



In vivo evaluation of a novel, wrist-mounted arterial pressure sensing device versus the traditional hand-held tonometer



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ABSTRACT

Although hemodynamic parameters can be assessed non-invasively, state-of-the-art non-invasive systems generally require an expert operator and are not applicable for ambulatory measurements. These limitations have restricted our understanding of the continuous behavior of hemodynamic parameters. In this manuscript, we introduce a novel wrist-mounted device that incorporates an array of pressure sensors which can be used to extract arterial waveforms and relevant pulse wave analysis biomarkers. *In vivo* evaluation is performed with Bland–Altman analysis to compare the novel sensor to a gold-standard hand-held tonometer by assessing their reproducibility and agreement in peripheral augmentation index (Alx) estimation at the radial artery. Arterial waves from 28 randomly selected participants were recorded in a controlled environment. Initially we assess the reproducibility of Alx results for both devices. The intra-class correlation coefficient (ICC) and mean difference \pm SD were $[0.913, 0.033 \pm 0.048]$ and $[0.859, 0.039 \pm 0.076]$ for the hand-held and the wrist-mounted tonometer respectively. We then show that the Alx values derived from the novel tonometer have good agreement, accuracy, and precision when compared against the Alx values derived from the reference hand-held tonometer (ICC 0.927, mean difference 0.026 ± 0.049). In conclusion, we have presented evidence that the new wrist-mounted arterial pressure sensor records arterial waveforms that can be processed to yield Alx values that are in good agreement with its traditional hand-held counterpart.

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1. Introduction

Age and lifestyle have been shown to alter global and proximal hemodynamic properties with pronounced impact on the stiffness of systemic vasculature. In the young, arterial pulses travel slowly within compliant vessels. As arteries age, the wave reflection topology is modified and vascular stiffness increases affecting unfavorably multiple facets of cardiovascular function [1,2].

Since direct, *in vivo*, measurement of vascular mechanical properties is not currently possible, we rely on non-invasive sensors and surrogate clinical indicators to assess vascular health and function.

The hand-held tonometer is the most widely used device for non-invasively recording arterial pressure waveforms. The device is comprised of a pressure sensor at the tip of a pen-like rod,

connected to a bench-top amplifier and digitizer [3]. The operator applies the sensor perpendicularly on the lumen of the measured arterial segment in order to record an uncalibrated pressure waveform [4,5]. Maintaining a constant level of applied force and minimizing vibrations require an expert's steady hand and a very compliant patient. Since the waveform acquisition is dependent on the quality of the mechanical coupling between the sensor and the arterial lumen, factors like breathing (operator and patient) and fatigue (from pushing the sensor at a constant force over long periods) can unfavorably influence the measurement quality [6,7].

A wide range of arterial tonometers and corresponding vascular assessment techniques have been reported. Table 1 presents the devices that are most frequently referenced in the corresponding literature. Among a wide variety of vascular health indices such as pulse wave velocity and total/regional compliance, the augmentation index (Alx) is a commonly assessed measure of arterial stiffness. Traditionally, Alx estimation has been performed via pulse wave analysis at the carotid artery [8,9]. However, recent work has proposed that peripheral Alx, calculated directly from radial

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Table 1
Previously developed technologies for arterial tonometry.

Device Name	Company Name	Sensor type	Location
Arteriograph	TensioMed Ltd	Inflatable cuff	Brachial
BPro	HealthSTATS International	Wrist applanation tonometer	Radial
Complior Analyse	Alam Medical	Piezoelectric sensor in neck cuff	Carotid
EndoPAT/WatchPAT	Itamar Medical Ltd.	Photoplethysmograph	Finger
HEM-9000 AI	Omron Healthcare	Inflatable cuff	Brachial
Mobilograph	I.E.M. GmbH	Inflatable cuff	Brachial
PulsePen	DiaTecne s.r.l.	Hand-held applanation tonometer	Radial
SphygmoCor	AtCor Medical	Hand-held applanation tonometer	Radial
Vascular Explorer	Enverdis GmbH	Inflatable cuff	Brachial
Vasotens	BPLab	Inflatable cuff	Brachial

pressure waveforms, can provide enough information on arterial stiffness and wave reflections to serve as a useful clinical risk indicator [10–12]. Alx estimation requires tonometric recordings at a single vascular location (in contrast to pulse wave velocity), making it a valuable target metric when the performance of a novel sensor is to be evaluated against a reference sensor [13].

