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Assessment of Local Venous Pulse Wave Velocity using Single-Site Methods- A Pilot Study

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***Abstract*—There has been a growing interest in assessing pulse wave velocity (PWV) in the veins with studies highlighting their potential in elucidating the vascular indices such as the venous pressure changes, venous return dynamics, venous insufficiency, and volaemic status. Despite their clinical significance, the measurements are limited due to the challenges associated with reliable venous pressure assessments. The local venous pulse wave velocity (vPWV) refers to the speed of pulse propagation within a targeted vein. Conventionally, PWV is calculated using a pulse-transit time-based approach where the venous pulses are measured from two known locations, necessitating the acquisition of high-fidelity venous pulses and demanding operator expertise. This study explores the feasibility of measuring local venous pulse wave velocity using established single-site measurement approaches employed in the arterial domain. These methods rely on simultaneous diameter and blood flow velocity signals from the vessel, employing the diameter-flow velocity (ln(D)U) and area-flow rate (QA) relationship in the vein. A pilot feasibility study was conducted on 16 participants aged 20-35 years, with the internal jugular vein selected as the target vein due to its proximity to the right atrium. Jugular venous diameter and flow velocity signals were captured at a resolution of 2 ms (frame rate = 500 Hz), and local vPWV values were derived. The in vivo measurements yielded local vPWV values, ranging from 0.5 ms^{-1} to 2.2 ms^{-1}, consistent with earlier literature findings. Furthermore, both measurement approaches demonstrated a significant correlation (r = 0.95, p < 0.05), validating their efficacy in assessing local venous pulse wave velocity.**

Keywords—Local venous pulse wave velocity, venous insufficiency, volaemic status, jugular veins, resolution, frame rate.

I. Introduction

Local pulse wave velocity is evolving as an important hemodynamic marker in assessing the health and function of the cardiovascular system [1]. It offers significant information on the intricate dynamics of the vessel characteristics, such as localized vessel stiffness and compliance [1], [2]. Numerous studies have been conducted in arterial vessels which demonstrated the close correspondence between local PWV and vascular characteristics. Few measurements have been directed toward measuring the local venous pulse wave velocity due to physiological differences and measurement challenges [3]. Unlike the distinct pulsatile nature of blood flow in arteries, the venous pulses are continuous but non-pulsatile, resulting in complex measurement approaches.

PWV in veins has garnered increasing interest, and several recent studies have focused on measuring pulse wave velocity majorly from peripheral veins [4], [5]. This can provide insights into venous pressure changes, insufficiency, venous return, vascular filling, and volaemic status [6]. Studies have also emphasized its potential as an indicator of bleeding response resulting in changes during venous constriction [7].

The reliable vPWV measurement approach involves invasive techniques where hemodynamic signals are measured directly from the target vein. The measurements are either transit-time-based or single-site approaches. The transit time method is simple and is conventionally implemented using two pressure catheters separated by a known distance [8]. Owing to the inherent non-pulsatile nature of venous pulses, the most common non-invasive measurement approach is based on artificially inducing venous pressure pulsations in a periphery location (basilic vein), and the propagation time is computed from the doppler shift in the blood velocity signal [5].

The jugular veins are the major neck vessels that carry deoxygenated blood from the cranial cavity back to the heart. The right internal jugular vein is connected directly to the superior vena cava, and the pressure changes in the right atrium are transmitted to the JV [9]. The JV pulsations can be observed on the skin surface as skin displacements and due to the pulsatile nature, the arterial PWV measurement approaches can be implemented on the JV. The JV pulsations are a result of right atrial contraction and the intrathoracic pressure changes during respiration [10]. The JV pulsations can be captured using ultrasound assessment and their pulse contour analysis can provide reliable instincts on cardiac anomalies. We had earlier demonstrated the feasibility of measuring local vPWV using the transit time-based approach, where JV diameter signals were measured from two locations along the vein [11].

