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Non-invasive cardiovascular disease assessment with miniaturized multi-beam laser Doppler vibrometry

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Abstract: A miniaturized 2×6-beam laser Doppler vibrometry sensor for non-invasive detection of cardiovascular disease is demonstrated. The pulse wave velocity is retrieved from preliminary experiments both on phantoms and on human subjects.
OCIS codes: (170.4580) Optical diagnostics for medicine; (170.3340) Laser Doppler velocimetry

1. Background

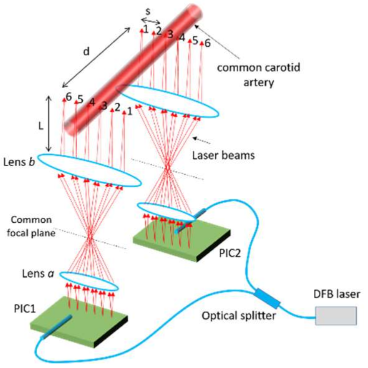
The assessment of an individual's risk of a major adverse cardiovascular event (e.g. myocardial infarction, stroke) is an important component of the clinical management of patients. There is compelling evidence that, besides the well-known classical risk factors (a subject's age, gender, cholesterol level, blood pressure and smoking status), additional prognostic information can be found in the stiffness of the large elastic and centrally located arteries. Increased stiffness of these arteries impedes their buffering capacity and leads to adverse effects including an increase in (the amplitude of) blood pressure, an augmented load on the heart and reduced perfusion of the heart [1].

The current clinical gold standard method to determine arterial stiffness is measurement of carotid-femoral pulse wave velocity [2]. Pulse wave velocity (PWV) is the speed with which the arterial pulse, generated by the heart, travels inside the arterial network. Carotid-femoral PWV is then calculated from the ratio of the estimated distance between the carotid and femoral measuring sites, and the time delay between the arrival of the foot of the pulse at the respective sites. The arrival of the wave can be measured with several techniques (ultrasound, applanation tonometry, magnetic resonance imaging) but also with Laser Doppler Vibrometry (LDV), detecting the vibrations that radiate from superficial arteries to skin level with each passage of a pulse wave. We and others previously have demonstrated the feasibility of detecting the pulse wave with LDV in the neck (common carotid artery) and groin (femoral artery) with conventional industrial LDV devices [3]. As the non-contact nature of the LDV measurement and its high spatial and temporal resolution of the technique may give LDV advantages over other measuring techniques, we have continued to explore the feasibility of developing a compact multi-purpose LDV scanning device with the potential to be used in a (pre)clinical setting. The envisioned device should not only allow measurement of carotid-femoral PWV with the same ease and level of accuracy as currently used devices, but would ideally also be capable of measuring the pulse transit time over a short distance to acquire the local PWV of the common carotid artery (CCA) itself, a large elastic artery that is expected to more specifically mirror changes in the elastic properties of large central vessels. Additional potential applications include the detection of narrowing of the CCA from a spectral analysis of the measured signal, and the detection of cardiac arrhythmia and dyssynchrony. All applications would require a device that allows for a simultaneous acquisition of skin vibrations from multiple spatially arranged measuring spots.

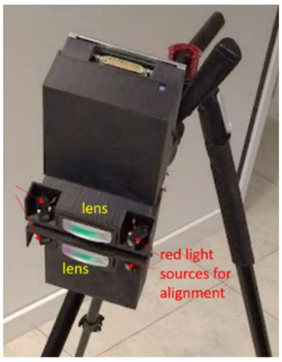
2. Device description

The local PWV measurement of a CCA involving two LDV beams has been realized with a silicon-based photonic integrated circuit (PIC) [4]. However, it turns out to be challenging to direct the two sensing beams to the right locations on the neck, since the CCAs are invisible. In this paper, we demonstrate an LDV sensor with two rows of six beams instead of two beams (see Fig. 1). Therefore, two rows of vibrations at 6 adjacent locations with a 5 mm spacing can be simultaneously measured. In each row, the beam closest to the common carotid artery can be derived based on the measured data. Since the separation of the two rows is known (25 mm or longer), the PWV can be calculated based on the two "best" beams in the two rows. With the help of the multi-beam LDV, the alignment difficulty in the PWV measurement is considerably reduced. Besides, the SOI platform also enables a potential low cost for large volume productions thanks to the CMOS compatible techniques [5].