Still, hand-held tonometry remains fundamentally non-ambulatory, thus providing clinicians with only a snapshot of vascular stiffness, even though diurnal patterns of hemodynamic parameter variation are known to carry risk-predictive information that is not available from single-point measurements [14,15]. Subsequently, it becomes of crucial importance to develop tools that will allow the continuous recording of arterial pressure waves and the ambulatory assessment of the corresponding vascular health biomarkers.

In the current study, we present a novel, wrist-mounted, non-hand-held arterial tonometer. We further compare its ability to capture the fine waveform features required for Alx estimation versus a commercial hand-held tonometer in a controlled environment. We evaluate the hypothesis that the wrist-mounted array of pressure sensors can record arterial pressure wave data that will produce Alx values with good reproducibility and good agreement against the data recorded with the traditional hand-held tonometer.

2. Methods

2.1. Subjects

Thirty subjects (18 male) were recruited for our study from the greater Seattle, Washington area. All subjects provided written informed consent for their participation in the study.

2.2. Data collection hardware

Arterial pressure waveforms were recorded from the radial artery using two devices: (1) a commercially available hand-held tonometer (SPT-301, Millar Instruments, Houston, TX, USA), and (2) the novel wrist-mounted tonometer.

The SPT-301 hand-held tonometer utilizes a micro-tip pressure transducer, embedded in a metal, pen-like casing that facilitates positioning and signal acquisition. The sensing tip is placed on the apex of the metal casing and is covered with a silicone type membrane for protection. Fig. 1 shows the hand-held tonometer as it is typically used for radial applanation tonometry. The SPT-301 was digitized at 1 kHz using a custom device that included a 24-bit analog-to-digital converter (ADC) (ADS1298, Texas Instruments, Inc., Dallas, TX, USA). The ADC also includes a programmable-gain amplifier, which for this experiment was set to 12x amplification. The ADS1298 was running in high-resolution mode and all the other registers were set to default values.

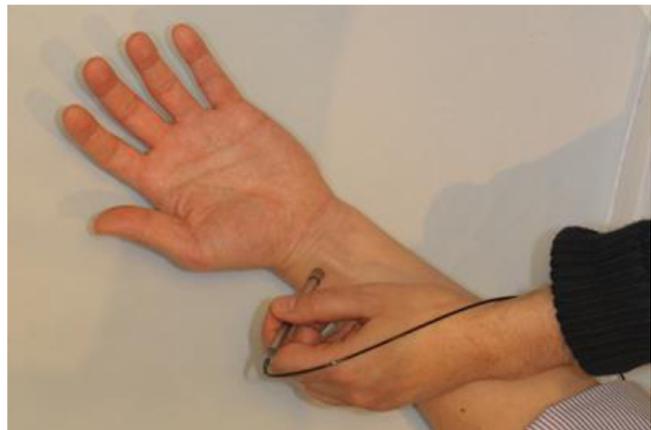


Fig. 1. An operator performing arterial tonometry on the radial artery using a Millar SPT-301 hand-held tonometer.

