



Università Politecnica delle Marche
Scuola di Dottorato di Ricerca in Scienze dell'Ingegneria
Ingegneria Industriale Curriculum Meccanico

Development of a measurement procedure for the assessment of carotid blood pressure by means of Laser Doppler Vibrometry

Ph.D. Dissertation of:

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Advisor:

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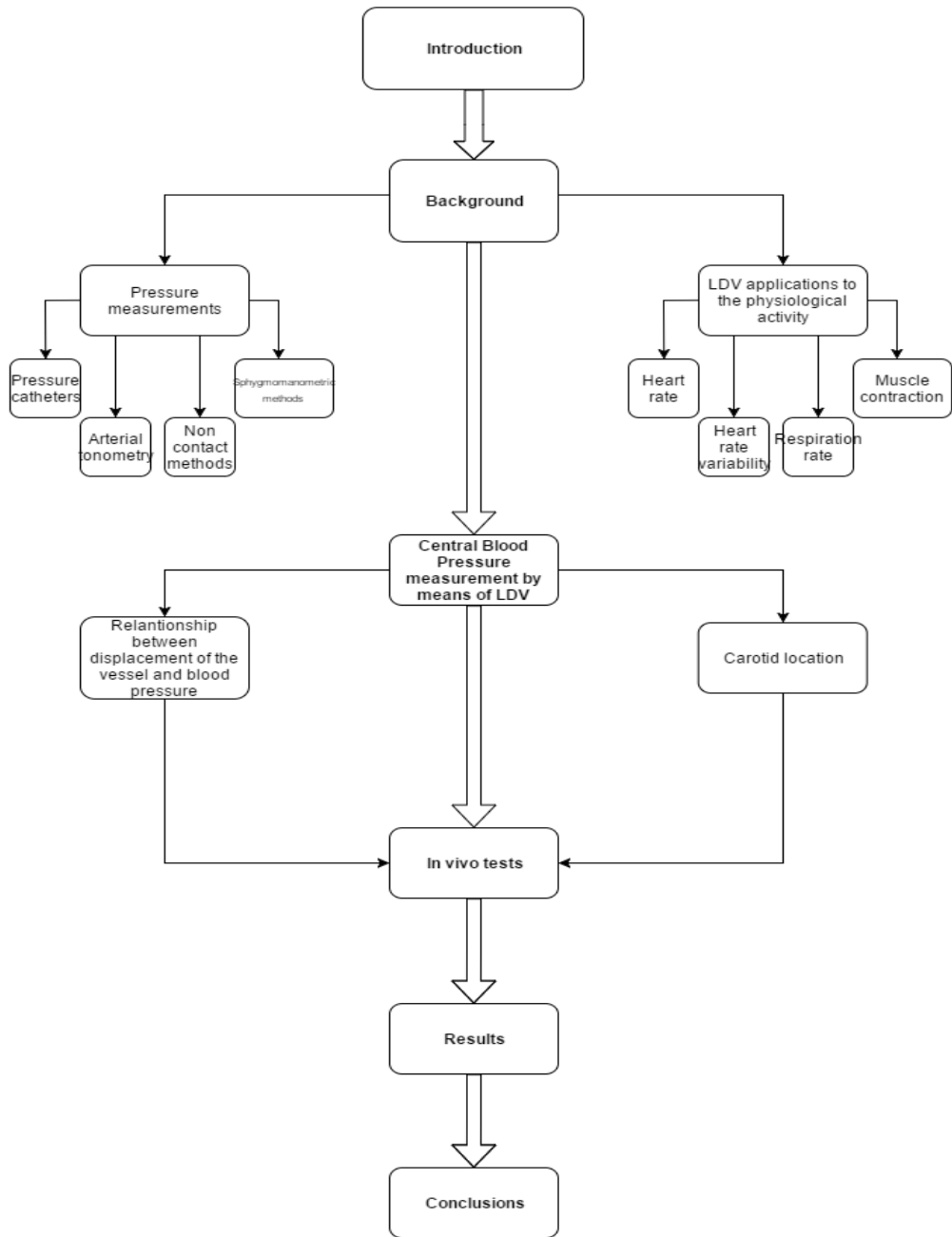
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Abstract

High blood pressure is a great risk factor for several physiological diseases, i.e. myocardial infarction, heart failure, stroke, renal failure, being the leading cause of death worldwide.

Therefore, blood pressure measurement is a fundamental aspect of health monitoring.

The aim of the present work is to validate a measurement procedure for the assessment of carotid blood pressure by means of Laser Doppler Vibrometry (LDV).

LDV is a non-contact technique with high sensitivity, able to detect the skin vibrations due to the cardiovascular activity.

It has been validated for the assessment of several physiological parameters, such as heart rate, respiration rate and muscle contraction.

In this study, LDV signal has been acquired from 28 healthy participants and it has been calibrated by means of an exponential mathematical model in order to obtain the carotid pressure waveform from the displacement of the vessel.

The results have been compared with two standard techniques for the assessment of blood pressure, sphygmomanometric method and arterial applanation tonometry.

The systolic peak of the calibrated waveform from LDV showed an average percentage deviation of 4% and 8% from the one assessed by means of sphygmomanometric cuff and arterial tonometer respectively.

The accuracy of the present measurement technique is discussed, considering the signal integration and the application of the calibration model as significant contributions to the total amount of uncertainty. An average percentage uncertainty of around 15 % has been obtained in the measure of carotid systolic pressure.

Moreover, other hemodynamic significant parameters, such as arterial stiffness and Left Ventricular Ejection Time, have been derived from LDV data, showing good correlation with the measures of the reference methods.

In conclusion, the proposed measurement technique, for the assessment of carotid blood pressure, shows good agreement with the reference techniques. Overall, some critical issues must be considered, such as the correct localization of the measurement point, the presence of movement artifacts and reflection phenomena not related to the pressure pulse in the investigated vessel.

Contents

Introduction	1
Chapter 1 Background.....	3
1.1 Blood Pressure measurements	3
1.1.1 Arterial Pressure catheters	4
1.1.2 Arterial tonometry	5
1.1.3 Indirect Blood Pressure Measurements	6
1.1.4 Non contact methods	8
1.1.5 Accuracy of blood pressure measurements	8
1.2 Laser Doppler Vibrometry principles and applications to physiological activity	9
1.2.1 Cardiac related measurements.....	10
1.2.2 Respiration rate measurement.....	13
1.2.3 Muscle contraction measurements	14
Chapter 2 Arterial Pressure measurement by means of LDV	15
2.1 Mathematical Models: relationship between displacement of the vessel and blood pressure	15
2.2 Application of the exponential model to LDV signal	17
2.3 Carotid location	17
2.4 Measurement setup.....	22
2.5 Signal processing.....	23
2.5.1 Preprocessing of LDV signal	23
2.5.2 Model implementation.....	26
2.5.3 Uncertainty of the proposed method	27
Chapter 3: Results	29
3.1 Pressure waveforms comparison	29
3.2 Stiffness evaluation	34
3.3 Left Ventricular Ejection Time computation	34
Concluding Remarks.....	37

List of Figures

- Figure 1: Physiological variation in pressure waveform throughout the arterial tree**
- Figure 2: Invasive pressure measurement by means of a catheter**
- Figure 3: applanation tonometry over the radial artery**
- Figure 4: The principle of measurement of an applanation tonometer**
- Figure 5: example of pressure cuff**
- Figure 6: amplitude of the oscillations measured by means of the oscillometric pressure meter**
- Figure 7: concept of a Laser Doppler Vibrometer**
- Figure 8: an example of main peak detection in ECG (above) and LDV (below) signals on the carotid site**
- Figure 9: example of QT time interval in ECG signal (above) and V_1V_2 time interval in LDV signal on the carotid site (below)**
- Figure 10: example of tacograms obtained by means of ECG (above) and LDV (below)**
- Figure 11: measurement point localization by means of thermal camera**
- Figure 12: Thermal image (above) with a zoom on the carotid area (below, with the bifurcation marked with a red dot)**
- Figure 13: representation of the measurement grid**
- Figure 14: averaged LDV signals of point 1 and point 3 (subject 1), above, and 5x7 matrix with the peak to peak values, below.**
- Figure 15: resampled carotid map (subject 1)**
- Figure 16: Example of two different carotid path, participant 6 (left), participant 16 (right)**
- Figure 17: the measurement grid, top, LDV traces of the fourth column and zoom on the area related to the velocity peaks, bottom.**
- Figure 18: Setup scheme: ECG electrodes placed on the skin according to the standard positioned scheme of the I-lead ECG; LDV spot perpendicularly directed on the skin surface**
- Figure 19: flow chart of the signal preprocessing procedure**
- Figure 20: raw LDV signal, above, filtered signal, below.**
- Figure 21: Filtered LDV signal, above, integrated and detrended signal, below.**
- Figure 22: individuation of onset and offset in single displacement waveforms, green dots**

Figure 23: an example of average LDV displacement signal
Figure 24: flowchart of the algorithm for the implementation of the exponential model
Figure 25: example of LDV pressure waveform
Figure 26: comparison between reference systolic pressure and LDV systolic pressure
Figure 27: average tonometric waveform (left), average LDV pressure waveform (right)
Figure 28: alfa average value as a function of age
Figure 29: LVET computation from tonometer and LDV, left and right respectively
Figure 30: scatter plot of LVET measured at carotid level by means of LDV versus LVET measured at radial level by means of arterial tonometer
Figure 31: Bland Altman plot as a comparison method for the measurement of LVET between LDV and arterial tonometer

List of Tables

Table I: physical characteristics of the tested participants

Table II: Gender of the participants, Measured brachial systolic pressure, Reference carotid systolic pressure calculated as $0.79 \times \text{Brachial Systolic Pressure}$ for male participants and as $0.85 \times \text{Brachial Systolic Pressure}$ for female participants, LDV Carotid Systolic pressure, Percentage deviation between LDV systolic pressure and reference systolic value

Table III: Gender of the participants, Measured radial systolic pressure, LDV carotid systolic pressure, Reference carotid systolic pressure computed as Measured radial systolic pressure +12 mmHg and Measured radial systolic pressure +8 mmHg for male and female participants respectively, percentage deviation between LDV and reference systolic pressure

Table IV: uncertainty in the measurement of systolic peak, study 1, left, study 2, right

Table V: average LVET measured by means of LDV and Radial Tonometer

Introduction

Hypertension, the systemic condition accompanying high blood pressure [1], is a relevant risk factor for several physiological diseases, e.g. heart failure, stroke, kidney failure[2].

This condition can be asymptomatic [2], moreover many different situations, such as physical activity or acute stress, can normally raise blood pressure. These temporary increases cannot be considered pathological: a diagnosis of hypertension can be made only when the patient has multiple high blood pressure readings over a period of time [3].

Several studies, [4] [5] [6], demonstrate that high blood pressure has a wide prevalence in the world population.

In fact, the World Health Organization (WHO) has defined hypertension as the first cause of death worldwide [7].

Therefore, blood pressure should be checked regularly, in order to monitor the health status of the cardiovascular system.

The gold standard method for the determination of the blood pressure waveform involves its direct measure by means of invasive techniques; the installation of an indwelling pressure transducer on the measurement site is required [8]. The continuous assessment of blood pressure waveform can furnish several types of information about cardiovascular activity, i.e. heart rate or location of the dicrotic notch.

In comparison, conventional blood pressure sensors, such as cuff based devices, are able to provide only the maximum and the minimum pressure values in a heart period, systolic and diastolic pressure respectively.

Cuff based techniques are the most common approaches for blood pressure assessment, in particular within the home monitoring environment. However, these devices are affected by an high degree of uncertainty and they pose some issues for long term monitoring, because of the discomfort caused by the cuff [8].

