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First experimental results of a novel arterial simulator with PWV adjustment

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***Abstract* – Pulse Wave Velocity (PWV) monitoring is a well-established method for both the diagnosis and prevention of cardiovascular diseases. Over the years, many arterial simulators have been made to study PWV dependency on the mechanical and geometrical characteristics of arterial surrogates; in particular, some of them are able to vary the tensional state of vessel walls to cause a change in PWV values. In this paper, a novel arterial simulator is presented, capable of varying the PWV of an arterial surrogate by acting independently on its inner and outer pressures. The simulator under assessment can manage pressures up to three times greater than the atmospheric one. This characteristic provides the possibility to explore many tensional states compared to its predecessors. The experimental outcomes confirm its working principle and an increasing trend in PWV is found. The result uncertainties are up to 10% of the corresponding PWV value.**

I. INTRODUCTION

Since 2000, cardiovascular diseases (CVDs) represent the leading cause of death worldwide [1]; only in 2019, about 15 million people died from heart attack and stroke [2]. In this regard, it is justified the importance to detect CVDs in order to properly diagnose and treat them. A clinical parameter that reflects the health status of the cardiovascular system is arterial stiffness: it's known that the elastic properties of large arteries change because of aging or diseases, e.g., atherosclerosis, hypertension, diabetes mellitus and others [3-5]. A parameter used since the early 20th century to measure and estimate arterial stiffness is the Pulse Wave Velocity (PWV) [6,7], i.e., propagation velocity through vessels of the pulse wave given by heartbeat. Today, the PWV measurement represents a standard method used to assess the health of blood vessels and, consequently, a possible cardiovascular risk for patients [8-10].

Over the decades, many arterial simulators have been developed in order to investigate *in vitro* the correlation between hemodynamic quantities. In this way, it is possible to isolate the phenomenon of interest to perform repeatable measurements without the influence of its variability due to human factor [11]. Recently, an arterial simulator was proposed to simulate variations of arterial stiffness by pre-tensioning the rubber hose which constituted the Arterial Surrogate (AS) [12]. In [13], another experimental setup was implemented with the same purpose. In this case, the arterial stiffness change was simulated by acting on the AS tensioning state by varying its transmural pressure, i.e., the difference between the pressure inside and outside the vessel. The outcomes in [13] are affected by the limited variation in external pressure taking off the possibility of analyzing the effect of various stress-strain conditions.

In this context, the present study focuses on a novel arterial simulator where the PWV of a vessel can be adjusted by operating with transmural pressures with mean pressure up to three times greater than the atmospheric one. This apparatus provides an experimental tool that will be used for a deeper understanding of how the tensional state of the AS, due to transmural pressure, affects its ability to transmit the pressure wave.

The next sections will explain the operating principle of the simulator, its main components, the acquisition protocol, and the main data processing steps. Finally, the first experimental results and their discussion will be reported.

II. MATERIALS AND METHODS

In the scientific literature it is known that the PWV in a vessel depends on its capability to strain upon the passage of a pressure wave, e.g., given by heartbeat [14]; in clinical environment, the Bramwell-Hill equation is commonly used to estimate the PWV in a vessel [6,7]:

$$PWV = \sqrt{\frac{A}{\rho} \cdot \frac{dp}{dA}} \tag{1}$$

where A is the cross-sectional area of the hose, while ρ and p are the density and the inner fluid pressure, respectively. The term:

$$\chi = \frac{1}{A} \cdot \frac{dA}{dp} \tag{2}$$

is called distensibility, i.e., the ability of the vessel to vary its area (dA) in relation to the hose internal pressure variations (dp) given by the heartbeat [7]. It is worth noting that Eq. (1) is valid under the assumption of small deformations only.

The operating principle of the simulator is based on varying the stress-strain state of the vessel by acting on its transmural pressure (ΔP):

$$\Delta P = p_{in} - p_{out} \tag{3}$$

where p_{in} and p_{out} are the inner and outer pressures of vessel walls, respectively. In fact, a change in ΔP induces a non-null stress-strain condition on the vessel constitutive material, that varies the capability of the hose to deform during pulse wave transit, therefore, the value of χ changes in Eq. (2) while keeping dp constant. To allow this, a silicon rubber hose, that constitutes the AS (Table 1), is put into a cylindrical polymethyl methacrylate (PMMA) case capable of withstanding pressures greater than the atmospheric pressure (until three times). The system is filled with distilled water as a working fluid. The transmural pressure (ΔP) can be adjusted through two hydraulic circuits connected to the inner and outer environments (Fig. 1).