The wrist-mounted tonometer uses three MS5805 sensors in a triangular configuration (Measurement Specialties, Inc., Hampton, VA, USA) (Fig. 2a). The MS5805 is a piezoresistive sensor that incorporates an analog front-end and a 24-bit analog-to-digital converter inside a protective plastic housing, providing absolute pressure measurements from 1 kPa to 200 kPa. The only configurable parameter on the MS5805 is the conversion time, which was set to 54 ms. The three sensors were interfaced with an Arduino Due microprocessor board (<http://arduino.cc>) and sampled at 204 Hz. The sensors were modified for use in this application; specifically, the smaller of the two plastic housing rings was cut off of each sensor to provide a larger and more comfortable contact platform, and the remaining (larger) ring was filled with a silicone elastomer (Sylgard 184, Dow Corning Corp., Midland, MI, USA). Sufficient silicone was applied to fill the housing and form a small bubble above the plastic. The silicone makes direct contact with the skin, and thus pressure is transmitted to the sensor without passing through an air gap. Three of these modified sensors were positioned on a custom printed circuit board to increase the possibility of one being directly over the arterial lumen (Fig. 2b). This PCB was then mounted in a custom plastic housing that attaches to an off-the-shelf fabric wristband (Timex Group USA, Inc., Middlebury, CT, USA), that includes a Velcro fastening loop. The entire device is shown in Fig. 2c. Schematic and PCB specifications are attached as supplementary material to the online version of this article, at [http://\[insert_final_doi_url_here\]](http://[insert_final_doi_url_here]).

2.3. Experimental protocol

2.3.1. Blood pressure measurement

The experiment was conducted under controlled conditions, in a quiet, climate-controlled (21–23 °C), human physiology laboratory

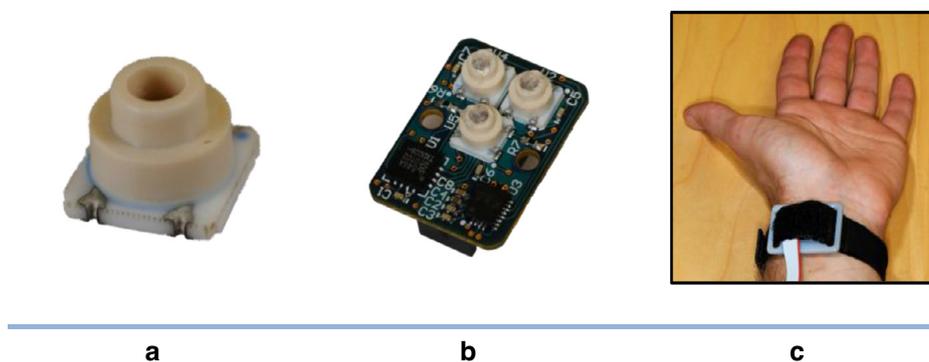


Fig. 2. (a) An unmodified MS5805 pressure sensor, (b) our modified sensors on a custom PCB and (c) The entire assembly, containing our PCB in its enclosure, mounted on a wristband.

within an industrial office building. Upon arrival, each subject was asked to rest for five minutes while filling out study-related paperwork. All the subsequent measurements and recordings were performed by the same expert operator and with the subject in a sitting position. The study protocol was explained to the subject, and the subject's brachial blood pressure and heart rate were collected using a validated sphygmomanometer (HEM-7222-Z, Omron Healthcare, Hoofddorp, NL).

2.3.2. Tonometry

Radial pressure waveforms were recorded sequentially (not simultaneously) with both tonometers. The hand-held tonometer was positioned above the radial artery, and once a strong pulse was detected through the visual feedback, waveforms were recorded for a period of 60 sec. The wrist-mounted tonometer was applied by the experimenter, the sensor with the best signal quality was noted, and 60 sec of data were collected.

Although simultaneous recordings on opposite wrists would have allowed analysis of the same sets of pulses on the two devices, the arterial pathways leading to the left and right wrists are by anatomic definition not identical and direct comparison would still not be possible or accurate. A recent study on pulse wave analysis by Martin et al. [16] found that "Simultaneously captured bilateral PWA variables demonstrated significant difference between arm differences in 88% (14/16) and 56% (9/16) of outcome variables when calibrated to within arm and equivalent PBP, respectively. Moreover, the right arm consistently demonstrated lower values for clinical PWA variables (for example, augmentation index, bias = -2.79%)." Using a single arm in a resting patient therefore minimized the potential complications to the validation study that would arise from left–right asymmetry.

2.3.3. Repeated measurements

The complete set of hand-held tonometer and wrist-mounted tonometer measurements was performed twice per subject. This yielded two 60-sec "sessions" of hand-held tonometry per subject, and two "sessions" with the novel tonometer.