Another common technique, which is able to provide the blood pressure waveform is the arterial applanation tonometry [9]. This technique is based on the use of a pressure transducer pressed against a blood vessel supported by a rigid structure, usually a bone. It can provide an accurate representation of the pressure waveform, but it requires the use of a calibration model [10]: this allows the waveform to be rescaled to its correct amplitude in typical units (e.g. mmHg). The application of such transfer function to the general population is subject to debate, and this represents one of the main limitations about the use of this technique [11]. Moreover, the correct installation of the pressure transducer is particularly challenging in obese patients, because of the significant presence of adipose tissue .

Other studies show the feasibility of alternative techniques to evaluate blood pressure non-invasively; in [12], intravascular magnetic resonance (MR) was used to assess the blood pressure waveform. A 1.5 Tesla [T] MR scanner was used, just above the sino-tubular junction, to evaluate the aortic area curves. This technique allows direct measurement of the variation of the vessel section during the cardiac cycle, but needs a calibration model to derive the pressure waveform from the aortic traversal area.

Pulse-Wave-based Ultrasound Manometry (PWUM) is another non-invasive method that combines Pulse Wave Imaging (PWI) and vessel diameter measurements for the

assessment of blood pressure[13]. It is based on the ultrasound scanning of the cross-section of the vessel, in order to measure its diameter variation during the cardiac cycle. The present work considers a method for non-contact measurements of the blood pressure waveform.

The proposed approach is based on the use of a Laser Doppler Vibrometer (LDV). LDV allows measurement of the vibrations of the skin surface due to the movements of arterial walls with an high degree of accuracy [14]. Several studies [15] [16] have investigated the use of LDV to assess heart rate and other cardiovascular parameters. The LDV technique has a high sensitivity and presents the significant advantage of being non-contact.

Therefore, the aim of this study is to validate a non-contact measurement procedure for the assessment of carotid blood pressure by means of Laser Doppler Vibrometry.

The rationale of this work has been developed according to the following steps:

- measurement of the mechanical vibration of carotid artery by means of LDV,
- calibration of the displacement curves from LDV for the calculation of carotid blood pressure
- discussion of the obtained results

The first step has required the development of a procedure for the localization of the correct measurement point over the investigated vessel, i.e. the carotid artery.

The findings show that an incorrect positioning of the Laser spot causes the incorrect measure of the carotid vibration amplitude as well as the measurement of velocity components which may not be related to the phenomenon of interest.

Two different approaches, based on the use of a thermal camera and a Laser Scanner system respectively, have been tested.

The calibration of acquired signals has been performed by means of a mathematical exponential model taken from scientific literature [10].

The results are discussed in terms of comparison between the calibrated LDV signals and standard reference techniques, e.g. cuff sphygmomanometry and arterial tonometry.

In chapter 1, a short review of the most significant blood pressure measurement techniques is presented. In addition, the main biomedical applications of Laser Doppler Vibrometry, developed over the past years, are described.

Chapter 2 discusses the basic steps to achieve a blood pressure waveform from LDV signal. Therefore, the main calibration techniques of blood pressure are reported, with a particular focus on the mathematical model chosen in the present study.

Then, the approaches used for the correct location of the measurement point, the measurement setup are described.

In the last section of the chapter, the steps of LDV signal processing are shown in detail.

Chapter 3 reports the results of this work, in terms of determination of the pressure waveform and achievement of parameters of physiological interest from the obtained signal, such as arterial stiffness and Left Ventricular Ejection Time.

The work ends with the discussion of the obtained results.

Chapter 1

Background

1.1 Blood Pressure measurements

The study of the physical variables related to the movement of blood in the cardiovascular system is called hemodynamics.[17]. Fluid cannot move through a system unless some energy is applied to it, in fluid-dynamics this energy is expressed as a pressure gradient between two points of the system. In hemodynamics, blood pressure is the pressure exerted by the blood against the walls of a vessel. The peak pressure during contraction of the heart is the systolic pressure and it is typically around 110-130 mmHg, whereas the minimum arterial pressure during relaxation of the heart is the diastolic pressure, usually around 70-90 mmHg [17]. The difference between the systolic and diastolic pressure is the pulse pressure [18]. Another important parameter of pressure waveform is the mean arterial pressure (MAP), the average arterial pressure during a cardiac cycle, calculated as follows:

$$MAP = \frac{1}{T} \int_0^T p(t) dt$$

where $p(t)$ is the pressure wave during a cardiac cycle and T is the cardiac period. Several empirical formulas were developed to estimate MAP when it is not possible to assess the blood pressure waveform [19]. The most common one is reported below:

$$MAP = \frac{1}{3}(2DBP - SBP)$$

where DBP and SBP are diastolic and systolic blood pressure respectively.

As blood flows along the aorta and into the other arteries, it is possible to notice significant changes in the arterial pressure waveform: as the pressure pulse moves away from the heart, the systolic peak rises while the diastolic pressure remains fairly constant. It is not completely clear why the pressure wave changes shape, it may be related to factors such as decreased compliance of distal arteries, the presence of reflected waves which add a contribution to the pressure pulse [20]. Moreover MAP declines, but its reduction is quite small, limited to a few mmHg [11]. The figure below [21] shows the changes in shape from aorta to distal arteries.

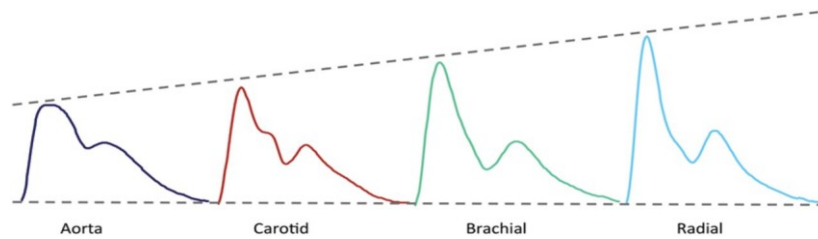


Figure 1: Physiological variation in pressure waveform throughout the arterial tree [21]

In the following sections, a review of the most important techniques used to assess arterial pressure is reported.

1.1.1 Arterial Pressure catheters

Direct measurement methods are the most accurate approaches for the assessment of intra-arterial blood pressure and they support measurement of the continuous pressure waveform [22]. They require a high level of specialization and they are associated with a higher degree of risk for the patient. These devices are based on the insertion of a pressure sensor in the measurement site by means of a catheter full of fluid in order to obtain a hydraulic coupling between the anatomic site and the pressure transducer.

Ideally, the fluid in the catheter should realize a perfect hydraulic coupling in order to transmit the pressure measured in the arterial site without introducing any error. In real conditions, the pressure transfer through a tube with a proper length, internal diameter and thickness generate an error due to the dynamic response of the system composed by blood, catheter and transducer. This is a typical dynamic response of a second order system. Another possible cause of error is the difference of height h between the pressure transducer and the catheter, this measurement uncertainty could be calculated as the product ρgh , where ρ is the density of the fluid in the catheter and g is the gravitational acceleration [22]. Moreover, if the fluid pressure can be considered as a constant in every direction in static conditions, in dynamic conditions, it is a function of kinetic energy $\rho v^2/2$.

This is a cause of error depending on the relative movement of the fluid with respect to the pressure transducer. A further factor of error could be the insertion of the instrument, this is a relevant issue in the vessels with a lumen comparable with the catheter diameter [23]. In these instances, the catheter insertion produces significant variations of pressure and velocity fields [22]. The insertion error can be computed from the ratio between vessel and catheter diameters.

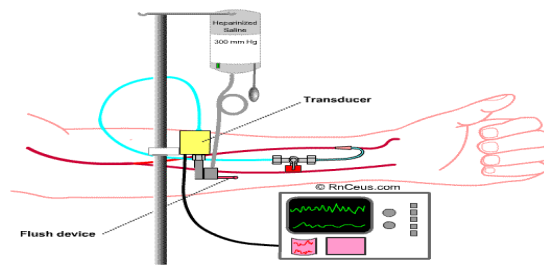


Figure 2: Invasive pressure measurement by means of a catheter

1.1.2 Arterial tonometry

Arterial tonometry is a technique for blood pressure measurement in which one or more pressure sensors are pressed against the skin over an artery [24]. The superficial artery is supported by rigid (e.g. a bone) structure, so that adequate applanation of the vessel can be achieved to obtain the pressure waveform. As tonometry can only provide the waveform, this signal has to be calibrated by means of an external method, for example a cuff technique giving peripheral blood pressure values [12]. This allows the waveform to be rescaled to its correct amplitude. Applanation tonometry is based on the Imbert-Fick principle [5].



Figure 3: applanation tonometry over the radial artery

The Imbert-Fick law states that the internal pressure (P_i) in a spherical body with an infinitely thin, dry and elastic membrane wall, equals the force (W) exerted on this body divided by the applanation surface (A). Hence, in an applanated spherical body, the Imbert-Fick law can be written as $P_i = W/A$; if one can measure W and A , P_i can be derived. In brief, a superficial artery (usually the radial one) is compressed and partially flattened against the underlying rigid structure. This flattened arterial surface acts as a "transducer" for intravascular pressures acting perpendicularly against the vessel wall. An array of piezoelectric crystals, positioned on the skin overlying this flattened portion of artery, senses arterial pressure changes and translates them into a continuous arterial pressure waveform.

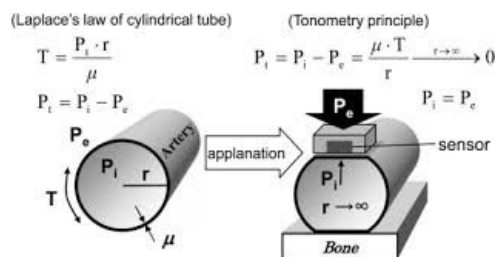


Figure 4: The principle of measurement of an applanation tonometer [25]

1.1.3 Indirect Blood Pressure Measurements

The indirect techniques to measure arterial blood pressure were introduced in Italy at the end of the 19th century by an Italian physician, Riva-Rocci [26]. This methods use a device called sphygmomanometer, which is an inflatable bladder covered by a cloth sleeve and a column to measure the pressure. The cuff is applied to the arm or leg over a major artery, and the bladder is inflated in order to reach a pressure able to compress the underlying artery. The bladder is then gradually deflated, so the artery is decompressed.



Figure 5: example of pressure cuff

It is important that the compression of the artery produced by the inflatable bladder in the cuff is uniform, this produce more reproducible sounds or vibrations. The length of the bladder should be at least 80% of the circumference of the upper arm in order to achieve an uniform compression of the interested area . If the dimension of the bladder is too small, the pressure measurements will be affected by a relevant error [26].. The use of a cuff with inappropriate size is called *miscuffing* and it is considered the most common cause of errors in the indirect measurement of arterial blood pressure.

There are different blood pressure measurement techniques based on the use of a sphygmomanometer cuff. The main ones are reported below.

Palpatory Method:

This method allows the measurement of the systolic pressure value. It is based on the following principle: the blood pulse cannot be palpated until the cuff pressure drops below systolic value.

Therefore, the operator touches the artery just above the cuff and he registers the systolic value when he is able to perceive the blood pulse.

Auscultatory Method:

This method considers the measurement of the blood pressure by means of the determination of sounds, the Korotkoff sounds, generated by the artery when it begins to open. These sounds are produced by the vibration of the artery related to the turbulent flow over the occlusion. The Korotkoff sounds, KS, are characterized by a very low frequency, in the range 25-50 Hz, and so they are just above the human threshold for hearing, that is 16 Hz [26]. When the artery is completely occluded, it does not produce any sound. Then, the opening of the valve causes a decrease of the pressure over the vessel. The first sound corresponds to the systolic pressure, which can be read by means of a manometer.

