Measurement: Sensors 18 (2021) 100240

Contents lists available at ScienceDirect

Measurement: Sensors

journal homepage: www.sciencedirect.com/journal/measurement-sensors

A preliminary approach based on numerical simulations for the design of a PWV-Varying arterial simulator

ARTICLE INFO

Keywords
Pulse wave velocity
Arterial simulator
Monte Carlo simulation
Design

ABSTRACT

Nowadays, in both scientific and medical communities, Pulse Wave Velocity (PWV) is commonly considered as a predicting factor of cardiovascular diseases. Such issue leads to the necessity of accurate PWV measurements as PWV non-local assessment is currently affected by low accuracy distance measurements. Despite the great interest on such predictor, a reference standard for PWV assessment is still awaited. In sight of the development of a reference standard able to reproduce PWV variations, the necessity arises of a mathematical model involving the main physical quantities influencing PWV. Therefore, the present study aims at giving a contribution in the development of such model as well as in the implementation of numerical simulations for the design of a sensorized PWV-varying arterial simulator as regards its metrological and physical characteristics. Despite the promising results, further developments could include a greater system parametrization, a system miniaturization as well as the investigation of other metrological characteristics.

1. Introduction

The Pulse Wave Velocity (PWV) has been defined as the propagation velocity of the pulse wave traveling along the arterial tree due to heart contraction [1]. In the current scientific literature, the strict relationship between such physical quantity and arterial stiffness is commonly accepted, therefore PWV assumes a key role in the early diagnosis and therapy of cardiovascular diseases worldwide [2,3]. To date, PWV is assessed as the ratio between the distance between two recording sites and the time delay a pulse wave takes to travel from one site to another (i.e., transit time) [4]. Despite the great interest around PWV on behalf of the scientific and medical community, *in vivo* PWV assessment over a long arterial portion is still affected by high distance measurement uncertainty [5]. Such issue could be overcome by designing and implementing measurement methods where PWV is locally assessed. This leads to the necessity of developing *in vitro* experimental set-up (e.g., arterial simulator) able to reproduce PWV variations, therefore constituting a reference standard for PWV assessment, which nowadays is still awaited. In the current state of the art, many studies focused their attention on *ad hoc* experimental set-up to investigate hemodynamic phenomena as well as the relationships subsisting between pressure, flow and the biomechanical and/or geometrical characteristics of the tube under analysis without any attempt to assess a reference PWV standard [6,7]. Furthermore, from a metrological point of view, the major part of the proposed solutions lacks a metrological characterization of the employed measurement chain.

The goal of the present study is to develop a mathematical model for an arterial simulator design and its measurement equipment, involving all the geometrical and mechanical characteristics influencing pulse wave velocity, starting from the most simple and consolidated ones (i.e., commonly accepted in the current scientific literature) [8,9]. Such a model has been implemented in MATLAB environment to numerically simulate PWV variations according to the parametrization of the main physical quantities involved (i.e., geometrical and mechanical). From such simulations, the transducers to be included in the design and development of a novel arterial simulator as well as the corresponding measurement chain, have been selected and their main metrological characteristics (e.g., measurement range, accuracy and bandwidth) have been evaluated.

2. Materials and methods

The numerical simulation presented in this preliminary study has been implemented starting from the mathematical model already proposed in [10]. By considering an elastic tube of given Young Modulus E, under inner and outer pressures, p_i and p_o, respectively, the following relationship for the static radial displacement u has been obtained:

$$u(r) = \frac{r r_o^2}{E\left(r_o^2 - r_i^2\right)}\left[(1-\nu)\left(p_i\frac{r_i^2}{r_o^2} - p_o\right) + (1+\nu)\frac{r_i^2}{r^2}(p_i - p_o)\right] \tag{1}$$

where r_i and r_o are the inner and outer tube radii (with $r_o - r_i \ll r_o$) respectively, and ν the Poisson ratio. When an over-pressure P is applied to the tube, the total inner pressure $p_{i,tot}$ is given by the sum $p_i + P$ therefore causing a maximum radial displacement $u_{\max}$ whose expression can be retrieved from (1) for $r = r_o$:

$$u_{max} = \frac{2 r_o r_i^2\left(p_{i,tot} - p_o\right)}{E\left(r_o^2 - r_i^2\right)} \tag{2}$$