2.4. Data processing

All data processing and analysis was performed in Matlab R2014b (The Mathworks, Inc., Natick, MA, USA).

2.4.1. Preprocessing

For uniformity of analysis, hand-held tonometer and wrist-mounted tonometer data were resampled to 200 Hz (from 1000 Hz and 204 Hz, respectively). Data were then filtered by an FIR low-pass filter at 18 Hz.

At this stage, all wrist-mounted tonometer data were visually re-examined by an expert to select the sensor that corresponded to the best signal quality. The design of the sensor array aims to place at least one sensor over the radial artery, but due to the large area covered by the array, it was never the case that all three sensors captured sufficient signal quality for Alx analysis.

2.4.2. Segmentation

Heart rate was estimated by computing the power spectrum of each recording; the frequency corresponding to the maximum power in the range of valid heart rates (40 bpm–210 bpm) was used as the heart rate estimate. Pulses were segmented by finding local minima in the filtered data (corresponding to candidate diastolic feet), enforcing a minimum time between peaks equal to two-thirds of the pulse duration. Though this allowed a small number of minima that were minor artifacts to be identified as candidate pulses (segmentation false positives), these were correctly identified as invalid pulses at the next processing stage (landmark identification).

2.4.3. Landmark identification, pulse validation, and Alx computation

In the following step, the systolic peak, dicrotic notch (incisura), and anacrotic notch (inflection point) were identified for each segmented pulse. The systolic peak was identified as the largest peak in the first half of the pressure wave. If there was a larger peak in the second half of the pulse, the pulse was discarded. Before searching for the dicrotic notch, the pulse was further smoothed using a 25-ms moving average. The dicrotic notch was identified as the first local minimum that was at least 100 ms after the systolic peak. In rare cases, the dicrotic notch appeared as a significant inflection point but not a local minimum; hence, if no local minimum was identified in the search region, the dicrotic notch was identified as the maximum of the first derivative in the search region.

We detected the anacrotic notch (inflection point) by searching for local maxima in the first derivative of the signal (the derivative is computed *prior* to applying the moving average used for dicrotic notch identification), subject to the constraints that the anacrotic notch has to be (1) after the systolic peak, (2) before the dicrotic notch, and (3) within 150 ms of the systolic peak. If no local minimum was found that satisfied these criteria, the pulse was discarded. If multiple local minima were found that satisfied these criteria, the most prominent local minimum was used, where prominence is defined as the sum of the height differences between this local minimum and the adjacent local maximum on each side.

An average of 3.2 pulses (std = 5.1) were discarded as invalid from each 60-sec hand-held tonometer session. An average of 1.6

Table 2

Descriptive characteristics of the study cohort. Blood pressure and heart rate measurements reflect the average of measurements taken at the beginning and end of the experimental session.

	Min	Max	Mean	SD
Age (years)	22	65	33.6	9.1
Height (cm)	147.3	188.0	172.9	10.7
Weight (Kg)	38.6	113.4	74.1	20.6
BMI	16.5	35.7	24.5	5.6
Systolic blood pressure (mmHg)	90	161	114.2	17.0
Diastolic blood pressure (mmHg)	57	102	78.1	8.9
Resting HR (bpm)	52	96.5	68.38	9.8

pulses (std = 3.4) were discarded as invalid from each 60-sec wearable tonometer session.

Augmentation index was then computed according to the conventional definition for peripheral analysis (Chowienzyk, 2011):

$$AIx = \frac{pANA - pDBP}{pSBP - pDBP}$$

...where pANA, pDBP, and pSBP are the pressure values at the anacrotic notch, systolic peak, and diastolic foot, respectively.

2.4.4. Alx Aggregation

Within each measurement session, augmentation index was aggregated by computing the median Alx value for all valid (i.e., non-discarded) pulses. This aggregation was performed because the hand-held and wrist-mounted tonometer data were not recorded simultaneously and beat-to-beat variation in Alx would have complicated the comparison. The aggregation creates two values of Alx per device, per person. Finally, we further aggregate data by averaging the two Alx values corresponding to the wrist-mounted sensor for each subject, and the two Alx values corresponding to the hand-held tonometer for each subject. This yields two unique values of Alx per subject: one for each device.