The sounds produced by turbulent blood flow last so long as the vessel is still compressed. When the KS disappear, the artery has recovered its original lumen, and the diastolic pressure can be measured. The auscultatory method is characterized by a high level of uncertainty, depending on the operator hearing capability and his time reaction in associating the starting sound or the last one to the pressure read on the manometer. Therefore, it is very difficult to quantify the performances of this technique in terms of accuracy and precision [22].

Oscillometric Method:

This approach is used to detect pulsatile pressure changes, oscillations, over an artery using the principles of plethysmography [26]. The processing of these periodic changes in oscillations is electronically performed and it allows measurement of the diastolic, systolic and mean arterial pressure. The instrument consists of a pneumatic circuit connected to a sphygmomanometer cuff and an electronic circuit able to detect the pressure in the cuff by means of a pressure sensor. The measurement procedure starts with the occlusion of the artery, this produces a total reflection of the pressure wave, inducing a small pressure pulse in the cuff. Then, the pressure in the cuff is gradually reduced by steps of 5 mmHg. When two oscillations of the same amplitude are detected, the pressure is reduced again, in order to reduce movement artifacts. The micro-processor receives, at each step, the cuff pressure and the amplitude of the oscillations. The first two oscillations with higher amplitude furnish the systolic pressure value. When the pressure is equal to its mean value (MAP), the oscillations reach their maximum amplitude. The diastolic value is registered when the oscillations become constant again [22].

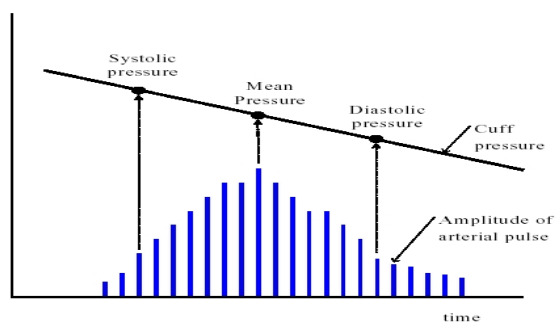


Figure 6: amplitude of the oscillations measured by means of the oscillometric pressure meter [22]

1.1.4 Non invasive methods

Different methods have been proposed in the past years to assess the pressure waveform non invasively. In [27] an approach based on the measurement of the distension wave of carotid artery by means of echo tracking has been shown. This technique requires the use of a calibration model [28] based on the assumption that the diastolic and mean arterial pressures are fairly constant through the arterial tree. The results of this work show reliable and reproducible results in comparing the approach with arterial tonometry. In [13] an ultrasound-based technique has been used to assess the local pulse pressure waveform without contact. Using raw radio frequency ultrasound signals at high frame rate the authors have measured the local distension waveforms. Moreover the local Pulse Wave Velocity (PWV) has been assessed, it gives significant information about the local stiffness of the vessel. The combination of PWV and distension waveforms has allowed the acquisition of a pulse pressure waveform strongly related to the one measured by applanation tonometry.

Another approach [12] consist of image processing techniques applied to cross-sections of the arteries obtained using magnetic resonance imaging. This technique is based on the fact that the relationship between pressure and arterial areas can be approximated by means of basic mathematic functions [10].

Therefore, the use of a mathematical model and the measurement of diastolic and mean arterial pressure allow a calibrated pressure waveform to be obtained.

In [12] three different mathematical models to derive the pressure waveform from the variation of the arterial section are compared, using an arctangent, a linear and an exponential function respectively. The results of this study show that arctangent and exponential methods are superior to the linear one in the assessment of the arterial pressure from the aorta.

1.1.5 Accuracy of blood pressure measurements

No matter which measurement device or method is used, blood pressure is an hemodynamic quantity, depending on many factors, including the circumstances of measurement itself.

In any case, it is important to underscore that an accurate device is fundamental to all blood pressure measurement [29]. In fact, attention to methodological details is not so relevant if the device is inaccurate [30].

The most accurate technique to measure blood pressure involves the use a pressure catheter. However, as reported in section 2.1.1, catheters too are affected by several causes of error: one of them is the blood kinetic energy which can produce what appear to be pressure variations. Therefore, the measured pressure depends on the orientation of the sensor with respect to the direction of blood flow.

In particular, in central districts, where systolic pressure is smaller, this could cause relevant errors. For instance, typical systolic pressure of the pulmonary artery is around 20 mmHg [18]; considering a blood velocity of 0.9 m/s, the dynamic contribution to blood pressure is 3 mmHg, and, therefore, the error is around 15 %.

With regard to cuff measurement devices, there are several sources of uncertainty, such as posture of the patient, arm support and position [30]. The American Association for the Advancement of Medical Instrumentation published a reference standard for sphygmomanometers for evaluating the accuracy of sensors[31]. In [32], several blood pressure measurement devices were tested in comparison to the reference standard. A mercury sphygmomanometer was used as the standard reference device, and the tested sensors were classified in dependence of the percentage of measurements inferior less than 5 mmHg, 10 mmHg and 15 mmHg with respect to the reference standard. None of the automated blood pressure measuring devices for self measurement at the upper arm were recommended. This confirms the high degree of uncertainty of the cuff sphygmomanometric devices. With regard to arterial tonometry, in [33] the accuracy of arterial tonometry was discussed in terms of comparison with an intra-arterial catheter. Results showed that the tonometric waveform is almost equal to the intra-arterial waveform. Inevitably, however limitations surrounding the use of arterial applanation tonometry refer to the application of a transfer function for the calibration of the pressure waveform. The validity of such transfer function to the general population is subject to debate [12]; this is due to the lack of studies validating the method versus invasive techniques in a general population. Moreover, the application of arterial tonometry is particularly challenging in obese subjects.[12].

1.2 Laser Doppler Vibrometry principles and applications to physiological activity

Laser Doppler Vibrometry (LDV) is a non-contact measurement technique used to assess the vibration of a surface, it is based on the Doppler effect. It is a frequency shift that happens when source and observer move relative to each other. The Doppler Effect can be used with the principle of interferometry to accurately measure surface velocity or displacement. An interferometer is an optical instrument which measures the position of the waves which have propagated through different paths. The interferometer splits an electromagnetic wave in two different parts using a beamsplitter. Then the two beams are delayed by unequal distances, redirected and recombined and so the intensity of the waves is detected. A Laser Doppler Vibrometer is a special kind of optical interferometer. Within the LDV hardware, the laser beam is split in two beams (reference and measurement) by means of a beamsplitter. The measurement beam then passes through the Bragg cell, which adds a frequency shift. Without a Bragg Cell, the system would not be able to distinguish whether the detected movement is towards or away from the laser. This frequency shifted beam then is directed to the target and the vibration amplitude and frequency are extracted from the Doppler shift of the reflected laser beam frequency due to the motion of the surface, once it is reflected back and collected to the photodiode by a second beam splitter together with the reference beam. The output of an LDV is generally a continuous analog voltage that is directly proportional to the target velocity component along the direction of the laser beam [34].

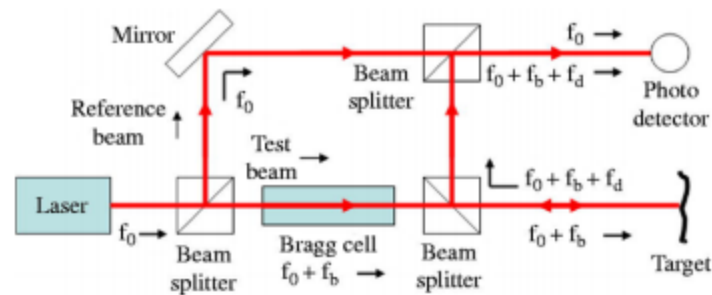


Figure 7: concept of a Laser Doppler Vibrometer

The relationship between the Doppler frequency f_d and the velocity v of the targeted surface in the direction of the Laser beam is shown below:

$$f_d = \frac{2v}{\lambda}$$

where λ is the wavelength of the Laser radiation.

Several studies, [14] [16] [15] [35] [36] have investigated the use of LDV to assess heart rate and other cardiovascular parameters. These studies show that this technique has a high sensitivity and presents the great advantage of operating without contact. Moreover, LDV has been also used to assess other physiological parameters such as respiration rate [37] [17] or muscle contraction [39], measuring the movements related to breathing or muscular activity respectively. A short review of the main biomedical applications of Laser Doppler Vibrometry is reported above

1.2.1 Cardiac related measurements

Several studies, [14] [16] [15] [35] [36], have investigated the applications of Laser Doppler Vibrometry to the monitoring of cardiovascular activity. One approach considers the measurement of the vibration activity over an artery, usually the common carotid artery. Therefore, the measurement point is, usually, fixed on the neck. In [16] a deep investigation of LDV signal over the carotid has been conducted. In particular LDV signal was studied at rest, and during and after rebreathing, a particular condition in which the participants were asked to raise upon cue an appropriately sized disposable surgical mask to their face and to hold it in that position with sufficient force to maintain a tight seal. The mask was connected to a anaesthetic bag, thus forcing the participants to rebreathe the same air. Vibration signals recorded with the LDV were studied both in terms of velocity, raw traces, and displacement, integrated signals. The rebreathing maneuver produced a relevant variation in the cardiovascular parameters such as Heart Rate, Blood Pressure and Pressure Pulse. Their variations were monitored by means of Electrocardiograph (ECG), arterial tonometer and Impedance Cardiogram (ICG). The focus of this study was to determine if the changes in cardiovascular conditions were mirrored in features of the LDV carotid pulse, suggesting that it can furnish significant information regarding cardiovascular function. Although considerable study remains, these findings suggest that the LDV method can be used as a surrogate for conventional measures. In [35] the movements of the chest wall were monitored by means of a single point Laser Doppler vibrometric system. A comparison has been performed with the gold standard method for the assessment of the cardiac activity, the electrocardiography (ECG). The measurement principle was based on the assumption that the peak in LDV signal is due to the muscle contraction triggered by the electrical signal measured by ECG. The main peak of the LDV signal, related to the R wave peak of the ECG, was identified following a procedure reported in [15]. All the results show an average bias in the measure of heart rate lower than 1 beat per minute (bpm).

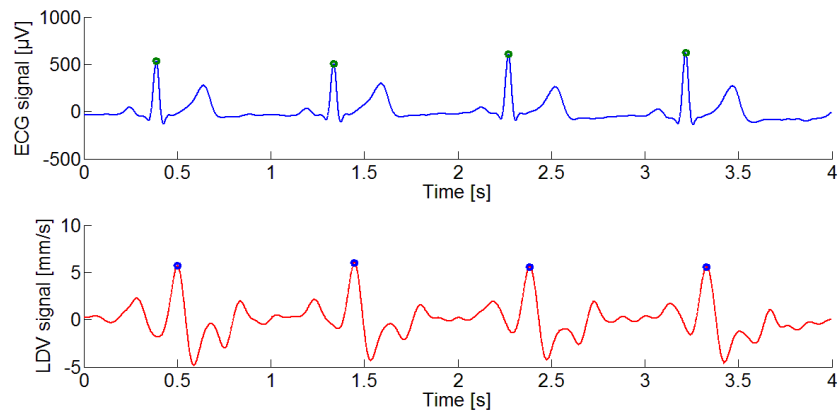


Figure 8: an example of main peak detection in ECG (above) and LDV (below) signals on the carotid site

Moreover in [40] an LDV single point system (Polytech PDV 100) was tested for the HR measurement over the common carotid artery. The reliability of such an approach was discussed in terms of sensitivity and positive predictivity with reference to the gold standard method (ECG). The obtained indicators were very closed to 1 for both the considered sensors (LDV and ECG), which means very good agreement with the reference method. This is confirmed by the fact that the average deviation between the two sensors for the 8 tested subjects was of 1.5 bpm. In this study, LDV and ECG have been also compared in order to evaluate if it is possible to estimate the QT time interval, the duration of ventricular contraction [41], by means of Laser Doppler Vibrometry. According to the results, a common bias of nearly 100 ms is noticed in the QT time interval with respect to the time interval between the two main peaks of LDV signal (V_1 and V_2).