Even though the PTT-based approaches are simple and easily amenable, their accuracy is compromised due to the presence of wave reflections. An alternate approach is based

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on single-site measurement, where two physiological signals are captured simultaneously from a single vessel location. These are based on the fundamental water-hammer theory or the characteristic impedance equations, where the PWV values are computed from hemodynamic signals such as pressure, diameter, and flow [1]. As the water-hammer equations were proposed on the arterial tree, the pressure, and blood flow directions are assumed to be unidirectional in nature [12]. Hence, the fundamental equations were modified owing to the fact that the blood flow direction in JV is opposed to the direction of the JV pressure pulse.

In this study, we propose the feasibility of indirect estimation of local vPWV from continuous jugular venous diameter and flow signals. The local vPWV was calculated using the two single-site measurement approaches, namely flow-area (QA) and the ln diameter-velocity ln(D)U methods [13]. The proposed measurement system can capture jugular venous diameter and flow signals at a frame rate of 500 Hz, ensuring a temporal resolution of 2 ms. The measurement approach and instrumentation system are discussed in section II. The key results and observations are elaborated in section III.

II. Materials and Methods

A. Measurement Principle

The assessment of local vPWV using single-site approaches requires the simultaneous measurement of any two distinct hemodynamic parameters, such as pressure, diameter or blood flow from the target vessel. Both ln(D)U and QA approaches rely on the simultaneous measurement of the diameter (D) and blood flow velocity (U) of the vessel. The ln(D)U technique is based on the fundamental water-hammer theory:

$$dP = \pm \rho C dU \tag{1}$$

where dP and dU are instantaneous pressure and blood velocity changes in the vessel and ρ is the density of blood and C is the wave speed [1], [12]. The positive sign applies in (1) if the wave moves downstream and a negative sign if the wave moves upstream [12]. The ln(D)U equation for calculating local vPWV is hence defined as:

$$vPWV = -\frac{dU}{2d\ \ln(D)} \tag{2}$$

The QA technique is based on the characteristic impedance of the wave equation, where the volume flow (Q) and cross-sectional area of the vessel are linearly related [1]. The QA equation is given by:

$$vPWV = -\frac{dQ}{dA} \tag{3}$$

The negative sign in the equation is that the blood flow direction is towards the heart while the right atrial pressure is transmitted from the heart towards the JV.

B. System Architecture

The instrumentation system consists of an A-mode ultrasound transducer (transducer frequency =10 MHz), for diameter measurement and an EMCO doppler (8 MHz EMCO Meditek, India) for blood flow measurement. The A-mode ultrasound transducer is interfaced to the acquisition hardware via an RF connector. The A-mode ultrasound transducer captures RF echo signals corresponding to the JV wall locations at a frame rate of 500 Hz [11], [14]. The acquired signals are amplified and are digitized by a voltage digitizer (PXI-5154, National Instruments, USA). The EMCO doppler is a battery-powered device, which is