The 2×6 LDV sensor consists of two identical PICs with 6 homodyne LDVs [6], and each PIC has a footprint of 2.5×5 mm^2 (see Fig. 1(a)). The PICs are fabricated based on an advanced silicon photonics platform [7] consisting of integrated germanium PDs with responsivities of ~1A/W. On each PIC, the six transmitting antennas are arranged in a line with a spacing of 300 µm. In order to direct the six beams to the right locations on the neck, a specific confocal lens system consisting of two lenses is placed in front of each PIC. The working distance of the confocal system is L = 75 mm. Each PIC is bonded to a PCB, on which an array of transimpedance amplifiers are placed to amplify the photo-currents from the PIC. Amplified signals are then sent to a decoder for the signal recovery. All twelve LDVs share the same laser source with 1550 nm wavelength and 800 kHz linewidth. Since 1550 nm light is invisible, four red guide beams are used to help users locate the beam positions easily (Fig. 1(b) and Fig. 2).



(a)



(b)

Fig. 1. (a) The 2×6 LDV device with confocal lens systems, where s = 5mm, d >=25mm, L = 75mm. (b) A picture of the 2x6 LDV system. The two front lenses and four red-light sources for alignment can be seen.

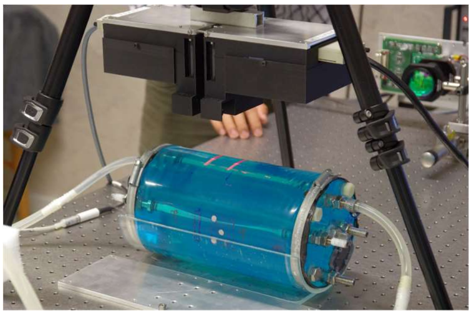


Fig. 2. Cylindrical neck phantom, showing vibrometer guide beams reflected by strips of adhesive retro-reflective tape. The latex tube at a depth of 20 mm below the skin surface is at the top. Note the second tube towards the front of the phantom, with depth below skin varying from 10 - 20 mm, not perfused in this experiment.

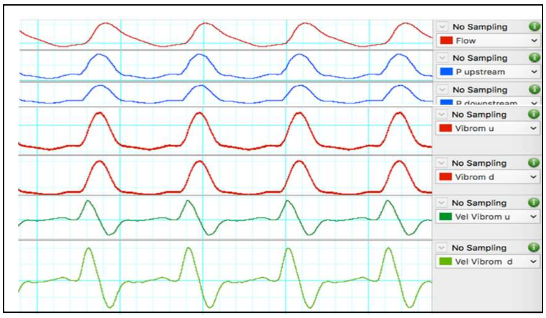


Fig. 3. Representative traces from the cylindrical phantom. Listed from the top: flow (red); upstream (U) and downstream (D) pressure (blue), U and D skin displacement derived from central beams (3U & 4D) in each set of 6 (red), U and D skin velocity (green). Similar signals were obtained from the other beam pairs (1U-6D, 2U-5D, etc.). The beam numbers are indicated in Fig. 1(a).