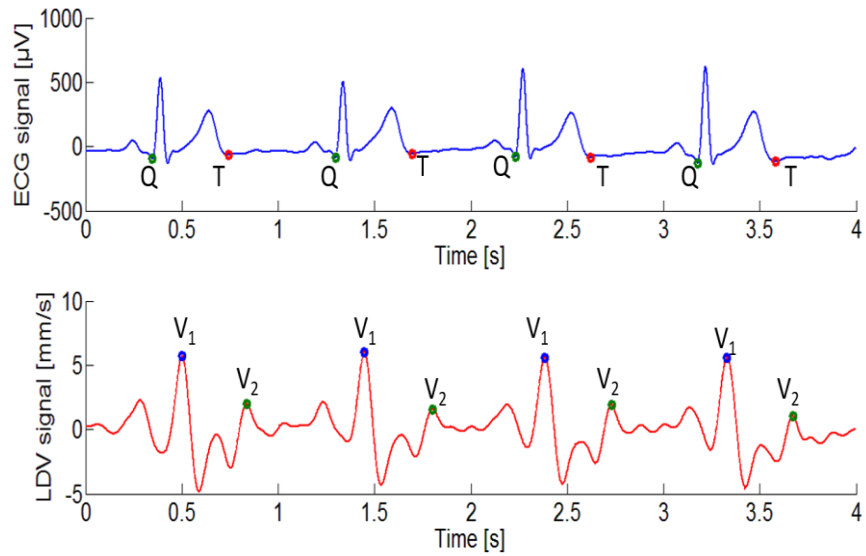


Figure 9: example of QT time interval in ECG signal (above) and V_1V_2 time interval in LDV signal on the carotid site (below)

This is due to the fact that V_2 is correlated to the T peak of the ECG signal, while the QT interval is computed by measuring the onset of QRS complex and the offset of T wave. The possibility of detecting a relevant feature, usually the main peak, in each cardiac cycle by means of LDV has permitted study of the Heart Rate Variability (HRV) without contact. HRV is the study of the physiological variability of the Heart Rate (HR), which is related to the health conditions of the subject. HRV is assessed measuring heart periods (HP) on a time window of >5 minutes [42].[22] In [35] a comparison between ECG and LDV was performed in time and frequency domain. The results showed no statistical difference between ECG and LDV in the studied HRV indices. In [36] LDV was compared with ECG and other devices for the cardiovascular monitoring (i.e. photoplethysmograph and phonocardiograph) in terms of heart rate and heart rate variability measurements. This work confirms that it is possible to accurately measure HRV by means of LDV. In figure 10, there is an example of the tachograms, the series of time intervals between two main features in a cardiac-related signal, obtained from ECG and LDV.

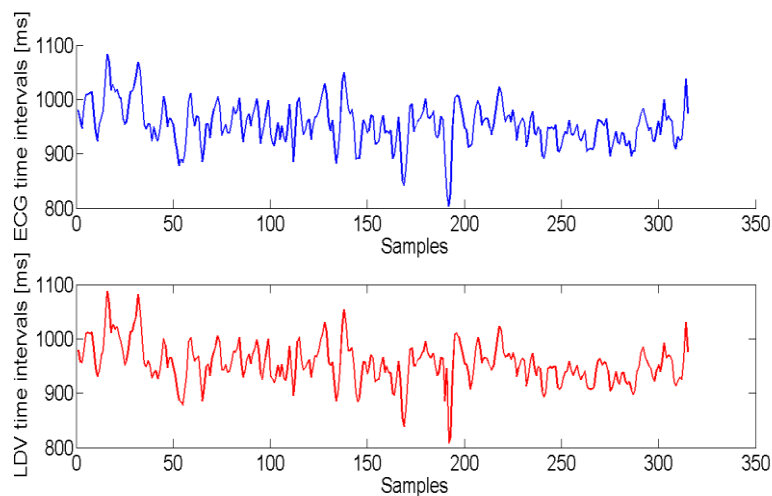


Figure 10: example of tacograms obtained by means of ECG (above) and LDV (below)

1.2.2 Respiration rate measurement

LDV systems have also been applied to the monitoring of respiration activity. The measurement principle is always based on the possibility of determining the velocity of a moving surface in the direction of the Laser spot. In respiration monitoring, the measurement point is fixed on the subject thorax, in order to reveal the movements related to the breathing act.

In [44] the velocity traces obtained by means of LDV on 10 different points fixed on the thorax have been compared with the signal measured by means of the reference device, i.e. the spirometer. The optical head of the vibrometer has been placed at a distance of 1.5 m from the tested subjects. The experiment has been conducted on 33 healthy subjects. The investigated breathing parameter was the respiration rate (RR), calculated from the time interval measured in seconds between two expiration maxima: the measurement principle is based on the assumption that the displacement signal measured by LDV is a consequence of the mechanical movement of the chest resulting from the respiration activity. The results of this study show an average deviation between the respiration periods acquired by means of the two systems of around 14 ms, therefore the authors suggest the use of LDV for the RR assessment in those cases where the standard use of a spirometer is impossible, e.g. with non-cooperative patients.

The same principle has been used in [38] for the assessment of Respiration Rate in pre-term infants. The main advantage of the proposed method was the possibility to measure a fundamental physiological parameter without contact with the patient and outside the incubator. Acquired data were compared with the ones obtained from the mechanical ventilators that assist the preterm infant. An uncertainty of ± 0.13 s in the RR assessment was revealed in this study.

1.2.3 Muscle contraction measurements

The LDV technique has been applied to the evaluation of muscular activity in [39] [45]. The aim of these studies was to assess isometric muscle contraction for two locomotor muscles by means of LDV, and to compare the results with the reference technique, the standard electromyography (EMG). The comparison between LDV and EMG has been performed in time and frequency domain. In the time domain, the timing of contraction, onset and offset of muscle contraction, and the amplitude of the signals have been discussed, while, in the frequency domain, the authors have focused their attention on the mean and median frequency of LDV and EMG spectral contents. EMG and LDV data were obtained from arm (flexor carpi ulnaris) and leg muscles (tibialis anterior), on both left and right sides, under two levels of instructed isometric force production. Overall, the times measured by the two techniques were in close agreement. The contraction onset times detected by the EMG and LDM methods were similar but larger differences were observed for measures of contraction offset times. The total contraction times were shorter for the LDV measures than for the EMG measures with a maximum standard deviation of 440 ms. The amplitude analysis was performed in terms of correlation between the Signal-Noise ratios (S/N) of LDV and EMG traces in the different measurement conditions: Pearson coefficient of 0.95 and 0.89 were obtained for flexor carpi ulnaris and tibialis anterior respectively. The frequency domain analysis showed similar Mean Power frequency (MPF) trends for the right and left flexor carpi ulnaris signals, for both the EMG and LDV signals. However, the MPF of the LDV signals were observed to be much lower than the MPF of the EMG signals. The authors suggest that this frequency difference between the LDV and EMG signals is related to the fundamental differences in origin and waveform of the mechanical and electrical muscle response components. LDV was also applied to facial myography to detect facial expression of emotion [46]. The study was assessed using simultaneously the LDV method, EMG and video recordings in order to describe the basic aspects of facial myography activity. The spatial distribution of the LDV muscle vibration patterns was consistent with the locations of the muscles engaged in the various expressions.

Chapter 2

Arterial Pressure measurement by means of LDV

The focus of this PhD thesis is to develop a measurement technique for the indirect measurement of blood pressure waveform in a central district, such as the carotid artery, by means of Laser Doppler Vibrometry.

LDV is a non-contact technique able to detect the vibrations of the skin surface due to the movements of arterial walls.

The use of LDV for blood pressure measure requires the calibration of the vibrational signal by means of a mathematical model in order to relate the displacement of the vessel to the arterial pressure. Moreover, a fundamental aspect of this study has been the correct location of the measurement point over the investigated vessel.

This chapter will discuss the most significant mathematical models for the calibration of a pressure signal, the techniques used to correctly detect the measurement point, the measurement setup used for the assessment of LDV signal and the signal processing applied to LDV traces.

2.1 Mathematical Models: relationship between displacement of the vessel and blood pressure

Most of the non-invasive techniques for the measurement of arterial pressure need a calibration model. It usually expresses the relationship between the arterial pressure and cross-sectional area of the blood vessel.

The application of these models starts from the assumption that diastolic and mean arterial pressure remain fairly constant throughout the whole length of the arterial tree [12]. This is an acceptable approximation, even if diastolic pressure is characterised by a small fall in peripheral sites, few mmHg [47].

In [12] the aortic area waveforms were calibrated using three different models. They all include the following parameters, in order to express the relationship between arterial pressure $p(t)$ and cross sectional area of the artery $A(t)$:

- p_d : diastolic pressure, assumed constant through the arterial tree;
- A_d, A_s : arterial diastolic and systolic areas, respectively;
- α : a scaling factor; its expression differs from one model to another. The α parameter can be considered as an indicator of the arterial stiffness of the considered vessel. As reported in [8], the arterial stiffness can be expressed in different ways, which include the two expressions of α reported below.

Linear model

$$p(t) = p_d + \alpha \cdot A(t)$$
$$\alpha = \frac{(BSP - p_d)}{(A_s - A_d)}$$

where BSP is the systolic pressure measured at brachial level.

Exponential model

$$p(t) = p_d e^{\alpha \left(\frac{A(t)}{A_d} - 1 \right)}$$
$$\alpha = \frac{A_d \ln\left(\frac{P_s}{p_d}\right)}{A_s - A_d}$$

In [12] calibration of both the models has been performed iteratively reducing the scaling factor α in order to minimize the difference between the measured mean brachial pressure and the synthesized averaged pressure curve.

Arctangent model

$$p(t) = P_0 + P_1 \operatorname{tg} \left(\pi \left(\frac{A(t)}{A_m} - \frac{1}{2} \right) \right)$$

where A_m express the maximal distension of the investigated vessel, P_0 is the pressure corresponding to the maximum compliance of the vessel and P_1 is the pressure at half of the maximum compliance of the vessel.

In [12] MR slices of descending aorta have been calibrated by means of three methods showing good correlation with arterial tonometry; $r^2=0.90$, $r^2=0.87$, $r^2=0.85$ for arctangent, exponential and linear model respectively. Moreover the exponential model showed the best agreement in terms of estimation of the systolic pressure value (bias 0.6 mmHg).

Therefore, the exponential model has been considered for the calibration of LDV signal in the present study, producing a satisfying shape for the pressure pulse and a good agreement in terms of estimation of the systolic peak.

2.2 Application of the exponential model to LDV signal

The application of the exponential model to the signal obtained by means of Laser Doppler Vibrometry requires three basic assumptions [48]:

- the shape of the considered vessel, the common carotid artery, can be assumed as a symmetric cylinder;
- the deformation of the carotid can be considered as a symmetric radial displacement;
- the values of diastolic pressure and mean arterial pressure are fairly constant through the arterial tree, while systolic pressure changes its value depending on the distance from the heart

The assumption of cylindrical shape has been used to consider the cross section of the vessel $A(t)$ as follows:

$$A(t) = \pi \frac{d^2(t)}{4}$$

where $d(t)$ is the vessel diameter, which was considered as the sum of two terms, as reported below:

$$d(t) = d_0 + \Delta d$$

where d_0 is the vessel diameter at rest; its value was taken from the literature [49] [50], while Δd is the diameter variation measured by LDV.

2.3 Carotid location

One of the critical issues of the present study is the correct localization of the common carotid artery over the neck of tests participants.