2.4.5. Statistical analysis

Agreement, accuracy, precision, and association between the repeated measurements and between the different devices were evaluated based on a previously described methodology [17,18]. Agreement between different estimations of Alx was assessed with the intra-class correlation coefficient (ICC), variability was assessed with the standard deviation (SD) of differences, and the root mean square error (RMSE) was used to evaluate accuracy. Finally, the Spearman's correlation coefficient and the coefficient of determination (R^2) were calculated and Bland–Altman analysis was performed.

3. Results

Hand-held tonometer sessions (60 sec each) yielded an average of 58.2 pulses (std = 7.6), of which an average of 55.0 (std = 8.0) were classified as valid pulses for purposes of Alx computation. Wrist-mounted tonometer sessions (60 sec each) yielded an average of 62.3 pulses (std = 7.8), of which an average of 60.1 (std = 7.9) were classified as valid.

Subjects were excluded if more than 20% of pulses were invalid in at least one recording from each device as previously described in the Data Processing section. Applying this rule, two male subjects were excluded, leaving twenty-eight (16 male) subjects in the pool used for analysis. The descriptive characteristics of the studied cohort are summarized in Table 2.

Initially we present a pair of sample waveforms for context and to clarify our definition of Alx. Fig. 3 shows two pressure waves (in blue) from the same person, one from the tonometer and one from the wrist-mounted tonometer.

Table 3

Reproducibility analysis for two repeated measurements of Alx with the hand-held tonometer (left column) and the wrist-mounted tonometer (right column).

$N = 28$ subjects	Hand-held tonometer Alx	Wrist-mounted tonometer Alx
Mean difference	0.033	0.039
SD of differences	0.048	0.076
Percent within limits (%)	96.4	92.9
RMSE	0.223	0.248
R^2	0.830	0.720

Table 4

Results of the comparison between the hand-held and wrist-mounted tonometer based on: bias, agreement, consistency and association.

$N = 28$ subjects	Comparison
Mean difference	0.026
SD of differences	0.049
Percent within limits (%)	92.8
RMSE	0.211
R^2	0.863

3.1. Reproducibility analysis of Alx estimation with the hand-held and wrist-mounted tonometers

We first assess each device's internal result reproducibility by comparing the first and the second Alx estimations made with each device. The mean difference (bias) between the two repeated estimations of Alx with the hand-held tonometer was 0.033 with SD of differences equal to 0.048. The mean difference between the two repeated Alx estimates for the wrist-mounted tonometer was 0.039 with 0.076 SD of differences. The Bland–Altman 95% limits of agreement were (−0.061–0.127) and (−0.109–0.188) for the hand-held tonometer and the wrist-mounted tonometer respectively. The corresponding Bland–Altman plots and scatter plots are shown in Fig. 4. Intra-class and Spearman's correlation coefficients were estimated for both devices and the analysis yielded the values (0.913, 0.932) and (0.859, 0.882) for the hand-held and the wrist-mounted tonometer respectively. All the calculated metrics of agreement, variation, association, bias, consistency and reproducibility for the reproducibility analysis are summarized in Table 3.

3.2. Comparison between the wrist-mounted and hand-held (reference) device

The mean value of the two Alx estimates from the hand-held tonometer was directly compared with the mean value of the two Alx estimates derived from the wrist-mounted tonometer using the same statistical metrics used above for reproducibility analysis. Table 4 summarizes the corresponding results. The ICC and the Spearman's correlation coefficient were equal to 0.927 and 0.952 respectively. Fig. 5 presents the Bland–Altman graph and the corresponding scatterplot. The Bland–Altman 95% limits of agreement were −0.071–0.1228.

