of a fluid filled phantom between probe and vessel which acts as an intermediate medium and prevents external pressure from the transducer from distorting the aortic wall motion [96].

Simultaneous acquisition may also be conducted with constant perpendicular placement of the ultrasound transducer via the perpendicular ultrasound velocimetry (PUV) technique. In this technique, velocity is not obtained via Doppler ultrasound but rather via cross-correlation techniques. The principle for measurement is like particle imaging velocimetry (PIV) [97] and PUV uses 2D cross-correlation in the time domain on raw RF data to determine the axial velocity distribution of the flow. In PUV, the ultrasound system is operated in fast B-mode or multiple M-line mode. A significant advantage of the perpendicular placement is the ability to measure diameter simultaneously without needing to account for angle correction [5].

Another simultaneous acquisition method akin to PUV similarly obtained measurements of diameter and velocity from B-mode images rather than M-mode and PW doppler. In this method, one dimensional (1D) cross-correlation techniques were employed to track wall motion and blood element speckle motion in the successive B-mode images [98]. For diameter measurement, 1D cross-correlation of successive frames was conducted separately for anterior and posterior walls and the wall motion waveform for each wall was given by the cumulative summation of displacements over time. Thereafter, diameter change waveform is obtained by the difference in wall displacement for anterior and posterior wall motion waveforms. The absolute diameter waveform can subsequently be obtained with knowledge of initial vessel diameter without distension. Meanwhile, velocity is determined by tracking and cross correlating the movement of the blood speckle pattern between frames wherein the highest correlation indicates the mostly likely location of blood element movement [98]. With knowledge of the displacement and imaging frame rate, velocity can be obtained. For accurate measurement, an ultrafast scanner is needed to adequately resolve the rapid acceleration and deceleration of blood during systole [98]. Akin to previous methods, ECG gating is used for time alignment while singular value decomposition (SVD) was used to separate weak blood and strong tissue signals [98].

Apart from the use of singular ultrasound beams as with the abovementioned methods, simultaneous acquisition can also be achieved with the use of multiple ultrasound beams. In multiple beam acquisition, colour Doppler is used blood flow velocity while diameter changes were measured using M-mode. The system consists of both the colour Doppler system and an echo-tracking subsystem that can use different ultrasound beams for velocity and diameter change respectively. These beams can be independently manipulated with an intersection between the beams at the range gate for both diameter and velocity measurement as shown in Figure 5 [99]. This method was found to have low variabilities in the maximum velocity and arterial diameter measurements despite the need to manipulate different beams, thereby supporting its reproducibility [100].

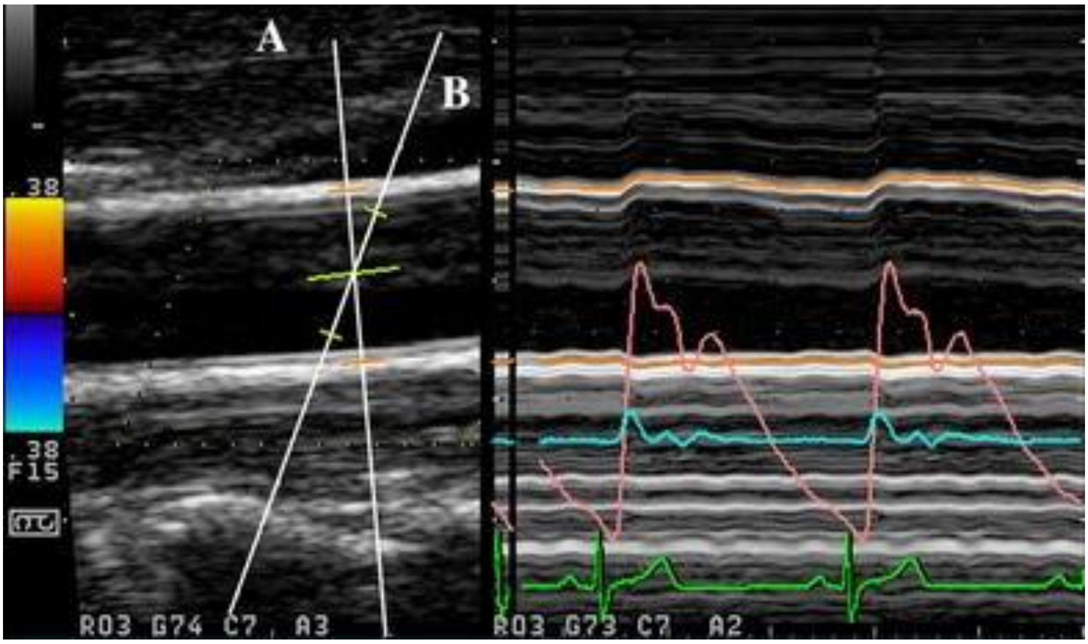

Figure 5. Simultaneous acquisition with two ultrasound beams (A and B) with overlap at the range gate region (from [99] with permission).

6.3. Comparison and Evaluation of Methods

Table 3 summarises the comparison of non-simultaneous and simultaneous methods in PWV parameter acquisition. In the acquisition of parameters for PWV measurement, non-simultaneous acquisition methods present as simpler and less computationally demanding options. However, a key limitation of non-simultaneous acquisition is the fact that velocity and diameter waveforms are not obtained at the same time [19,60]. This lack of simultaneity is a source of error in PWV assessment due to an inaccurate time alignment between the two curves despite methods to ensure as close an alignment as possible. Additionally, the possibility of inter-cycle variations between diameter and velocity acquisition implies that even with accurate time alignment [101], the measured diameter at each instance may not correspond to the velocity measured at the same timepoints. This issue may be overcome by estimating velocity and diameter from the same data or with the use of one transducer angled oblique to the vessel and another perpendicular to the vessel for respective velocity and diameter measurement at the same region of interest [32,99].