In fact, an incorrect localization of the measurement point causes an inaccurate assessment of the vessel vibration, and, consequently, the application of the calibration model to a signal which does not quantify accurately the vessel displacement. In a preliminary study, as reported in [40], a thermal camera (VarioCAM HD, InfraTec) was included in the test bench, in order to improve the identification of the optimal acquisition point. The inclusion of thermal imaging was based on the differential temperature distribution in the area of the carotid, supporting localization efforts.

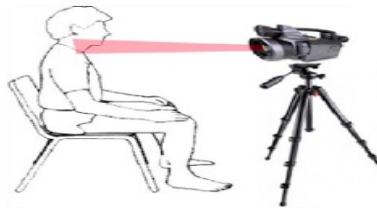


Figure 11: measurement point localization by means of thermal camera

Thermal images were acquired asking the participants to sit quietly with the left side of the neck uncovered. An example of a thermal image, with a zoom on the carotid area, where it is possible to visualize the carotid bifurcation is reported below. The optimal LDV measurement point was located after a 20 s imaging period.

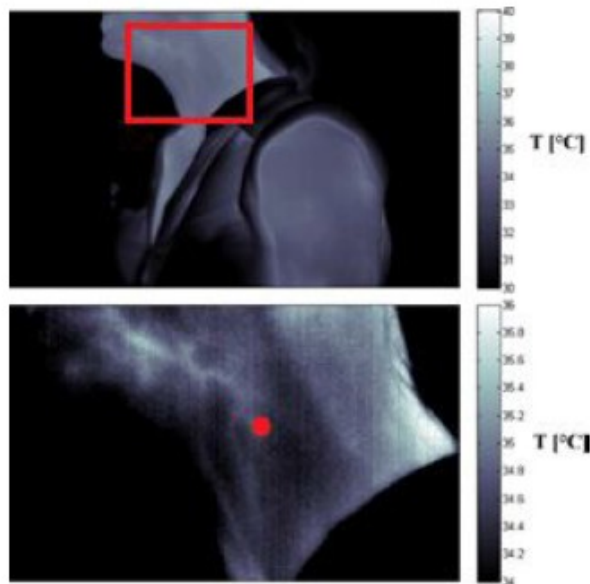


Figure 12: Thermal image (above) with a zoom on the carotid area (below, with the bifurcation marked with a red dot)

However, the differential temperature distribution did not always support correct detection of the measurement point, in fact when the blood pulse passes through the vessel, the heat spreads to the surrounding tissues, and it is not possible to identify the precise location of the carotid lumen.

For this reason, a different approach has been proposed, as reported in [51]. Data measured by means of a scanning LDV system, Polytec PSV-300, were collected from 22 adult participants. Signals were obtained from a patch subtending 4.8 cm horizontally by 4.0 cm

vertically, which bounded 35 individual measurement points arranged in a 7 x 5 grid (horizontal spacing = 0.8 cm, vertical spacing = 1.0 cm).



Figure 13: representation of the measurement grid

Data were measured from each point for a 9 s period, starting at the upper left corner. After that, the Laser beam was advanced to consecutive points in a serpentine pattern. The LDV velocity pulses for all available beats within individual 9 s measurement periods were averaged, using the R wave in the ECG as reference for the synchronization. The basic idea was that the vibration amplitude related to the blood pulse over the carotid artery had to be greater with respect to the surrounding points. Therefore, the peak to peak amplitude was computed for each of the 35 averaged LDV waveforms. The 5x7 matrix with the peak to peak value was resampled in order to achieve the carotid maps.

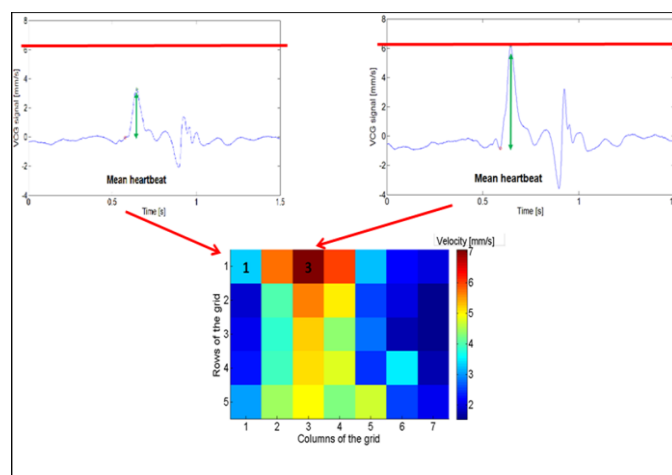


Figure 14: averaged LDV signals of point 1 and point 3 (subject 1), above, and 5x7 matrix with the peak to peak values, below.

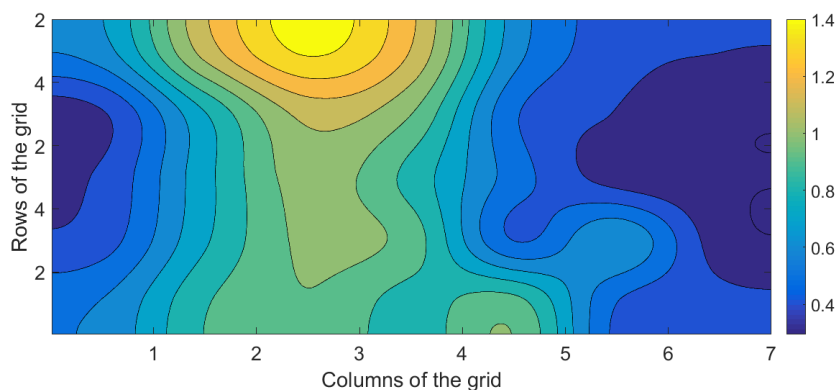


Figure 15: resampled carotid map (subject 1)

Most individuals showed a vertically oriented trace of maximum amplitude that is anatomically consistent with the location of the carotid.

There are, however, substantial individual differences in the path of the carotid. This suggests corresponding anatomical differences. The majority of participants showed maximum amplitude at the top locations. This is localized in a small zone in which the carotid is not overlaid with the sternocleidomastoid muscle, at the site of the bifurcation of the common carotid into the internal and external components. The level of variability is generally consistent with other reports based on imaging and anatomical methods [52] [53].

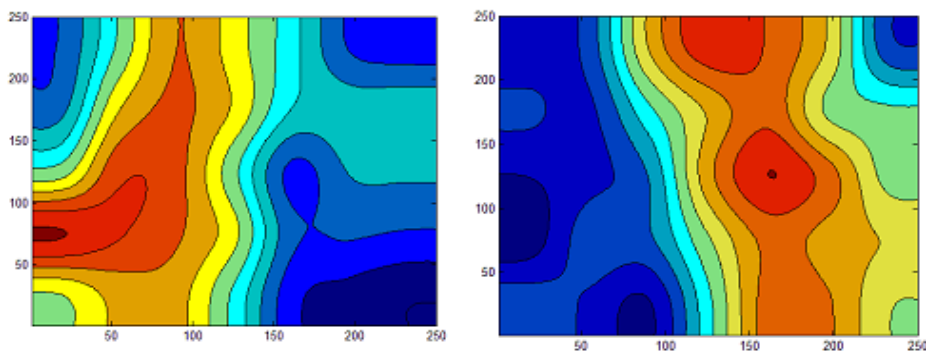


Figure 16: Example of two different carotid path, participant 6 (left), participant 16 (right)

Vertical transmission of the pulse, revealed in most of the subjects, has been confirmed by the study of timing in the velocity peak measured by LDV.

Time delays in the velocity peak from bottom to top are consistent with the transmission of the pressure pulse over the carotid.

Figure 17 shows an example of LDV traces , participant 16, in a column of the measurement grid. It is possible to see the time delay in velocity peak from bottom to top.

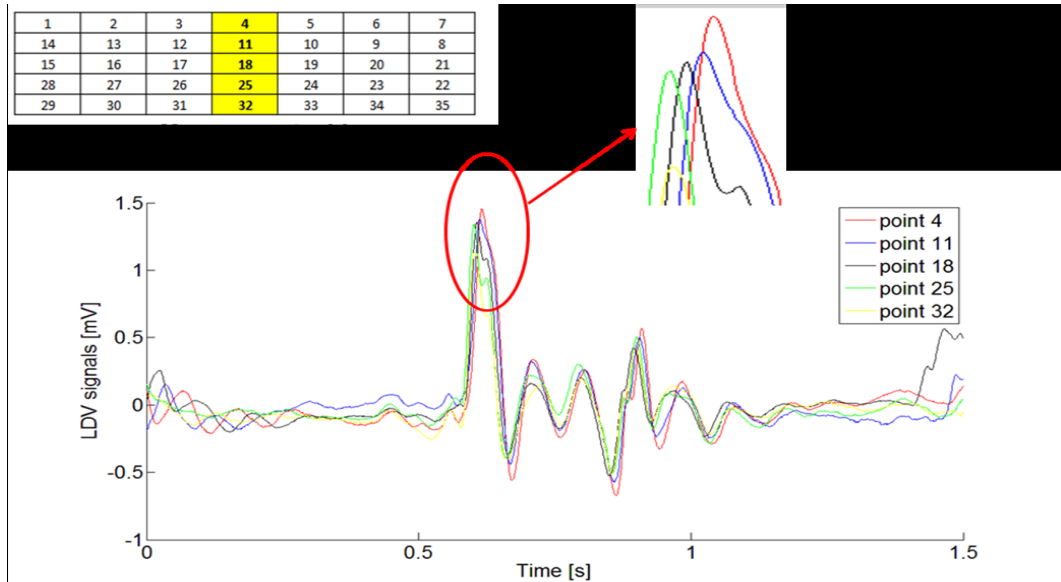


Figure 17: the measurement grid,top, LDV traces of the fourth column and zoom on the area related to the velocity peaks, bottom.

2.4 Measurement setup

A first study,as reported in [48] [54] [55], has been conducted on 6 healthy participants. aged 26 ± 3), whose characteristics are reported in the table below.

	Height [m]	Weight [kg]	BMI [kg/m ²]
Subject 1	1.81	82	25.3
Subject 2	1.78	65	20.5
Subject 3	1.66	53	19.2
Subject 4	1.81	93	28.1
Subject 5	1.67	56	20.1
Subject 6	1.65	48	17.6

Table I: physical characteristics of the tested participants

The experimental setup included the following instruments:

Laser Doppler Vibrometer (PDV 100, Polytec, sensitivity of 0.2V/(mm/s));

Electrocardiograph (ECG) (ADInstruments MLA2540 5 Lead Shielded Bio Amp Cable).

LDV and electrocardiographic (ECG) signals were acquired simultaneously using a proper A/D board (12-bit); a conventional oscillometric method was used to assess simultaneous blood pressure at the brachial level (accuracy: ± 3 mmHg).

The participants were asked to lie supine and stay relaxed.

The vibrometer was placed on a tripod at a distance of 50 cm from the subject and it was pointed perpendicularly to the skin of the participant, over the left common carotid artery.

A sketch of the measurement setup is represented in the figure below.