4. Discussion

In the current study, we presented a new wrist-mounted device for acquiring pressure signals from the radial artery. This type of pressure sensor can be used for the analysis of arterial waveforms and relevant pulse wave biomarkers, such as augmentation index, or – in conjunction with electrocardiogram data – pulse transit time. Given the possibility of this family of devices to record data continuously, this emerging class of wrist-mounted sensors could

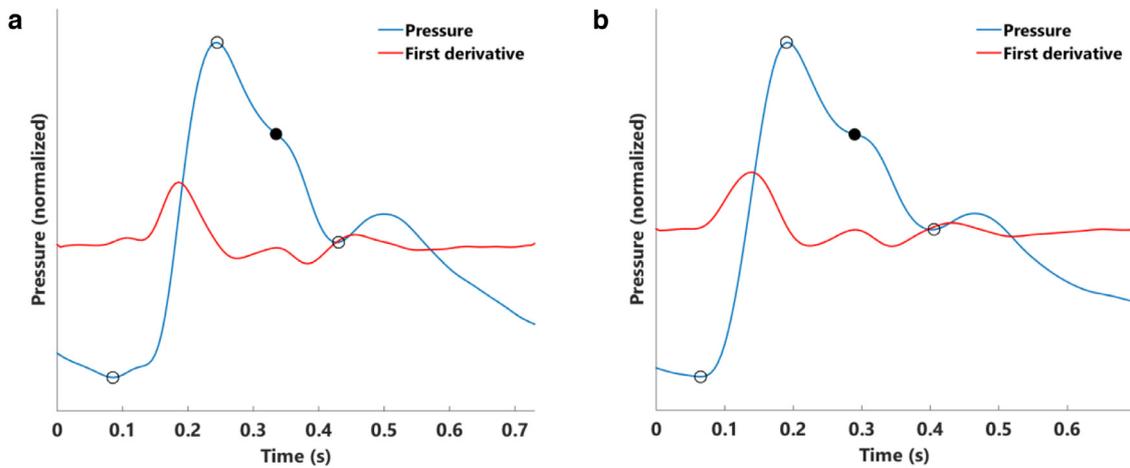


Fig. 3. Pressure waves recorded non-simultaneously from the same subject, using the hand-held tonometer (left) and wrist-mounted tonometer (right). The solid black point corresponds to the location of the anacrotic notch. Other open circles correspond to diastolic foot, systolic peak and dicrotic notch. (For interpretation of the references to color in this figure, the reader is referred to the web version of this article.)