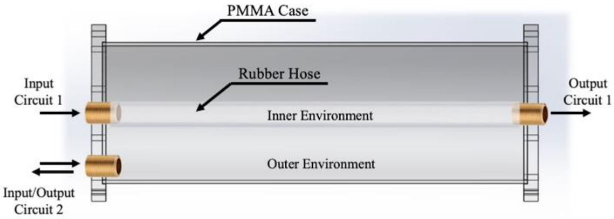

Fig. 1. Principal components of the pressurization case. "Circuit 1" and "Circuit 2" are the hydraulic sections connected to the inner and outer environments, respectively.

Firstly, a centrifugal pump was used to set both p_{in} and p_{out} pressures to the same value which represents the minimum ΔP of the system; then, closing a valve, p_{in} value was changed via air infills inside a hydropneumatic accumulator. Both pressures were continuously monitored with two digital manometers (Keller 23SY). A piston connected to the inner environment generated a pressure perturbation propagating through the whole AS (Fig. 2).

Two strain gauges were attached to the hose at a known distance (ΔL = 25.0 ± 0.1 cm), in order to detect the transit of the pulse wave: the transit time (Δt) is intended as the difference between the time instants in which the pulse passes through the first and second strain gauge.

Table 1. Main characteristics of the silicon rubber hose used as Arterial Surrogate; values expressed as mean ± standard deviation (STD).

Characteristic	Value
Length	42.0 ± 0.1 cm
Inner diameter	16.0 ± 0.4 mm
Thickness	2.0 ± 0.1 mm

An *ad hoc* electronic circuit was developed for amplification and impedance matching of the strain gauge resistance variations, with the aim to make signals readable for a Data Acquisition System (DAQ).

The PWV in every condition of transmural pressure was then derived by calculating:

$$PWV = \frac{\Delta L}{\Delta t} \tag{4}$$

Therefore, a measurement campaign was carried out to provide a preliminary validation of the working principle of the simulator (Table 2). The pressure of the outer environment was set to a fixed value, whereas the inner pressure was adjusted by steps, in order to change the value of ΔP; this pressure regulation is similar to the human body, where the pressure outside arteries remains approximately constant, instead of the inner one.

The temperature of the system (T) was kept constant.

Table 2. Characteristics of the measurement campaign; values expressed as mean ± standard deviation (STD).

Characteristic	Value
System temperature [°C]	20.0 ± 0.5
Outer pressure [kPa]	50.0 ± 2.5
Inner pressure [kPa]	80.0 to 150.0 ± 2.5
Inner pressure steps [kPa]	10.0 ± 2.5

Tests were repeated for 8 values of ΔP and, for each of them, 16 acquisitions were carried out.

With the aim to acquire values from strain-gauge sensors, a DAQ (NI USB-6251) with a software

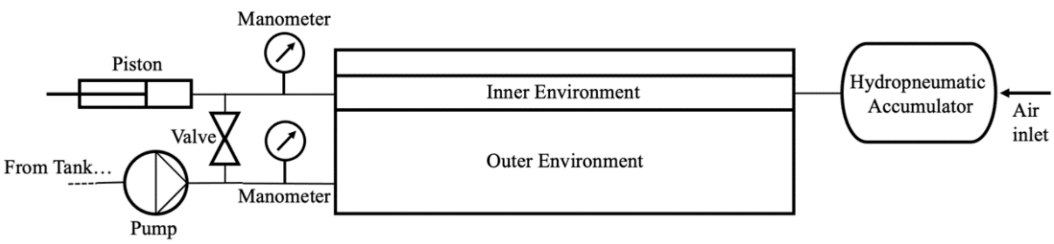

Fig. 2. Scheme of the main components of hydraulic circuit.

(LabView) was used. The main DAQ settings for data acquisition are listed in Table 3.

Table 3. Main settings of DAQ.