Through the Bramwell-Hill formula [8], the relationship between the PWV, the variation of cross-sectional lumen area ΔA and the pressure variation $\Delta p = p_{\max} - p_{\min}$ can be derived as follows:

https://doi.org/10.1016/j.measen.2021.100240

Available online 20 September 2021

$$PWV = \sqrt{\frac{A_{min}}{\rho}\frac{\Delta p}{\Delta A}} \tag{3}$$

where ρ is the inner fluid density and $A_{\min} = \pi\,(r_o + u)^2$ is the cross-sectional lumen area before the over-pressure P is applied. In particular, the variation of cross-sectional lumen area ΔA can be expressed as the difference between the maximum cross-sectional lumen area $A_{\max} = \pi\,(r_o + u + \Delta u_{max})^2$ after the over-pressure application and $A_{\min}$ as follows:

$$\Delta A = A_{max} - A_{min} = \pi \Delta u_{max}(\Delta u_{max} + 2r_o + 2u) \tag{4}$$

where Δu_{max} is the maximum radial displacement variation given by

$$\Delta u_{max} = u_{max} - u(r_o) \tag{5}$$

Therefore (3) can be rewritten as a function of both P and Δu_{max}:

$$PWV = \sqrt{\frac{P}{\rho}\frac{(r_o + u)^2}{\Delta u_{max}(\Delta u_{max} + 2r_o + 2u)}} \tag{6}$$

Nowadays PWV is determined both in *in vitro* and *in vivo* experiments as the ratio of the distance between two different sensors Δs and the transit time Δt:

$$PWV = \frac{\Delta s}{\Delta t} \tag{7}$$

From (7), it is possible to retrieve the maximum frequency (i.e., the minimum sensor bandwidth) of the pulse wave propagation phenomenon, when the distance Δs between the two sensors is fixed, as follows:

$$f_{max} = \left(\frac{\Delta s_{min}}{PWV_{max}}\right)^{-1} \tag{8}$$

On the basis of (1)-(8), a custom-written algorithm has been developed in MATLAB environment in order to carry out the numerical simulations in sight of the arterial simulator design. In such simulations different components should be included: the elastic element which has been chosen with geometrical characteristics (i.e., inner and outer tube radii) as similar as possible to the ones of an adult healthy subject's aorta [11], whereas the mechanical characteristics (i.e., Poisson ratio and Young Modulus) have been retrieved from the ones of natural rubber [12]. Furthermore, in the numerical simulation, the elastic element is supposed to be straight and infinitely long, to neglect pulse wave reflections as well as sharp travel direction changes. As regards the inner fluid flowing in the simulated tube, it has been supposed to be distilled water. The parameters describing the abovementioned simulated tube as well as the inner fluid characteristics have been reported in Table 1 and they have been kept constant throughout all the simulation steps.

3. Results

The ideal arterial simulator has been designed according to the following three steps for its metrological characteristics determination. In all cases, the over-pressure P has been kept constant to 5.3 kPa (~40 mmHg), by supposing a physiological over-pressure due to heart pumping action between systolic and diastolic phases.

3.1. Inner pressure evaluation

In the first step, the tube inner pressure p_i has been evaluated for a pathological PWV value of 15 m s^{-1} [13,14], by imposing an outer pressure $p_o = 0.05 \cdot p_i$, on the basis of *in-vitro* experiments carried out in [10]. The computation of p_i value has been carried out by inverting (6) after applying (1) and (5). The obtained p_i value has been reported in Table 2.

3.2. Outer pressure evaluation

In the second step, from the p_i value computed above, it has been possible to retrieve $p_{o,j}$ (j = 1, …, 6) values corresponding to PWV ranging from 10 to 15 m s^{-1} with steps of 1 m s^{-1}. Such range has been chosen to simulate a progressive tube stiffening which is related to PWV values reflecting human pathological conditions [13,14]. The $p_{o,j}$ values have been computed by inverting (6) after applying (1) and (5). Such step allows to simulate both an increment of PWV as well as the consequent decrement of Δu_{max} due to a stiffening process analogous to the one occurring in human physiology. The obtained $p_{o,j}$ values have been reported in Table 2.

3.3. Monte Carlo simulation

In the third step, PWV and Δu_{max} measurement accuracies have been retrieved through the implementation of a series of Monte Carlo Simulations (MCSs). In fact, in the current scientific literature, MCS is a widespread and robust tool, employed in many different studies [15–20] for the uncertainty evaluation of software-derived measurements. Six MCSs have been carried out for all the $p_{o,j}$ values with a number of iterations of 10^5 each, by assigning a distribution to the quantities involved in (5) and (6). The distributions and their characteristics have been reported in Table 2. The inner and outer radii standard deviations (SDs) have been retrieved from [21]. The inner and outer pressures SDs have been chosen according to the measurement accuracy reported in digital manometers datasheets as 0.1% with respect to a full scale of 1 MPa, by supposing a 95% confidence level. The SD of the over-pressure P has been set to 0.7 kPa (~5 mmHg). The standard deviation of the fluid density ρ has been set at 1 kg m^{-3} considering the density variation for temperature changes of 5 °C. Finally, the Young Modulus SD has been chosen to 6% with respect to its mean value accordingly to the percentage errors previously determined in [21].