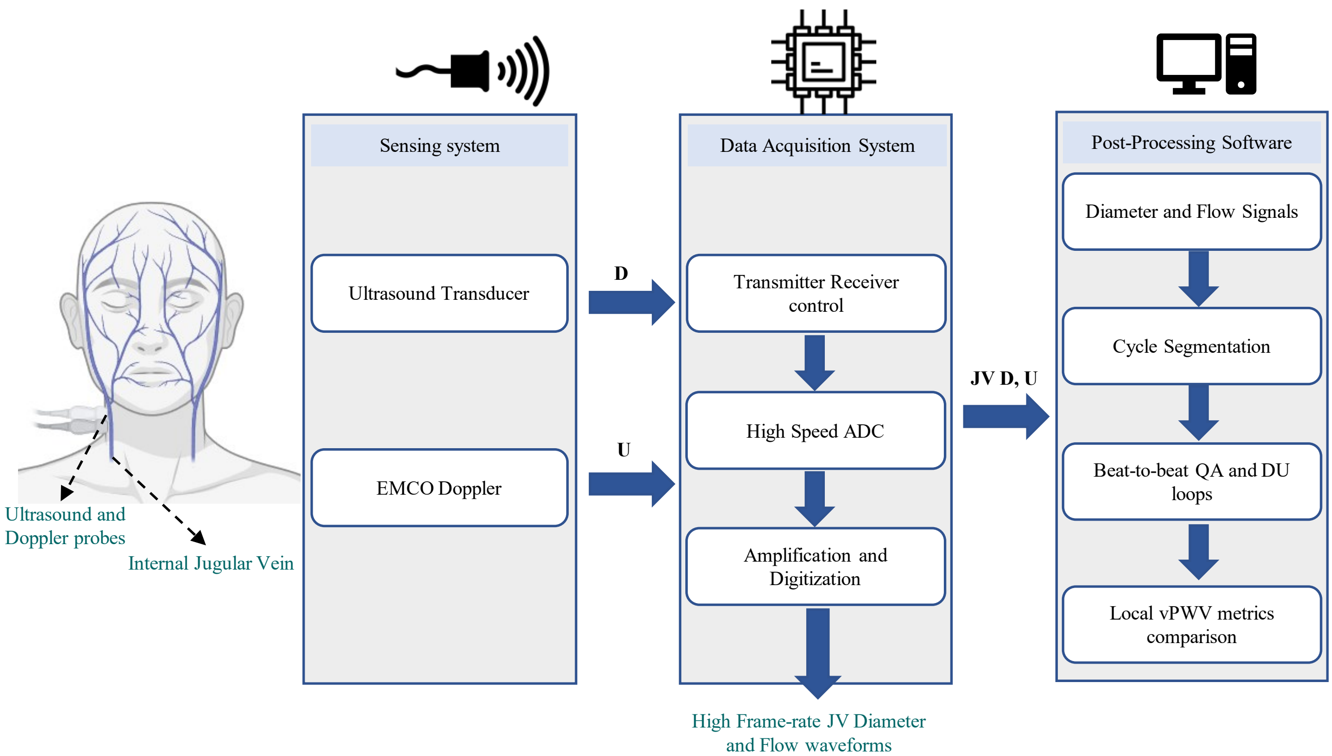

Fig. 1. The architecture of the proposed local vPWV measurement system

TABLE I. SUBJECT DEMOGRAPHICS

Parameter	Range (*Mean ± SD*)
No of Participants (Male/ Female)	16 (8/8)
Age	20-35
Height (cm)	163.06 ± 7.20
Weight (Kg)	64.38 ± 6.11
BMI	20.72 ± 2.63
Brachial SBP (mmHg)	106.50 ± 6.79
Brachial DBP (mmHg)	69.56 ± 4.30
Mean Arterial Pressure (mmHg)	77.94 ± 15.92
Heart Rate (BPM)	79.13 ± 4.69

connected to the same acquisition system ensuring time-synchronized acquisition of diameter and blood flow signals. The audio feedback from the doppler system permits the operator to differentiate between arterial and venous flow signals. As the system operates at a higher frame rate, the real-time processing demands high computation features, and hence, we have implemented separate software applications for acquisition and data processing. The local vPWV measurement system architecture is given in Fig.1.

The acquisition and post-processing software applications were implemented in the LabVIEW platform (LabVIEW 2019, 32-bit, National Instruments, USA). The acquired A-mode frames were filtered using a Butterworth filter (Bandpass, passband range: 1 to 10 MHz). The semi-automated gating feature allows the operator to manually identify and correct the tracking locations of the distal and proximal echoes of the JV vessel. A cross-correlation-based algorithm identifies the vessel wall motion, continuously tracks the wall locations, and is recorded as the JVP distension waveform [15]. A low frame rate tracking of the frames is enabled in real-time to aid as immediate feedback to the operator to ensure robust acquisition of JVP signals [16]. This is achieved using a real-time frame decimator that selectively tracks a subset of total frames. Additionally, the quality of wall echoes is monitored using a signal quality score that indicates the sharpness and strength of the echoes. The doppler device measures the blood flow envelope at the same sampling rate of 500 Hz. The doppler provides the flow envelope morphology while it can't measure the amplitude. Hence, the captured flow envelope needs to be calibrated to the actual flow velocity by measuring it using the Ultrasonix imaging system in PW mode.