Characteristic	Value
Channel sample rate [kS/s]	500
Number of channels	2
Voltage range	± 1 V

To estimate the transit time (Δt) from the data acquired, the following post-processing operations were implemented in MatLab. A low-pass filter was used to remove frequencies above 200 Hz: from the spectral analysis of raw signals, contributions beyond the adopted cutoff frequency were less than 1% with respect to the fundamental frequency amplitude. Then, a cross-correlation was applied to the two filtered strain gauge signals for the estimation of the transit time.

III. RESULTS AND DISCUSSIONS

The PWV results obtained for increasing transmural pressure values are shown in Fig. 3.

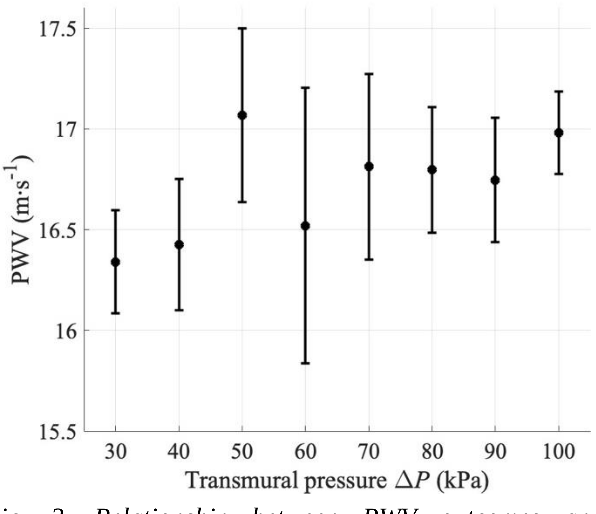

Fig. 3. Relationship between PWV outcomes and transmural pressure applied on AS. Results are represented with error bars, expressed in terms of standard deviation.

The plot shows that mean PWV values have a growing trend as ΔP increases. This behavior is in agreement with [6]: in fact, as p_{in} increases, PWV value raises. This behavior can be explained by making the following considerations: (a) the greater the internal pressure, the greater the volume of water contained in the AS, consequently the greater the value of the cross-sectional area A in Eq. (1); (b) according to [15], the increase of silicon rubber stiffness is related to the increase of its deformation, that implies a reduction of χ, thus an increase of PWV.

On the other hand, the measurement uncertainty was estimated by applying the propagation of the relative standard deviations of the quantities in Eq. (4). The uncertainty of ΔP was considered negligible.

About the standard deviation of PWV results, Fig. 3 shows that (a) error bar sizes are between 2% and 10% with respect to the relative PWV mean value, (b) some error bars are wider than others, e.g., the STD relative to ΔP = 60 kPa is higher about three times with respect to the relative to ΔP = 100 kPa one. This uncertainty values heterogeneity can be attributed to the manual actuation of the piston: pulse duration depends on the actuation force given to the piston. According to [16], strain rate affects the mechanical behavior of the vessel since its constituent material (silicon rubber) has viscoelastic characteristics. In this context, if the pulse is fast, the deformation of vessel walls is less than if the pulse is slower, keeping dp constant. In relation to Eq. 1, a faster pulse causes a decrease in χ (so, an increase in PWV), a slower one causes an increase in χ (then, a decrease in PWV), in the same condition of ΔP. Also, when a high actuation force is provided, the small deformations assumption does not hold and nonlinear behaviors occurred. Since the piston is actuated manually, the variability in the pulse wave magnitude and duration causes unpredictable error bar sizes.

IV. CONCLUSIONS

This paper focuses on a new arterial simulator able to vary the PWV of an arterial surrogate by changing the tensional state of its walls, thus, reproducing the variation of arterial stiffness in the human body. The stress-strain condition can change by varying, independently, inner and outer pressures of the AS, which is embedded in a sealed case and filled with water. A hydraulic circuit, connected to inner and outer environments allows changing liquid pressure. A piston, manually actuated, generates the pulse wave. Two strain gauges were glued at a known distance on the AS, in order to measure the transit time of the perturbation running through the vessel by deformation of its walls during pulse transit. The simulator working principle has been confirmed by first experimental results from a measurement campaign. In particular, the trend of results is in agreement with the reference mathematical model. The non-repeatability of measurements due to manual generation of pulse causes error bars up to 10% of PWV value. More acquisitions are required with a controlled pulse generator to properly characterize the system.

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