In general, while simultaneous acquisition was more computationally complex, the advantage and limitations of each method varied. Of the discussed methods, the cross-correlation-based methods have a unique advantage in the ability to perform measurements with the use of B-mode imaging, meaning that the transducer is kept in one position throughout acquisition. This ensures that the imaged region is constant, thereby preventing errors that may arise from Doppler angle adjustment. However, this method is computationally intense and may not be use in regions of excessively high velocities due to the limitations on the ultrasound system, which can be problematic for clinical use [5]. In contrast, while the dual ultrasound beam method required positioning of two beams, the results had good reproducibility [99,100]. Additionally, the ability to independently manipulate the beams may allow for flexibility in conducting measurement.

In all, while no one method is currently optimal, simultaneous acquisition methods have a distinct advantage in preventing errors due to delays or possible physiological differences between cardiac cycles. Each discussed method has advantages that can be leveraged for improving acquisition, hence, apart from comparisons between the methods, for future work, it is crucial to note the various means by which acquisition can be further improved. For instance, the use of ECG gating allows for consistent measurements over each cardiac cycle which improves repeatability of measurement. Meanwhile, the use of filters such as singular value decomposition to separate tissue signals can improve signal to noise ratio in data acquisition, particularly in Doppler ultrasound wherein noise can result in aliasing and affect velocity measurement.

Table 3. Comparison of non-simultaneous and simultaneous acquisition methods for diameter and velocity.

Acquisition type	Imaging method and key acquisition details	Advantages	Limitations	Ref.
Non-simultaneous	• B-mode imaging and PW Doppler imaging method. • ECG gating used for time alignment.	• The low computation demand and low complexity • Application at different arterial sites is convenient	• Requires a method to ensure proper alignment of haemodynamic loops. • Delays, heart rate variations between measurement time periods of velocity and diameter or calculations with different timescales cause significant error and reduces precision	[60]
	• M-mode imaging and PW Doppler imaging method. • Ultrasound data is recorded over several cardiac cycles	• Diameter distension measured more accurately and precisely with the use of M-mode		[19]
Simultaneous	• M-mode imaging and PW Doppler imaging	• Fairly reproducible results	• Manual adjustment of gates and transducer angles are needed which may introduce errors in measurement.	[33,34,96]
	• B-mode imaging with cross correlation techniques	• Use of B-mode imaging for both variables circumvents issues arising from manual transducer angling.	• Unable to use if axial velocities are excessively high due to the limited framerate of the ultrasound system. • More computationally demanding.	[5,98]
	• M-mode imaging and colour Doppler with two ultrasound beams positioned at different angles	• Independent manipulation of ultrasound beams for acquisition is possible with good reproducibility	• Arterial movement due to normal artifacts such as respiration and pulsation may affect diameter measurements	[99,100]

7. Conclusions

This paper has summarised the use of ultrasound imaging in vessel data acquisition, covered the different ultrasound-based imaging modalities for acquiring area and velocity data, and compared between simultaneous and non-simultaneous data acquisition for PWV estimation. Based on the reviewed literature, despite its challenges and considerations, ultrasound remains a promising means by which PWV can be obtained non-invasively. It is key, therefore, to carefully adjust the key parameters when using the various imaging modalities for measurement, particularly in the use of Doppler ultrasound for velocity measurement. In the comparison of simultaneous and non-simultaneous acquisition, it is evident that there is currently no optimal method for data acquisition, however, simultaneous acquisition, once optimised, would allow for the acquisition of both diameter and velocity waveforms that prevents errors arising due to physiological differences between two cardiac cycles.

Future developments in the use of ultrasound for PWV measurement will likely focus on improvements to be made in the acquisition phase as well as improvements in processing the ultrasound data post-acquisition. Firstly, experimental investigations between non-simultaneous and simultaneous methods can be conducted to better compare the accuracy and feasibility of each method and to improve upon the best-performing method. For other improvements in haemodynamic variable acquisition via ultrasound, the discussed challenges present possible

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avenues of work. Given that wave reflections can greatly affect data acquisition, further research into wave analysis methods to effectively separate forward and backward flow is warranted. Additionally, operator reliance is another key limitation that significantly affects data quality wherein further study into machine learning may reduce operator-based errors by automating part of the acquisition process or providing feedback to operators during acquisition. Apart from addressing challenges, working around the limitations of ultrasound imaging is another area of improvement such as considering the use of mediums, the design of the ultrasound transducer, or developing a standardised method to limit the effect of motion or differences in acoustic impedance and ensure consistently high data quality. Another area for development includes improvements in processing of ultrasound data after acquisition. These include determining the most accurate models for PWV estimation and subsequent applications of PWV such as in pressure estimation.

Overall, ultrasound is a promising non-invasive alternative to the current non-invasive gold standard of carotid-femoral PWV (cfPWV) measurement via direct tonometry and further research needs to be conducted to overcome current constraints and ensure accuracy, reliability, and repeatability for clinical use.

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Glossary

ABP	Arterial Blood Pressure
CCA	Common Carotid Artery
cfPWV	Carotid-Femoral Pulse Wave Velocity
CT	Computed Tomography
ECG	Electrocardiography
lnDU	lnDiameter-Velocity
MRI	Magnetic Resonance Imaging
PIV	Particle Image Velocimetry
PRF	Pulse Repetition Frequency
PUV	Perpendicular Ultrasound Velocimetry
PWUM	Pulse Wave-Based Ultrasound Manometry
PWV	Pulse Wave Velocity
QA	Flow-Area
SVD	Singular Value Decomposition
TGC	Time Gain Compensation

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