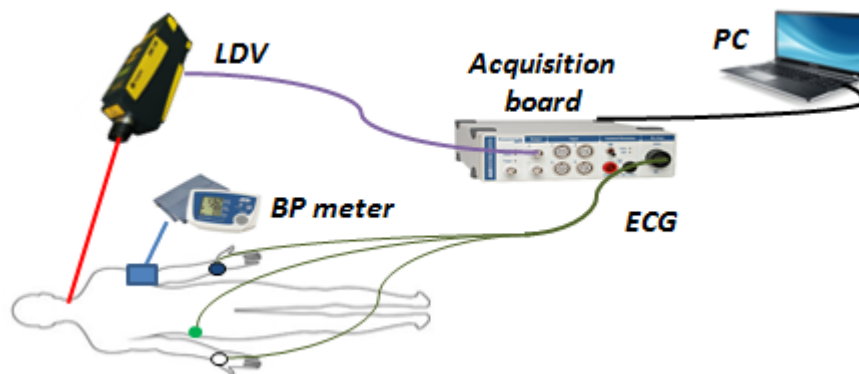


Figure 18: Setup scheme: ECG electrodes placed on the skin according to the standard positioned scheme of the I-lead ECG; LDV spot perpendicularly directed on the skin surface

Three repeated 1-minute measurements were made on each participant. The experimental setup included also a blood pressure meter using a proper cuff positioned on the subject's left arm. It was used to measure Diastolic Blood Pressure, DBP, and Systolic Blood Pressure, SBP, at the brachial level. The achieved values were used to estimate Mean Arterial Pressure (MAP), by means of the following empiric formula:

$$MAP = \frac{1}{3}(2DBP - SBP)$$

Before each acquisition, three consecutive measurements of brachial blood pressure were performed and the average value of DBP and MAP were considered in the application of the calibration model.

A second study has been conducted on data collected from 22 healthy participants at Washington University in Saint Louis.

LDV signals were acquired by means of the scanning Laser system, Polytec PSV-300, described in section 2.3. Moreover an electrocardiograph and a radial tonometer were included in the measurement setup.

2.5 Signal processing

2.5.2 Preprocessing of LDV signal

The data processing procedure is reported in figure 19.

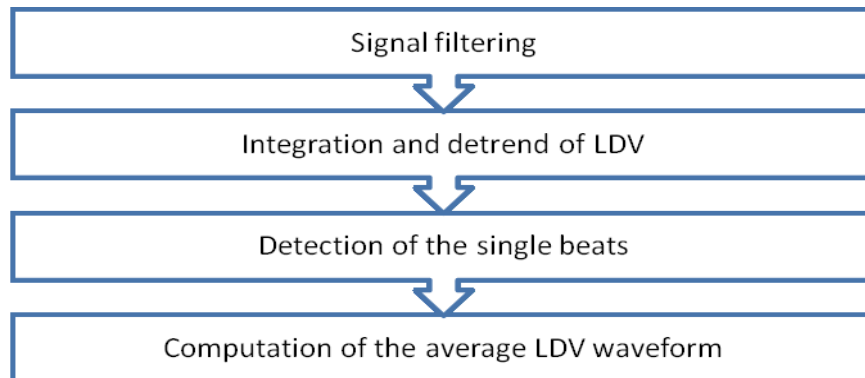


Figure 19: flow chart of the signal preprocessing procedure

Signal filtering: LDV and ECG signals were filtered by means of a 3rd order Butterworth bandpass filter with the following cutoff frequencies: 0.1 Hz (high pass filter) and 40 Hz (low pass filter) for ECG; 0.1 Hz (high pass filter) and 30 Hz (low pass filter) for LDV.

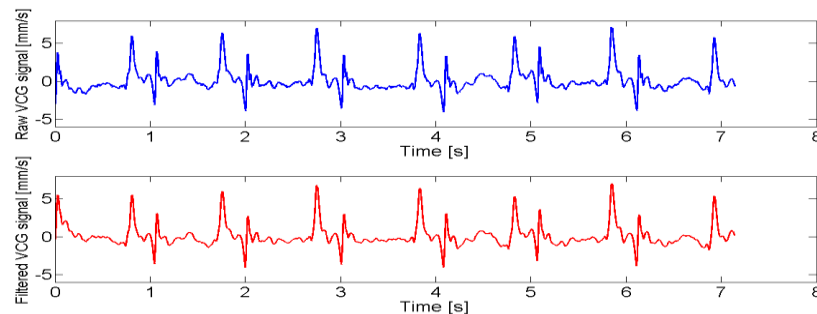


Figure 20: raw LDV signal, above, filtered signal, below.

Integration and detrending of LDV: The LDV signal was integrated in order to obtain a displacement signal from the measured velocity data. An operation of detrending was performed on the displacement signal to achieve a mean value equal to zero.

The detrending was applied to the signal in order to remove the linear trend caused by the operation of integration applied to LDV signal (performed to obtain a displacement trace). The detrending was performed in Matlab environment, computing the least-squares fit of a straight line to the data and subtracting the resulting function from the data.'

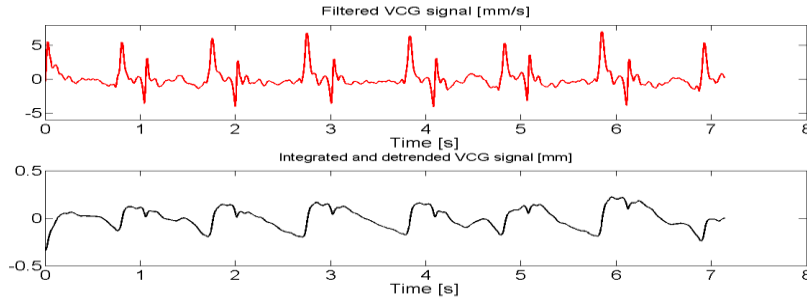


Figure 21: Filtered LDV signal, above, integrated and detrended signal, below.

Detection of the single beats: The ECG signal was used to correctly detect every single heartbeat in the LDV signal.

An algorithm based on the geometric shape of the signal [40] was applied to the LDV displacement signal in order to detect the onset and offset of the LDV pulses associated with single heart beats. This algorithm performs the computation two straight lines on a small subset of points, by means of a moving window. Then, the angle included between the two straight lines was computed. Detecting local maxima of the angle time it was possible to locate the onset and the offset of the single displacement waveforms.

Then, each LDV pulse was re-sampled according to the mean heart period detected from ECG signal.

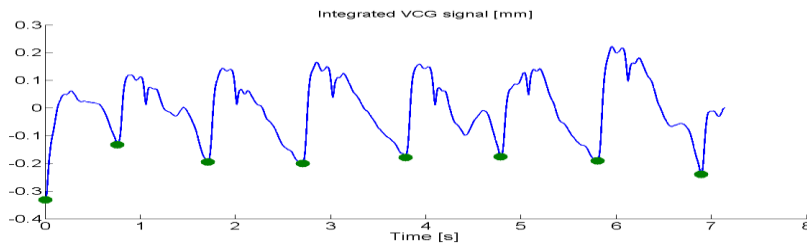


Figure 22: individuation of onset and offset in single displacement waveforms, green dots

Computation of the average LDV waveform: the re-sampling of the single heartbeat allowed to calculate the average displacement waveform for each acquired signal.

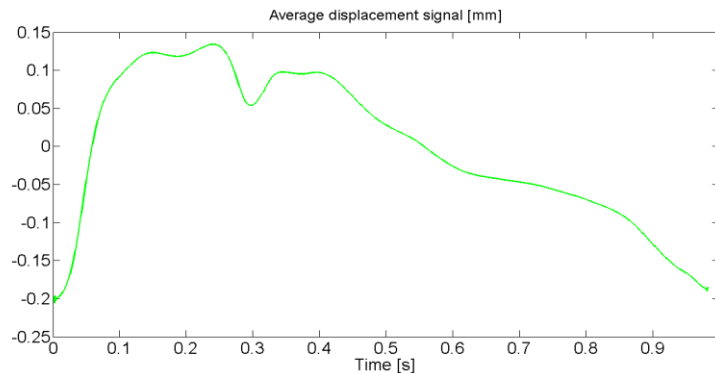


Figure 23: an example of average LDV displacement signal

2.5.2 Model implementation

The exponential model described in section 3.1 was applied to the average displacement signal; in this way, the calibrated pressure waveform was obtained. The algorithm used for the model implementation is reported in the following flowchart.

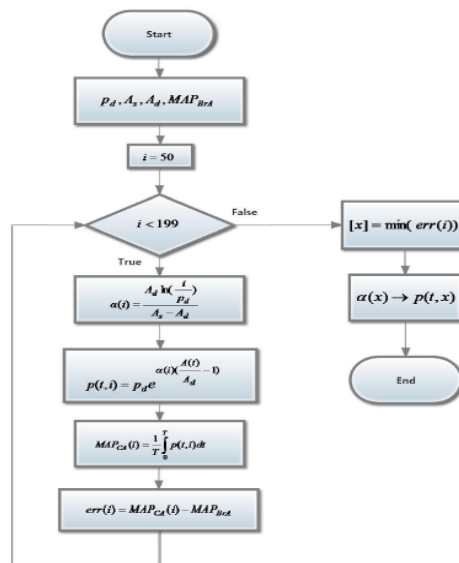


Figure 24: flowchart of the algorithm for the implementation of the exponential model

A range equal to 80-130 mmHg was utilized for carotid systolic pressure.

An iterative procedure composed by 50 cycles was performed: the stiffness value α depends on the carotid systolic pressure, as reported in section 3.1, therefore, a different α was computed at each cycle, and, starting from it, a correspondent pressure waveform was obtained, applying the exponential model reported in 2.1. The calibration procedure was based on the minimization of the following cost function:

$$ERR = MAP_{car} - MAP_{meas}$$

where MAP_{car} is the Carotid Mean Arterial Pressure, computed from the calibrated LDV data, as reported in the formula below, and MAP_{meas} is the Mean Arterial Pressure, measured at brachial or radial level. This starts from the assumption that MAP is fairly constant through the arterial tree.

$$MAP_{car} = \frac{1}{T} \int_0^T p(t) dt$$

where T is the mean cardiac period.

Therefore, the LDV pressure waveform was chosen, among the 50 calibrated waveforms, as the one which minimized the cost function ERR.

An example of LDV pressure wave is reported in the following figure.

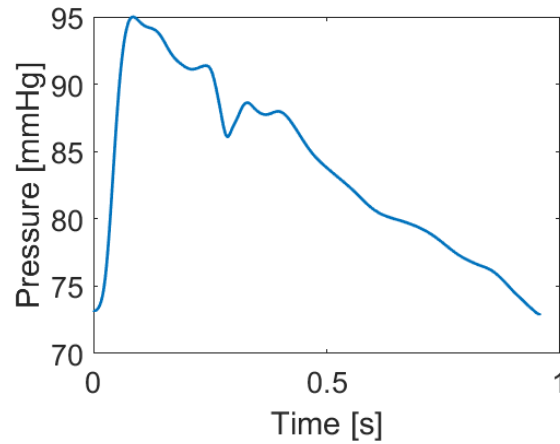


Figure 25: example of LDV pressure waveform

2.5.3 Uncertainty of the proposed method

In order to estimate the uncertainty of the proposed method, it should be considered that the present procedure is composed of three main steps: measurement of the velocity of carotid vibration by means of LDV, integration of the LDV signal and application of the exponential model. It is important to emphasize that each of these steps produce a contribution to the total uncertainty μ .

Velocity measurement: The adopted LDV device, Polytech PDV 100, has an accuracy of $\pm 0.2\%$ in the frequency range 0.05 Hz-22 kHz [56].

Considering the ideal condition in which the device is pointed perpendicularly to the skin of the participant, the measured velocity value has an accuracy of around ± 0.02 mm/s.

Integration: the integration of the digital velocity signal has been performed by means of the trapezoidal rule; it is one of a family of formulas for numerical integration called Newton–Cotes formulas [57]. The trapezoidal rule approximate the region under the graph of the function $f(x)$ as a trapezoid and calculating its area:

$$\int_a^b f(x)dx \approx (b-a) \left[\frac{f(a)+f(b)}{2} \right]$$

where a and b are the integration's extremes. For a domain divided into N equally spaced intervals, the approximation becomes:

$$\int_a^b f(x)dx \approx \frac{(b-a)}{2N} \sum_{i=1}^N (f(x_{i+1}) + f(x_i))$$

The trapezoidal approximation improves when the number of considered intervals increases. The error of the composite trapezoidal rule is the difference between the value of the integral and the numerical result [58]. It can be demonstrated that there is a value ξ in the $[a,b]$ interval for which the error is given by:

$$err = -\frac{b-a}{12N^2} h^2 f''(\xi)$$

where $h = \frac{b-a}{N}$.