The acquired diameter and flow cycles were processed offline, and cycles were segmented using the valley-to-valley cycle segmentation approach in the flow cycle. The QA loop was constructed by plotting the flow rate (Q), which is the product of flow velocity (U) and the cross-sectional area (A). While the ln(D)U loop was constructed by plotting flow velocity (U) against the natural logarithm of the JV diameter. The local vPWV values were computed as the slope of the linear region measured from these loops. To evaluate the beat-to-beat repeatability in local vPWV measurement, corresponding JV diameter and flow cycles were monitored for 10 cardiac cycles. The real-time low frame rate distension waveform, coupled with the auditory feedback from the doppler serves as a validation tool confirming the reliable acquisition of JVP signals.

C. Study Objectives

The pilot study was designed to:

a) Evaluate the feasibility of combined acquisition of jugular venous diameter and blood flow signals

b) Verify the functionality of local vPWV measurement using QA and ln(D)U methods

c) Compare and contrast the local vPWV measurements by the two approaches.

D. Study Design

The designed pilot study was conducted on a cohort of 16 healthy volunteers aged between 20 and 35 years. None of the recruited subjects had any history of venous or CVD anomalies. All the in-vivo measurements were conducted in accordance with the guidelines and regulations approved by the Institutional Ethical Committee, IIT Madras (compliant with the Helsinki Declaration 1975, revised in 2013). The subject demographic details are indicated in Table I. Participant information, including demographic details, lifestyle, and medical history were collected with a standardized questionnaire. The participant was advised to rest in a supine posture for a duration of 5 minutes. Oscillometric blood pressure measurements (SunTech ®247™, SunTech Medical, Halma, UK) were recorded once the participant was relaxed. The right internal JV was selected for the measurement as it is directly connected to the right atrium [10]. The ultrasound transducer and the doppler probe were placed in proximity over the internal jugular vein. Care was taken to ensure minimal hold-on pressure on the JV to prevent flattening of the vein. The diameter and flow signals were recorded and processed offline to evaluate the local vPWV. Simultaneous diameter and flow signals were captured for a period of about 2 minutes. The baseline flow conditions were recorded using the Ultrasonix system operating in pulse wave doppler mode to calibrate the flow envelope amplitude.

E. Statistical Analysis

Population characteristics and measurement variables are represented as mean ± standard deviation (SD) format. The