3.4. Discussion

The PWV and Δu_{max} results according to the variation of p_o together with the PWV percentage error $\varepsilon_{PWV\%}$ have been reported in Table 3. As shown in Fig. 1, PWV increases for decreasing outer pressure values. Moreover, the obtained PWV percentage error for all the p_o values is ≤ 5%. The PWV standard deviation values computed with MCS suggest that an arterial simulator designed with the abovementioned characteristics could be able to reproduce PWV values where it is possible to distinguish about the tenth of m·s^{-1}, in theory.

The outcomes show a decreasing trend of Δu_{max} in correspondence of

Table 1
Geometrical and mechanical characteristics of the simulated tube.

Parameter	Description	Value
r_i (mm)	Inner radius of the elastic tube	12.5
r_o (mm)	Outer radius of the elastic tube	14.0
ρ (kg·m^{-3})	Inner fluid density	1000
ν	Poisson's ratio	0.5
E (MPa)	Tube Young Modulus	1.5

Table 2
Parameters distributions in Monte Carlo Simulations.

Parameter	Measurement unit	Distribution	μ ± SD
r_i	mm	Uniform	12.5 ± 0.4
r_o	mm	Uniform	14.0 ± 0.4
p_i	kPa	Gaussian	386.8 ± 0.5
$p_{o,j}$	kPa	Gaussian	107.7 ± 0.5
			83.6 ± 0.5
			63.3 ± 0.5
			46.2 ± 0.5
			31.7 ± 0.5
			19.3 ± 0.5
P	kPa	Uniform	5.3 ± 0.7
ρ	kg·m^{-3}	Uniform	1000 ± 1
E	MPa	Gaussian	1.5 ± 0.1

Table 3
PWV and Δu_{max} results for each p_o value.

j	p_o (kPa)	Δu_{max} (mm)	PWV ($m \cdot s^{-1}$)	$\varepsilon_{PWV\%}$
1	107.7 ± 0.5	1.00 ± 0.36	10.0 ± 0.5	5.0%
2	83.6 ± 0.5	0.89 ± 0.36	11.0 ± 0.5	4.5%
3	63.3 ± 0.5	0.79 ± 0.36	12.0 ± 0.4	3.3%
4	46.2 ± 0.5	0.71 ± 0.36	13.0 ± 0.3	2.3%
5	31.7 ± 0.5	0.64 ± 0.36	14.0 ± 0.4	2.9%
6	19.3 ± 0.5	0.59 ± 0.36	15.0 ± 0.5	3.3%

The values have been reported as mean ± SD. $\varepsilon_{PWV\%}$ is the PWV percentage error.

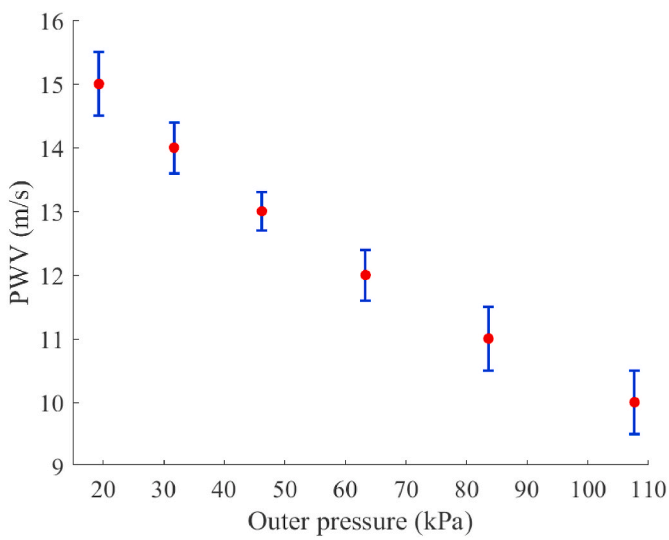

Fig. 1. PWV and outer pressure relationship with error bars.

increasing PWV values therefore successfully reproducing the tube stiffening process, simulated through the outer pressure decrease. From the outcomes retrieved in MCSs it is possible to assess the measurement range (e.g., until at least 1 mm) of the displacement transducers which should be able to detect the pulse wave passage along the elastic tube through the maximum radial displacement variation Δu_{max}. Furthermore, Δu_{max} standard deviations allow to establish the accuracy of the abovementioned transducers, e.g., at least tenth of mm.