3. Measurement and results

The 12-beam device described above was used to measure the velocity of the pulse wave detected at the surface of a cylindrical neck phantom (Fig. 2) filled with a soft-tissue-mimicking viscous gel (Aquasonic, Parker Labs, Fairfield, NJ. Length 400 mm, width 150 mm, height 100 mm), with an embedded latex tube (i.d. 6.5 mm, wall thickness 0.25 mm) representing the CCA (depth below gel surface 20 mm). The outer surface of the gel was covered with a thermoplastic polyurethane sheet 0.1 mm thick, (Platilon, Epurex Films, Bomlitz, Germany), to mimic the skin. The perfusion system was water-filled, pressurized from a header tank and pulsatile flow, imposed with a pump (type 55305, Harvard Bioscience Inc.). Pressure in the tube was measured with 2 catheter-tip manometers (6f gauge, Gaeltec, Dunvegan, Scotland). Each set of 6 beams was aligned at right angles to the tube axis and the surface wave speed derived from corresponding beams in each set of 6 was compared to the pressure wave speed within the tube measured with the manometers. Data were sampled at 10 kHz (Powerlab 16/35, AD Instruments, Oxford, UK), typically for 10 seconds and displayed in real time with associated Labchart software. Pulse wave transit time between measurement sites was calculated from the first derivatives of the two pressure signals and corresponding beams from the upstream and downstream set of six beams. Fig. 4 compares the PWV derived from the phantom surface velocity with that obtained from the first derivative of the pressure signals within the embedded tube. For the central beam pairs (3-4, 4-3 & 5-4) the agreement is reasonable, although there is more variability in the vibrometer values.

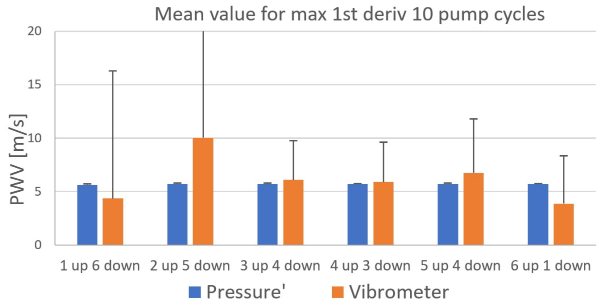


Fig. 4. The pulse wave velocity derived from the phantom surface velocity and that obtained from the first derivative of the pressure signals within the embedded tube. The beam numbers shown under the color bars are indicated in Fig. 1(a).

Using a commercial 2-beam laser Doppler vibrometer (SIOS Meβtechnik, Ilmenau, Germany), we have also carried out in-vivo measurements of skin displacement over the carotid artery in 10 subjects ranging in age from 23 to 70. We obtained pulsatile waveforms with similar characteristics (Fig. 5) to those derived by, for instance, tonometry [7], although this depended critically on the beam position, with the most repeatable signals being obtained from the more proximal positions. The lower trace in Fig. 5 was obtained from a miniature 3-axis MEMS accelerometer (ADXL 337, Analog Devices, Norwood MA.) to provide an independent measure of skin movement. PWV values in the range 4.6 to 10.1 m/s were recorded, with the older subjects having the higher values, as expected. Fig. 5 shows that the shape and timing of the skin displacement obtained from the vibrometer and independently from the doubly integrated z-axis (normal to the skin) accelerometer signal are similar. This preliminary study was carried out at Queen Mary University of London with the approval of The Queen Mary Ethics of Research Committee (QMERC2017/05). In-vivo measurements using the 12-beam device described here are awaiting approval from the ethics committee of Ghent University.

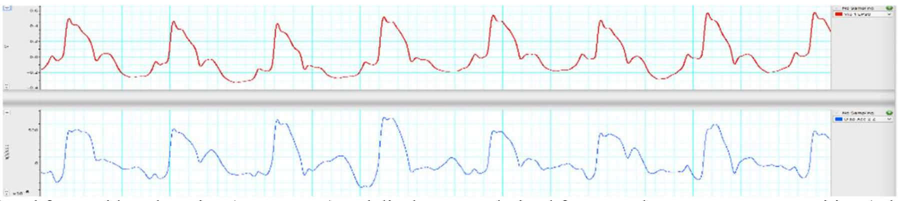


Fig. 5. LDV signal from mid neck region (upper trace) and displacement derived from accelerometer at same position (arbitrary units) as functions of time.

In conclusion, we have shown that, in a simple neck phantom containing an embedded compliant tube representing the common carotid artery, measurements of surface displacement using the 12-beam device described herein allow a reasonable estimation of pulse wave velocity (PWV) within the tube, as determined by direct measurement of the pressure PWV. In-vivo measurements using a 2-beam commercial device have yielded plausible PWV values, increasing with age as expected.

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