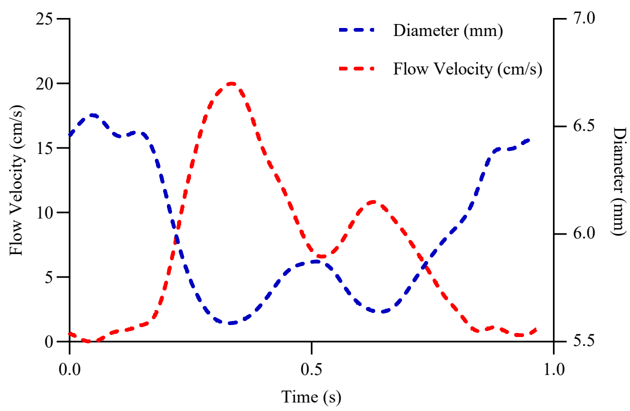

Fig.2. The acquired JV diameter and flow cycles for a cardiac cycle

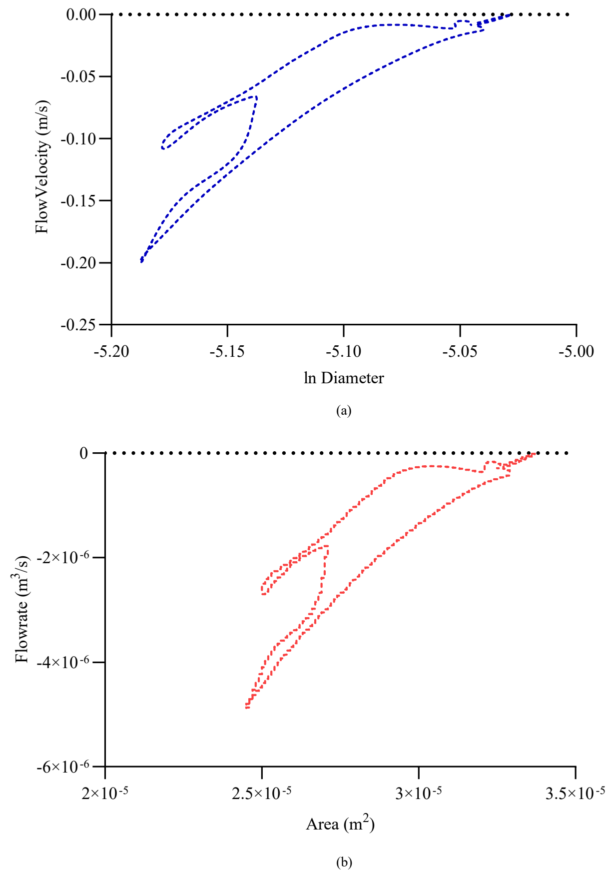

Fig.3. The (a) ln (D)U and (b) QA loops constructed from the diameter and flow signals in a cardiac cycle

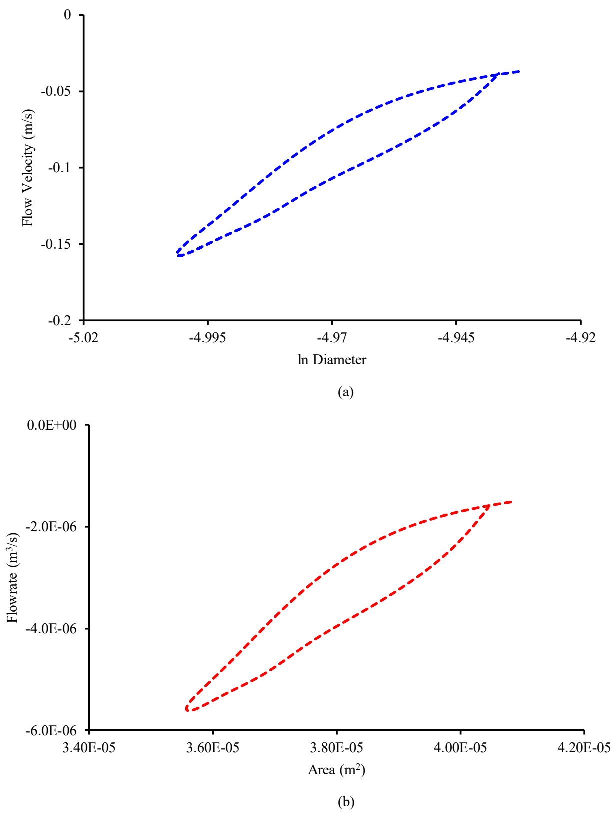

Fig.4. The QA and ln(D)U loops constructed out of selected subsection of flow and diameter cycles.

Bland-Altman analysis was employed to compare the local vPWV estimates measured using the QA and ln(D)U methods. The agreement between the estimates was further analyzed through Box-Whisker analysis to investigate the similarities and differences in agreements. The beat-to-beat repeatability in measurements was quantified in terms of the coefficient of variation (represented as the % CoV) for 10 continuous JVP cycles. The statistical analysis was performed using the GraphPad Prism software.

III. RESULTS

A. Reliability of JV Diameter and Flow Measurements

The acquisition system could capture JV diameter and flow signals from all recruited participants. The measurement system operates at a frame rate of 500 Hz (temporal resolution = 2 ms), ensuring high-fidelity signal acquisition. The higher frame rate of acquisition ensures reliable measurement of all the JVP fiduciary markers. The low frame rate (50 Hz) visual feedback enables real-time quality check of the captured diameter cycles. The beat-to-beat JV diameter and flow velocity cycles were recorded with an SNR > 20 dB. The mean maximum and minimum JV diameter for 10 cardiac cycles are 9.4 ± 2.43 mm and 7.35 ± 1.43 mm, respectively. While the flow velocity range in the cohort was observed to be 16.62 ± 5.37cms^{-1}. The measured diameter and flow velocity ranges were in concurrence with the ranges reported in earlier studies. Fig.2. indicates the simultaneous JV diameter and flow velocity measurements for a single cardiac cycle (0.93 s). The beat-to-beat JV diameter and flow velocity measurements show good repeatability ($\%CoV|_D = 12\ \%$, $\%CoV|_U = 18\ \%$). The minima-to-minima algorithm was used to segment flow signals for beat-to-beat analysis. The developed algorithm selects high-fidelity JV flow cycles and rejects poor-quality cycles with a higher sensitivity and specificity. The JV diameter cycles were further segmented to the corresponding locations of the flow cycle.