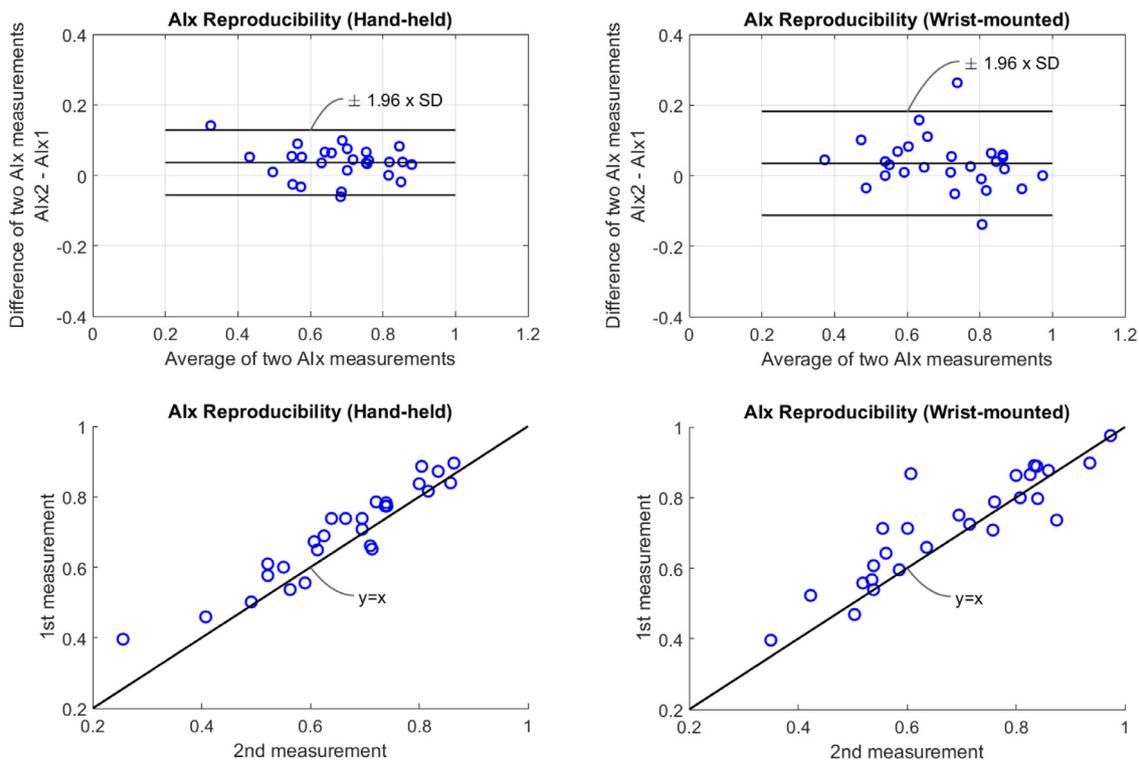


Fig. 4. Reproducibility results for the hand-held tonometer (left) and the wrist-mounted tonometer (right).

open the door to new, ambulatory approaches in cardiovascular health assessment that allow ambulatory monitoring of these signals and derive information from their real-world variability.

It was demonstrated that the new wrist-mounted tonometer sensor records arterial waveforms that derive peripheral augmentation index values which are in good agreement and accuracy compared to the values computed from a reference hand-held tonometer.

Since direct comparison of non-simultaneous pressure waveforms was not feasible, we utilized Alx as a target metric for assessing the agreement of the tonometer outputs.

We assessed the internal reproducibility for each device by comparing the Alx values computed from two separate 60-sec recordings. The estimation of Alx was highly reproducible and precise by both devices. ICC values were higher than 0.85 reflect-

ing very good to excellent agreement. The narrow limits of agreement further supported this, although for the case of the wrist-mounted sensor the limits were slightly wider than for the hand-held tonometer (Fig. 4). The low values of the SD of differences further indicated the high reproducibility of measurements. Both the reference SPT-301 hand-held tonometer and the new wrist-mounted tonometer presented very low values of mean difference (< 4%), and for both devices the bias was positive between the first and second measurement sessions. The presented values compare well with previous findings on intra-observer differences for Alx estimation. Wilkinson et al. studied a mixed cohort of 33 subjects (including: controls, diabetics, hypertensive) and reported an intra-observer mean difference of 0.049 with very low SD of differences [19]. Similar studies have also reported very small intra-observer differences in Alx estimation [20,21]. However, existing literature