Therefore, the trapezoidal approach underestimates the integral when the function is concave down and it overestimates the integral when the fuction is concave up.

Implementation of the model: Beyond the error intrinsic to the process of integration, errors associated with the implementation of the exponential model must also be considered. $p(t)$ is related to the displacement $d(t)$ by the relationship:

$$p(t) = p_d e^{\alpha \left(\frac{\pi d^2(t)}{4A_d} - 1 \right)}$$

assuming cylindrical shape of the vessel, as reported in sections 3.1 and 3.2. This is a case of uncertainty propagation: the uncertainty Δx of a certain variable x is known, there is a functional relationship $y=f(x)$ between x and y , and it is required to evaluate the uncertainty Δy of the y variable [59]. The uncertainty Δy , for a given value x_0 of x variable, is:

$$\Delta y = \left. \frac{df}{dx} \right|_{x=x_0} \Delta x$$

Therefore, in the present case, the uncertainty Δp is given by:

$$\Delta p = p_d \left(e^{\alpha \left(\frac{\pi d^2}{4A_d} - 1 \right)} \frac{\pi \alpha}{2A_d} d(t) d'(t) \right) \Bigg|_{d=d_0} \Delta d$$

where Δd is the uncertainty in the measurement of the displacement of the vessel, d_0 is a given value of displacement, $d'(t)$ is the derivative of displacement signal.

Chapter 3

Results

3.1 Pressure waveforms comparison

The signal processing provided the displacement waveforms by means of the integration of the original LDV signal (i.e. a velocity signal). Subsequently, the averaged waveform was obtained by resampling the LDV pulse for each heartbeat to the mean cardiac period computed from the ECG signal. By applying the calibration model, the pressure waveform was obtained; its maximum was considered as the Systolic Carotid Pressure value. Such a pressure value is expected to be lower than the peripheral one, because of the contribution of the reflected waves. In [60] a study of systolic pressure amplification from carotid to peripheral artery was conducted. It has revealed an average systolic pressure reduction of 79 % in a male population of 72473 subjects, and an average systolic pressure reduction of 85 % in a female population of 52714 subjects. These results were adopted here to compare the LDV data, measured at the carotid level with the peripheral pressure (radial and brachial pressure for the first and the second measurement setup respectively, as reported in section 2.5).

Results of the first study

A comparison between the systolic pressure measured by means of the oscillometric cuff at brachial level and the one obtained from the calibration of the LDV signal has been performed as reported below.

	Gender	Brachial Systolic Pressure [mmHg]	Reference Carotid Systolic Pressure [mmHg]	LDV Carotid Systolic Pressure [mmHg]	Percentage Deviation [%]
Subject 1	Male	111	88	84	-4
Subject 2	Female	126	100	104	4
Subject 3	Female	117	99	100	1
Subject 4	Female	107	91	92	1
Subject 5	Male	98	77	85	10
Subject 6	Female	99	84	80	-5
Average		110	90	91	4

Table II: Gender of the participants, Measured brachial systolic pressure, Reference carotid systolic pressure calculated as $0.79 \times$ Brachial Systolic Pressure for male participants and as $0.85 \times$ Brachial Systolic Pressure for female participants, LDV Carotid Systolic pressure, Percentage deviation between LDV systolic pressure and reference systolic value

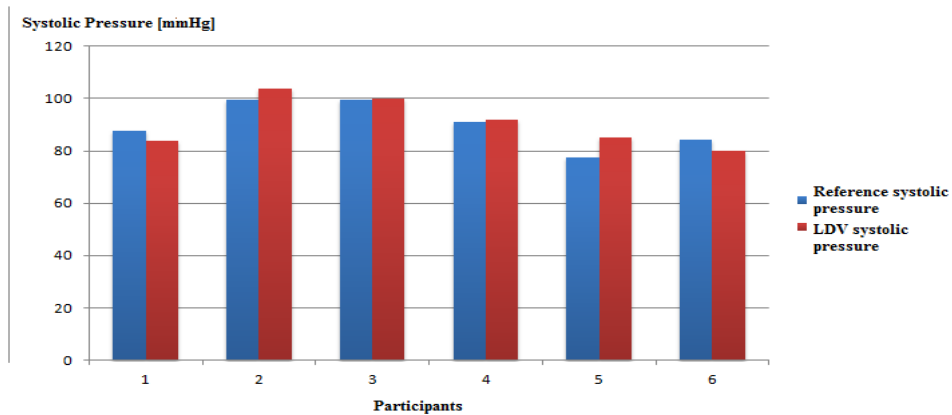


Figure 26: comparison between reference systolic pressure and LDV systolic pressure

Results show an average deviation between LDV systolic pressure and reference systolic pressure of 4 %, with a maximum deviation of 10 % in subject 5.

Results of the second study

In this study, the pressure waveforms calibrated from the LDV signal are compared with the signals acquired from the radial artery by means of an arterial tonometer in 22 healthy subjects.

An example of comparison between the average pressure waveform from LDV and arterial tonometer is illustrated in the figure below.

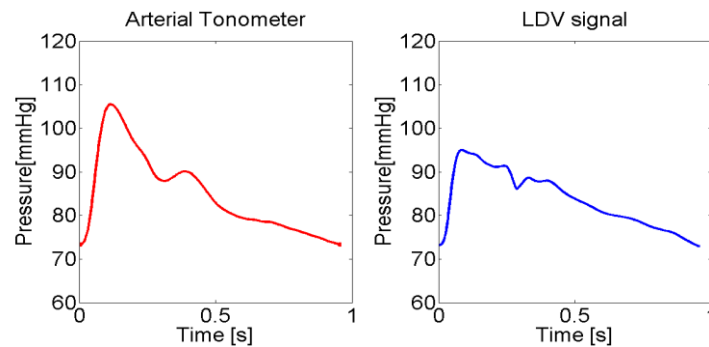


Figure 27: average tonometric waveform (left), average LDV pressure waveform (right)

The results are reported considering a correction of the systolic tonometric peak, based on the results of [61], of 12 mmHg and 8 mmHg for male and female participants respectively, in order to compensate the amplification of maximum blood pressure from carotid to radial artery. This value was considered as the reference systolic pressure and it is compared here with the systolic peak of the LDV calibrated signal.

	Gender	Carotid systolic pressure [mmHg]	Radial systolic pressure [mmHg]	Reference carotid pressure [mmHg]	Percentage deviation [%]
Subject 1	Male	104	129	117	-11
Subject 2	Female	99	121	113	-12
Subject 3	Male	113	120	108	5
Subject 4	Female	95	105	97	-2
Subject 5	Male	92	106	94	-2
Subject 6	Male	106	119	107	-1
Subject 7	Female	97	116	108	-10
Subject 8	Male	89	125	113	-21
Subject 9	Female	86	100	92	-7
Subject 10	Female	89	103	95	-6
Subject 11	Male	99	113	101	-2
Subject 12	Female	95	116	108	-12
Subject 13	Female	90	111	99	-9
Subject 14	Female	82	100	92	-11
Subject 15	Male	81	95	83	-2
Subject 16	Female	87	111	103	-16
Subject 17	Male	110	129	117	-6
Subject 18	Female	117	134	126	-7
Subject 19	Male	80	97	85	-6
Subject 20	Female	78	97	89	-12
Subject 21	Female	99	123	115	-14
Subject 22	Male	116	136	124	-6
Average		96	114	104	-8

Table III: Gender of the participants, Measured radial systolic pressure, LDV carotid systolic pressure, Reference carotid systolic pressure computed as Measured radial systolic pressure +12 mmHg and Measured radial systolic pressure +8 mmHg for male and female participants respectively, percentage deviation between LDV and reference systolic pressure

An average percentage deviation of -8% was obtained between LDV systolic pressure and reference systolic pressure, with a maximum deviation of -21% (participant 8).

Computation of uncertainty

The proposed method is affected by several causes of uncertainty.

In particular this section, considering ideal measurement conditions, focus on the uncertainty produced by the integration of the signal and the application of the exponential model for calibration of LDV traces, starting from the measurement accuracy of the considered LDV device, 0.2 % in the frequency range 0.5 Hz - 200 kHz. An estimation of the uncertainty has been performed by means of the methods described in section 2.5.1. Table IVa and IV b show the uncertainties for the 6 participants of the first study and the 22 participants of the second study, in the measure of the carotid systolic pressure. Uncertainty is reported in percentage of the measured systolic value.

	Measured carotid systolic peak [mmHg]	μ [%]
Participant 1	84	14,5
Participant 2	104	18,1
Participant 3	100	10,3
Participant 4	92	13,2
Participant 5	85	9,5
Participant 6	80	16,4
Average		14

	Measured carotid systolic peak [mmHg]	μ [%]
Participant 1	104	14,5
Participant 2	99	5,2
Participant 3	113	13,1
Participant 4	95	27,7
Participant 5	92	18,2
Participant 6	106	29,5
Participant 7	97	14,6
Participant 8	89	13,2
Participant 9	86	22,4
Participant 10	89	15,4
Participant 11	99	28,5
Participant 12	95	6,5
Participant 13	90	7,6
Participant 14	82	18,3
Participant 15	81	18,4
Participant 16	87	4,2
Participant 17	110	20,4
Participant 18	117	19,9
Participant 19	80	8,5
Participant 20	78	15,7
Participant 21	99	17,2
Participant 22	116	26,9
Average		17

Table IV: uncertainty in the measurement of systolic peak, study 1, left, study 2, right

3.2 Stiffness evaluation

The parameter α of the adopted mathematical model express the arterial stiffness [12] [62]. Therefore its value has been computed, evaluating if it is able to quantify the elastic properties of carotid artery. Data from the 22 tested participants have been classified in three age groups (20-30 years, 30-40 years, 40-55 years). Table IV shows the average α value for the three considered age groups, and the relative standard deviation:

Age [years]	Number of participants	α []
20-30	8	1,5 \pm 0,5
30-40	11	2,0 \pm 0,4
40-55	4	2,5 \pm 0,5

Table IV: the average α value computed for the three age groups

It is possible to see that α , which depends on the systolic pressure indirectly measured by means of LDV, has a linear increasing trend as function of age, figure 27.

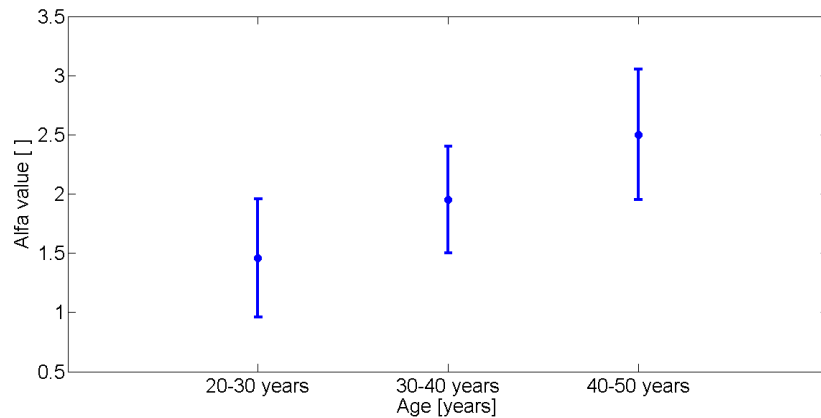


Figure 28: alfa average value as a function of age

3.3 Left Ventricular Ejection Time computation

Left Ventricular Ejection Time (LVET), e.g. the time of ejection of blood from the left ventricle beginning with aortic valve opening and ending with aortic valve closure, can be measured clinically from onset to incisural notch of the carotid or other pulse [58]. In the present section, a comparison between the pressure waveform obtained from LDV signal and the tonometric signal from radial artery is reported in terms of computation of the LVET from the 22 tested participants.