B. Feasibility of Local vPWV Assessment using QA and ln(D)U Methods

The slope of the constructed QA and ln(D)U loops gives the corresponding local vPWV. Fig. 3 indicates the typical QA and ln(D)U loop constructed from a single participant. The typical local vPWV ranges measured using QA and ln(D)U methods were 1.15 ms^{-1} and 1.18 ms^{-1}, respectively. It was observed that the linear region in the loops corresponds to the first half of the flow cycle, and hence, for the ease of the measurement, the half duration of the flow cycle and its corresponding diameter regions were selected for local vPWV calculation. The subsection selected from the QA and ln(D)U loops for local vPWV assessment are indicated in Fig. 4.

C. Comparison of local vPWV Measurement Methods

To compare the local vPWV measurements using the two techniques, Bland-Altman and Box-Whisker analysis were performed. The Bland-Altman analysis revealed a significant level of agreement between the two local vPWV assessment techniques with a mean bias of 0.03. A statistically significant correlation ($r = 0.95$, $P < 0.05$) was observed between the QA and ln(D)U methods. The comparison plots between the local vPWV values measured using the QA and ln(D)U approaches is depicted in Fig. 5.

D. Limitations and Future Scope

The local venous pulse wave velocity is a relatively novel marker with only a single validated approach based on pulse

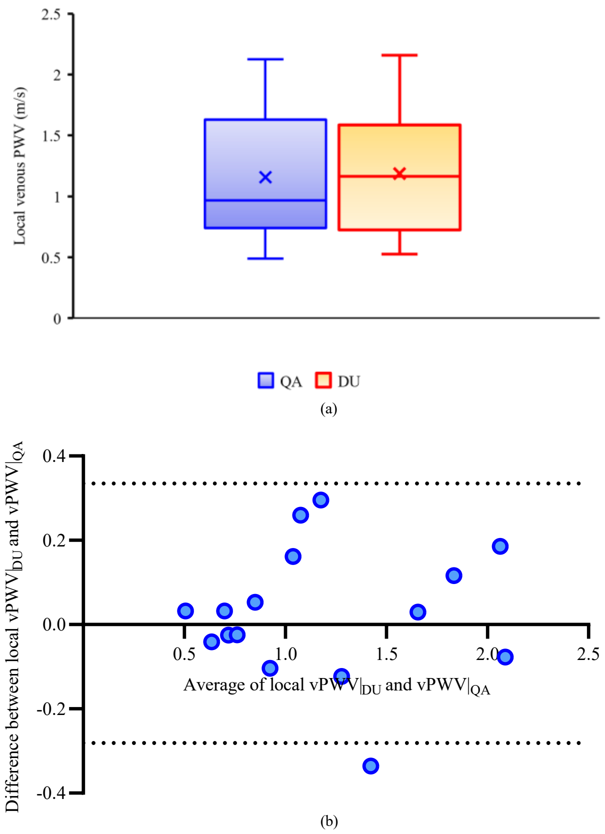

Fig.5. Comparison of local $vPWV|_{QA}$ against $vPWV|_{DU}$ methods using (a) Box-Whisker plot and (b) Bland-Altman analysis