In addition, from these preliminary results it is also possible to estimate the minimum bandwidth that allows the transducer to detect the pressure wave passage. In particular, by supposing the two transducers diameter of about 10 mm each, as well as a fixed distance Δs of 5 cm between the transducers central axis and, by considering the maximum PWV provided in this study (15 m s^{-1}), the minimum bandwidth can be estimated from (8) to be 300 Hz. Finally, from the considerations above, it can be assessed that (a) the transducers, satisfying those specifications and currently available on the market, are displacement transducers such as inductive, capacitive and optical and (b) the measurement chain should involve an analog to digital converter (ADC) able to sample the input signal at a sampling frequency of at least 1 kHz.

4. Conclusions

In the present study, numerical simulations implemented through an *ad hoc* algorithm developed in MATLAB, for the design of an ideal arterial simulator able to reproduce pulse wave velocity variations have been proposed. As a first step a mathematical model has been derived from consolidated and commonly accepted ones, by considering both geometrical and mechanical quantities involved. In particular, such model resulted from the combination of the Bramwell-Hill formula and the static radial displacement mathematical expression with the periodic pressure variation simulating the heart pumping action. The second step has been the implementation of a series of Monte Carlo Simulations to retrieve useful data for the metrological characterization (e.g., measurement range, accuracy and bandwidth) of some elements involved in the measurement chain (e.g., pressure manometers, displacement transducers). The outcomes seem to confirm that with decreasing outer pressure, by keeping constant the elastic tube inner pressure, PWV increases and the maximum radial displacement variation decreases, therefore properly simulating the tube stiffening (i.e., progressive pathological condition). Despite the promising results, the algorithm proposed may be improved by (a) studying PWV variations according to changes of a higher number of mechanical quantities involved (e.g., Young Modulus, tube inner pressure), (b) investigating the system output with different geometrical characteristics in sight of a system miniaturization and (c) including further metrological characteristics (e.g., sensitivity, resolution). A further future development is the realization of an *ad hoc* experimental set-up on the basis of the numerical simulations data. Such set-up could be used for the validation of the proposed model by the comparison between the PWV values impressed on the basis of the simulator physical characteristics and the ones experimentally retrieved from the ratio of the distance between the two displacement transducers and the transit time.

Acknowledgments

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

References

[1] H.-L. Kim, S.-H. Kim, Pulse wave velocity in atherosclerosis, Front. Cardiovasc. Med. 6 (41) (2019).
[2] B. Williams, G. Mancia, W. Spiering, E.A. Rosei, M. Azizi, M. Burnier, et al., 2018 ESC/ESH guidelines for the management of arterial hypertension: the task force for the management of arterial hypertension of the European society of cardiology and the European society of hypertension, J. Hypertens. 36 (10) (2018) 1953–2041.
[3] S. Laurent, J. Cockcroft, L. Van Bortel, P. Boutouyrie, C. Giannattasio, et al., Expert consensus document on arterial stiffness: methodological issues and clinical applications. European Network for Non-invasive Investigation of Large Arteries, Eur. Heart J. 27 (21) (2006) 2588–2605.
[4] A. Milan, G. Zocaro, D. Leone, F. Tosello, I. Buraioli, D. Schiavone, F. Veglio, Current assessment of pulse wave velocity: comprehensive review of validation studies, J. Hypertens. 37 (8) (2019) 1547–1557.
[5] L. Van Bortel, Is arterial stiffness ready for daily clinical practice? J. Hypertens. 24 (2) (2006) 281–283.
[6] M. Jang, M.W. Lee, J.U. Kim, S.Y. Seo, S.H. Shin, Development of a cardiovascular simulator for studying pulse diagnosis mechanisms, Evid. base Compl. Alternative Med. 1 (2017) 1–9.
[7] E.O. Kung, A.S. Les, C.A. Figueroa, F. Medina, K. Arcaute, R.B. Wicker, M. V. McConnell, C.A. Taylor, In vitro validation of finite element analysis of blood flow in deformable models, Ann. Biomed. Eng. 39 (7) (2011) 1947–1960.
[8] J.C. Bramwell, A.V. Hill, The velocity of the Pulse Wave in man, Proc. Roy. Soc. Lond. B. 93 (1922) 298–306.
[9] R.G. Budynas, J.K. Nisbett, *Mechanical Engineering Design*, Shigley's, McGraw-Hill, New York, 2015.
[10] F. Fuiano, G. Fiori, F. Vurchio, A. Scorza, S.A. Sciuto, Transit time measurement of a pressure wave through an elastic tube based on LVDT sensors, in: Proc. Of the 24th IMEKO TC4 International Symposium & 22nd International Workshop on ADC Modelling and DAC Modelling and Testing, Palermo, Italy, 14 – 16 September 2020.
[11] A. Evangelista, F.A. Flachskampf, R. Erbel, F. Antonini-Canterin, C. Vlachopoulos, G. Rocchi, R. Sicari, P. Nihoyannopoulos, J. Zamorano, European Association of Echocardiography; Document Reviewers: M. Pepi, O. A. Breithardt and E. Plonska-Gosciniak, "Echocardiography in aortic diseases: EAE recommendations for clinical practice", Eur. J. Echocardiogr. 11 (8) (2010) 645–658.
[12] Materials Data Book, Cambridge University Engineering Department, 2003 (available in June 2021), http://www-mdp.eng.cam.ac.uk/web/library/enginfo/cueddatabooks/materials.pdf.
[13] T. Pereira, C. Correia, J. Cardoso, Novel methods for pulse wave velocity measurement, J. Med. Biol. Eng. 35 (5) (2015) 555–565.
[14] E.J. Kim, C.G. Park, J.S. Park, S.Y. Suh, C.U. Choi, J.W. Kim, S.H. Kim, H.E. Lim, S. W. Rha, H.S. Seo, D.J. Oh, Relationship between blood pressure parameters and pulse wave velocity in normotensive and hypertensive subjects: invasive study, J. Hum. Hypertens. 21 (2) (2007) 141–148.
[15] G. Fiori, F. Fuiano, A. Scorza, J. Galo, S. Conforto, S.A. Sciuto, A preliminary study on an image analysis based method for lowest detectable signal measurements in PW Doppler ultrasounds, ACTA IMEKO (2021). "in press".