The incisural notch was detected by means of the algorithm reported in [40], based on the geometrical shape of the signal, explained in section 2.5. The incisural notch point was

detected as a local maximum of the angle between the onset and the offset of the pressure waveform.

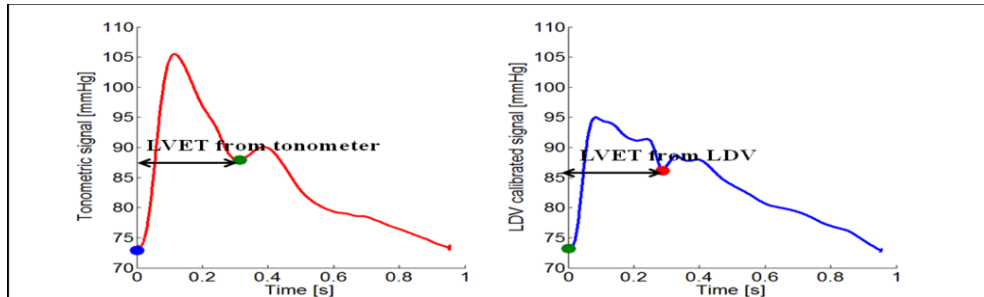


Figure 29: LVET computation from tonometer and LDV, left and right respectively

Table V shows the average LVET, with relative standard deviation, measured by means of LDV and tonometer, from carotid and radial artery respectively.

	Carotid artery(LDV)	Radial artery(Tonometer)
LVET [ms]	312±32	325±31

Table V: average LVET measured by means of LDV and Radial Tonometer

A scatter plot and a Bland Altman test [55] have been performed in order to compare the LVET time intervals measured from the 22 participants by means of the two considered sensors.

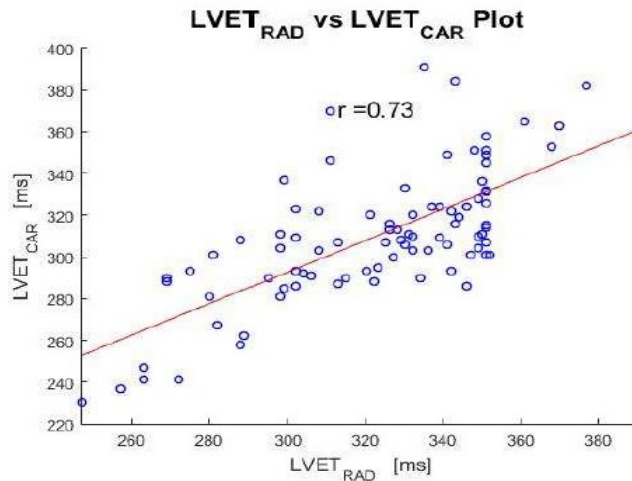


Figure 30: scatter plot of LVET measured at carotid level by means of LDV versus LVET measured at radial level by means of arterial tonometer

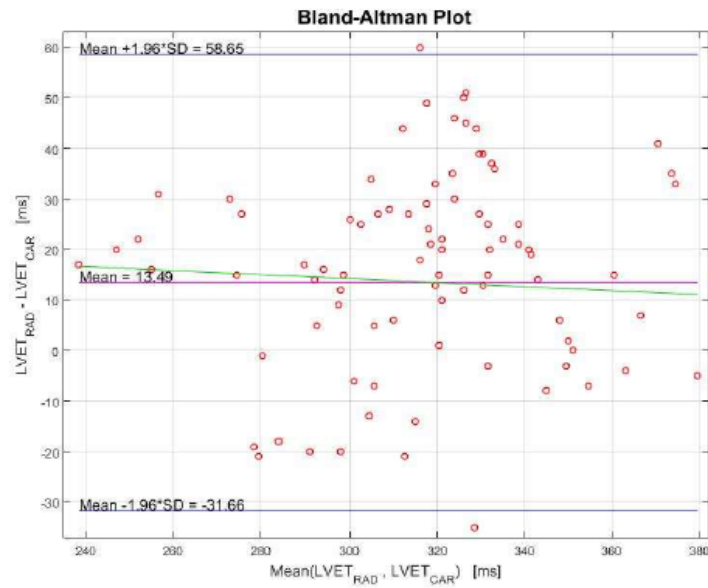


Figure 31: Bland Altman plot as a comparison method for the measurement of LVET between LDV and arterial tonometer

Scatter plot reveals a good degree of correlation, $r=0,73$; while Bland Altman shows a bias of 13 ms between the two methods in the measure of Left Ventricular Ejection Time.

Considering the definition of agreement provided by Bland and Altman, the limits of agreement of the two measurement methods are $13 \text{ ms} \pm 45 \text{ ms}$, considering a coverage factor $k=1.96$. This may be unacceptable by a clinical point of view, but the experiment should extend to a larger number of participants in order to be statistically significant.'

Concluding remarks

Blood pressure monitoring is fundamental for the prevention of several physiological diseases. In fact, hypertension is considered as the main cause of death worldwide [7].

The present work can be introduced in the field of blood pressure measurement techniques. All the commonly used approaches for the assessment of arterial pressure are characterized by the contact with the patient, or, in some cases, i.e. in the use of arterial catheters, are fully invasive.

This PhD thesis had a challenging task: the development of a non-contact technique for the measurement of a fundamental physiological parameter as blood pressure.

For that purpose, an approach based on the use of a Laser Doppler Vibrometer was developed.

LDV can detect the mechanical vibration due to the blood pulse passage through a superficial vessel, such as carotid artery[14] [16] [35] .

The measured velocity signal was integrated in order to obtain the displacement of the investigated vessel during the cardiac cycle.

Starting from the assumption of cylindrical shape of the vessel, the displacement signal was calibrated by means of a mathematical exponential model, which relates the variation of the cross section of the vessel to the internal blood pressure.

Diastolic (p_d) and mean arterial pressure (MAP), measured by means of a reference method at brachial or radial level, were used to calibrate the LDV signal, starting from the assumption that p_d and MAP remain fairly constant throughout the arterial tree while systolic pressure increases from central to peripheral sites.

Systolic peaks of the calibrated signals were compared to the systolic pressure measured in a peripheral site. The reference systolic pressure was computed from the one measured at brachial or radial level, applying a proper correction factor taken from the literature, in order to adapt the peripheral value to the carotid site [60] [61].

Moreover, the LDV calibrated waveforms were characterized in terms of computation of the carotid stiffness and of the Left Ventricular Ejection time.

This allowed two other fundamental cardiovascular parameters to be obtained by means of the non-contact measurement technique presented in this work.

A first study, conducted on 6 healthy participants, aged 26 ± 3 years, showed an average percentage deviation of 4 % between the systolic peak of calibrated LDV signal and the reference systolic pressure, computed from data acquired by means of a sphygmomanometric cuff.

This study verified the feasibility of the discussed LDV-based technique in the assessment of pressure waveform without contact.

In a second study, LDV data from 22 healthy participants, aged 19 to 51 years, collected at Washington University in Saint Louis, were calibrated by means of the proposed method and were compared with the signals acquired by means of radial applanation tonometry.

The average percentage deviation between systolic pressure of LDV signal and systolic reference value, computed from tonometer data corrected with a proper factor in order to

compensate for the physiological increase of systolic pressure from central to peripheral site, was around 8 %.

The results, achieved by means of the discussed measurement technique, were comparable with the ones obtained by two techniques, sphygmomanometer cuff and arterial tonometry, as are commonly used in clinical and home environments, in terms of measure of the systolic pressure, considered as the main indicator of hypertension [29].

The computation of arterial stiffness from the LDV pressure waveform was performed considering a model parameter, α , and verifying if it was able to characterize the elastic properties of carotid artery in dependence on the age of the tested participants.

The test verified that α , which depends on the systolic pressure indirectly measured by means of LDV, has a linear increasing trend as function of age.

This is consistent with the consequences of ageing on the arterial stiffness and, consequently, on the possible occurrence of hypertension.

Left ventricular ejection times computed from LDV calibrated data and tonometer signals showed a good correlation, $r=0.73$, and a bias between the two methods of around 13 ms was achieved.

This finding provides that the LDV can be able to measure the time of contraction of the left ventricle with a good agreement in relation to the reference method.

The present work demonstrates that LDV can, on a non contact basis, estimate fundamental physiological parameters such as blood pressure, Left Ventricular Ejection Time and arterial stiffness .

In particular, it can provide blood pressure waveform and systolic pressure, the main indicator of hypertension, fully non-invasively.

This is a great advantage in terms of comfort for the patient but also for the quality of the measure: in fact, the standard techniques for blood pressure measurements are affected by insertion uncertainty, due to the contact within the patient, while LDV does not suffer of this issue.

Anyway, it must be considered the need of calibration of the discussed technique by means of a reference method, for the assessment of diastolic and mean arterial pressure.

Moreover, it is important to underline that the proposed measurement technique is characterized by several causes of uncertainty, which limit its accuracy.

The main causes of uncertainty of LDV approach in the blood pressure measurement are reported below:

- correct pointing of the Laser Spot,
- movement artifacts,
- presence of reflection phenomena,
- integration and application of the exponential model,

Correct pointing of the Laser Spot: LDV measures the velocity component in the direction of the Laser spot. Therefore, the Laser spot has to be perpendicular to the measurement surface.

As the neck does not have a regular shape, in some cases, it is difficult to correctly direct the laser spot and to achieve the condition of perfect perpendicularity between LDV and measurement surface.

Moreover, a critical issue of this technique is the localization of the measurement point. In previous works, the carotid artery was localized by means of palpation of the neck surface [36] [40]. As the aim of the present study was particularly challenging, two more systematic approaches were applied: the use of a thermal camera and of a Laser scanner over the measurement area, as reported in section 2.3. Even if the Laser scanner approach has conducted to good results, it is not always possible to correctly detect the optimal measurement point.

Movement artifacts: LDV is a non-contact technique with very high sensitivity. For this reason, it is potentially affected by a variety of movements not related to the investigated phenomenon.

The participants in the study were asked to stay relaxed and as still as possible during the acquisition. Nevertheless, movements related to the breathing activity or swallowing invalidate the execution of the test.

Presence of reflection phenomena: the use of LDV at carotid level can involve the measure of reflection phenomena, which may be not related to the investigated vessel.

The presence of other vessels near the carotid can produce contribution to the measured vibrational signal.

A deeper investigation of the physiological dynamics is required in order to distinguish carotid features from the other mechanical events detected by LDV and to have a more accurate pressure waveform.

Integration and application of the exponential model : the signal processing of LDV traces produces significant factors that increase the total amount of measurement uncertainty.

The uncertainty due to the integration of the velocity signal and to the application of the exponential model, starting from the measurement accuracy of the adopted LDV device, has been discussed in sections 2.5.3 and 3.1. An average uncertainty of around 15,5 % in the measure of systolic pressure has been computed.

However, it must be noticed that the most common techniques used to assess blood pressure, such as sphygmomanometers, are affected by comparable amounts of uncertainty, as reported in section 2.1.5.

In conclusion, the present work can be considered as a further step in the development of a commercially viable LDV system which produce a signal encoding multiple parameters, including Heart Rate, Heart Rate Variability, cardiac-related time intervals and also features extractable from the blood pressure waveform.

For that purpose, the various issues pertaining to the LDV technique reviewed above should be resolved, including a fuller understanding of the physiological meaning of the measured vibrational signals, and effort to reduce the effects of the several causes of uncertainty.

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