transit time quantification [11]. Hence, there exists no standardized reference measurement approach to validate our measurement. Even though about 70 percent of the blood volume flows through veins at any cardiac instant, the pulse wave velocity measurements are least explored. The single-site approaches listed in this study are derived from the fundamental arterial PWV equations. But unlike the arterial tree where both the pulse direction and the blood flow are unidirectional, the direction of pulse propagation and the blood flow are opposite in veins. This demanded the amendment of the current equations with a negative polarity. The local vPWV measurements using the QA and ln(D)U approaches offered significant repeatability in this study, but further analysis by acquiring multiple hemodynamic parameters such as pressure, impedance, etc., and verifying the performance of each PWV assessment metric is essential to identify the best-suited approach. The measurements were performed in a semi-automated fashion where the acquired ultrasound echoes were processed offline to obtain the distension waveform. Automated algorithms are to be developed to aid in real-time processing [17], [18]. Also, the current study was a limited cohort study including only healthy participants. Dedicated clinical trials on a diverse population is necessary to compare the efficiency of each local vPWV assessment approach and its association with other functional markers and cardiovascular diseases.

The local vPWV, has the potential to provide valuable insights on the functioning of the venous system. Understanding this parameter can aid in early diagnosis and treatment of venous disorders, making it a valuable tool in clinical practice [4]. By accurately assessing the functioning of the venous system, healthcare professionals can better understand the extent of venous insufficiency and other vascular conditions, guiding treatment decisions [19], [20]. The relationship between the venous pulse wave velocity and other clinical markers such as arterial pulse wave velocity and vessel stiffness are to be explored [21] -[23]. In addition to its diagnostic value, local venous pulse wave velocity also serves as a valuable tool for monitoring the effectiveness of interventions aimed at improving venous health. Hence, future directions would focus on developing a standardized local vPWV measurement approach and verifying its functionality in identifying the changes during venous interventions such as passive leg raise and valsalva maneuver. Studies are also planned to explore the ability of local vPWV, in identifying various cardiac anomalies that can be predicted using the pulse contour analysis of JV.

E. Discussion

The local vPWV is a potential marker that venous hemodynamic assessment. Owing to the difficulty in measuring the lower pressures in the jugular vein, local vPWV approaches based on pressure values can't be implemented directly. Among the different single-site approaches the ln(D)U and the QA methods can be easily implemented as the measurements are quite straightforward. Both these methods differ in the fundamental principles, where the ln(D)U is based on the water-hammer equation while the QA method is based on transmission line characteristics. Taking into account that these methods differ in fundamental principle, there is no univocal opinion on which method is superior to the other. This study is the first to evaluate the feasibility of implementation of these methods to evaluate the local vPWV. Here, being an initial approach, we have derived the cross-sectional area from the diameter and the mass flow rate as the product of the velocity and area. Dedicated image processing tools permit the measurement of diameter and area, which can be used for independent local vPWV analysis.

The proposed measurement system operates in a semi-automated framework demanding offline processing. The possibility of carotid artery influence on the measurement is manually verified, and future efforts are in progress for automated rejection of the arterial influence to ensure higher signal quality. The observations reported in the study are based on non-invasive jugular venous diameter and flow signal measurement, and it's challenging to compare them against reference invasive PWV measurements. Future studies on animal models and diverse populations are necessary to validate the functionality of the proposed system. Computerized recognition, segmentation, and detection mechanisms have become the cornerstone of imaging-based diagnostic applications [24]-[29]. The development of advanced algorithms can aid in reliable real-time measurements and has the potential to measure multiple physiological parameters.

IV. Conclusion

We have demonstrated the feasibility of indirect assessment of local venous pulse wave velocity using single-site measurement approaches. The diameter and flow signals were acquired at 500 Hz, ensuring high-fidelity signals (SNR >20 dB, temporal resolution = 2ms) for processing the local vPWV. The measured in-vivo local vPWV ranged from 0.5 ms^{-1} and 2.12 ms^{-1}, which were consistent with the venous

PWV ranges reported in previous literature. The local vPWV measurement using both the ln(D)U and QA approaches demonstrated a significant correlation ($r = 0.95$, $p < 0.05$), validating the accuracy of measurements. This preliminary pilot study, conducted on a healthy cohort, assesses the feasibility of single-site local PWV measurement approaches on the venous tree. Future studies are underway to ascertain the applicability and accuracy of the proposed technique in assessing local vPWV across a larger and more diverse population, with the potential to contribute valuable insights into venous function.

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