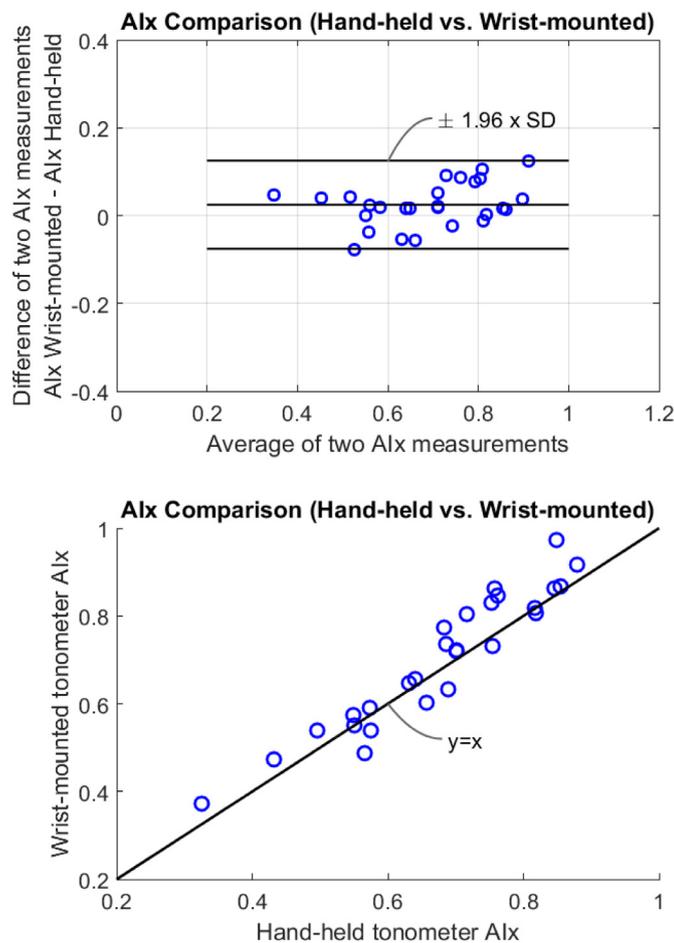


Fig. 5. Comparison results for hand-held tonometer vs. wrist-mounted tonometer.

has investigated primarily central Alx, while data on the reproducibility of peripheral Alx are not available to our knowledge.

The data analysis for the direct comparison between the reference method (hand-held) and the new device showed a very good agreement and accuracy. The ICC was larger than 0.9 while the mean difference was equal to 0.026 and the RMSE was equal to 0.211. The new device was also characterized by great precision and low variability, which is reflected in the low value of standard deviation of differences ($SD=0.049$) and the narrow limits of agreement (Fig. 5). Previous approaches to alleviate the disadvantages of pen tonometry have also focused on wrist-mounted devices that incorporate either a single micro-tip pressure transducer or a hemispheric plunger placed on the radial artery. Our findings of good agreement between hand-held and wrist-mounted tonometers compared well with existing data of Beck et al., but in that study the values of Alx were estimated after the peripheral arterial signals were reconstructed to resemble central pressure waveforms with a dedicated transfer function [13].

In the measurements presented above, the experimenter observed all three sensor channels of the wrist-mounted tonometer while placing the device and selected through visual inspection the channel with the optimal signal quality for the subsequent data analysis. However, automating the channel selection process is critical for further augmenting the applicability of arterial tonometry. Fortunately, a significant amount of research has been focused on the closely related problem of signal quality estimation for photoplethysmography, using machine learning [22–24], cross-correlation with an expected waveform [25], Kalman filtering [26], and morphological heuristics [27]. Extending these approaches to

the domain of signal quality estimation for pressure waveforms is a promising area for future work, both for automatic channel selection and for automatic determination of when a measurement is feasible in ambulatory scenarios.

5. Limitations

Simultaneous signal acquisition with both types of tonometer is not feasible and as such, a direct comparison of waveforms was not possible. Arterial signal acquisition did not fully comply with the Artery Society's guidelines for tonometry, since the subjects were not in the supine position [28]. Measurements that comply with the supine positioning will be included in our future research.

In the presented evaluation study, an expert user supervised the application of the wrist-mounted device for optimal signal acquisition quality, and an expert manually selected channels for further analysis. To enable real-world applicability of wrist-mounted devices, future work will have to develop and validate techniques for automated signal quality estimation and channel selection.

The current study did not aim at providing clinically relevant associations between the derived Alx values and other disease markers; the sole aim of the data acquisition was to investigate the agreement between the new wrist-mounted device and the hand-held tonometer. The capacity of the novel sensor to capture surrogate biomarker values for specific age groups and pathologies in good agreement with published clinical investigations will be the subject of future research.

6. Conclusions

In conclusion, we have presented evidence that the new wrist-mounted arterial tonometer provides Alx values that are in good agreement with its traditional hand-held counterpart. The provided results support the advance and use of tonometric devices for arterial stiffness studies that extend beyond clinical scenarios and pave new directions in the domain of hemodynamic assessment.

Conflicts of interest

The authors are employees of Microsoft Corporation, or were employees of Microsoft Corporation at the time this work was conducted. This work was conducted and funded by Microsoft Corporation. The device described here is being developed at part of a research project at Microsoft Corporation.

Approval

This work followed the approval process for human subjects research at Microsoft Corporation. All subjects provided written informed consent for their participation in the study.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at [doi:10.1016/j.medengphy.2016.06.022](https://doi.org/10.1016/j.medengphy.2016.06.022).

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