[16] G. Fiori, F. Fuiano, A. Scorza, J. Galo, S. Conforto, S.A. Sciuto, Lowest detectable signal in medical PW Doppler quality control by means of a commercial flow phantom: a case study, in: Proc. Of the 24th IMEKO TC4 International Symposium & 22nd International Workshop on ADC Modelling and DAC Modelling and Testing, Palermo, Italy, 14 – 16 September 2020.
[17] G. Fiori, F. Fuiano, F. Vurchio, A. Scorza, M. Schmid, S. Conforto, S.A. Sciuto, A preliminary study on a novel method for depth of penetration measurement in ultrasound quality assessment, in: Proc. Of the 24th IMEKO TC4 International Symposium & 22nd International Workshop on ADC Modelling and DAC Modelling and Testing, Palermo, Italy, 14 – 16 September 2020.
[18] G. Fiori, F. Fuiano, A. Scorza, J. Galo, S. Conforto, S.A. Sciuto, A preliminary study on the adaptive SNR threshold method for depth of penetration measurements in diagnostic ultrasounds, Appl. Sci. 10 (2020) 18.
[19] F. Orsini, F. Fuiano, G. Fiori, A. Scorza, S.A. Sciuto, Temperature influence on viscosity measurements in a rheometer prototype for medical applications: a case study, in: IEEE International Symposium on Medical Measurements and Applications (MeMeA), Istanbul, Turkey, 26 – 28 June 2019.
[20] G. Fiori, F. Fuiano, A. Scorza, M. Schmid, S. Conforto, S.A. Sciuto, ECG waveforms reconstruction based on equivalent time sampling, in: IEEE International Symposium on Medical Measurements and Applications (MeMeA), Bari, Italy, 1 – 3 June 2020.
[21] F. Fuiano, G. Fiori, A. Scorza, S.A. Sciuto, A novel experimental set-up for Young modulus assessment through transit time measurements in biomedical applications, in: IEEE International Workshop on Metrology for Industry 4.0 & IoT, Rome, Italy, 7 – 9 June 2021. "in press".

Fabio Fuiano*, Giorgia Fiori, Andrea Scorza, Maurizio Schmid, Silvia Conforto, Salvatore Andrea Sciuto
Department of Industrial, Electrical and Mechanical Engineering, Roma Tre University, Rome, Italy

* Corresponding author.
E-mail addresses: fabio.fuiano@uniroma3.it (F. Fuiano), giorgia.fiori@uniroma3.it (G. Fiori), andrea.scorza@uniroma3.it (A. Scorza), maurizio.schmid@uniroma3.it (M. Schmid), silvia.conforto@uniroma3.it (S. Conforto), salvatore.sciuto@uniroma3.it (S.A. Sciuto).