Towards ultrasound wearable technology for cardiovascular monitoring: from device development to clinical validation

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Abstract—The advent of flexible, compact, energy-efficient, robust, and user-friendly wearables has significantly impacted the market growth, with an estimated value of 61.30 billion USD in 2022. These wearable sensors have revolutionized in-home health monitoring by warranting continuous measurements of vital parameters. Ultrasound is used to non-invasively, safely, and continuously record vital parameters. The next generation of smart ultrasonic devices for healthcare integrates microelectronics with flexible, stretchable patches and body-conformable devices. They offer not only wearableness, and user comfort, but also provide higher tracking accuracy of immediate changes of cardiovascular parameters. Moreover, due to the fixed adhesion to the skin, errors derived from probe placement or patient movement are mitigated, even though placement at the correct anatomical location is still critical and requires a user’s skill and knowledge. In this review, the steps required to bring wearable ultrasonic systems into the medical market (technologies, device development, signal-processing, in-lab validation, and, finally, clinical validation) are discussed. The potential of the next generation of vascular ultrasound and its future research directions offer many possibilities for modernizing vascular health assessment and the quality of personalized care for home and clinical monitoring.

Index Terms—Blood pressure, capacitive micromachined ultrasound transducers (CMUTs), flexible lead zirconate titanate (PZTs) ultrasound transducers, non-invasive monitoring, piezoelectric micromachined ultrasound transducers (PMUTs), real-time monitoring, vascular stiffness.

I. INTRODUCTION

Cardiovascular diseases (CVDs) remain the leading global cause of death, surpassing cancer fatalities for both sexes [1]. In 2020, CVDs accounted for 19 million deaths, while cancer caused 10 million deaths [2, 3]. Early detection of chronic CVDs is challenging, necessitating mobile and continuous vital sign measurements for primary prevention.

The emergence of new portable technologies for ambulatory monitoring is having a profound impact on society. The wearable medical market, valued at 61.30 billion USD in 2022, continues to grow, particularly with the increasing adoption of mobile health (mHealth) technologies for remote, non-invasive, and non-obtrusive heart disease monitoring [4–7].

The industry and research sectors have shown an increasing interest in non-invasive medical monitoring devices due to their user-friendly interface, portability, safety, and wireless features. Ambulatory blood pressure (BP) monitoring and ultrasound-based BP transducers have witnessed substantial growth in recent years. For instance, in-home wearable BP monitoring is projected to reach a market size of nearly 1.8 billion USD by 2025 [8].

Continuous non-invasive home monitoring of not only BP but also blood flow is of significant importance. Vascular ultrasound provides a means to assess blood flow using diverse techniques, including Transient Time and Doppler Ultrasound. The market for blood flow measurement devices reached 533 million USD in 2021, with a market growth rate of 8.2% between 2022 and 2032 [9].

In addition to BP and flow velocity, wearable sensors can simultaneously record multiple biomedical and physiological signals, including pulse rate, artery thickness, stiffness, and pulse wave velocity (PWV), which serves as a gold-standard descriptor of vascular age [10]. Current wearable systems predominantly employ photoplethysmography (PPG) through optical sensors to capture these vital signs [11, 12]. In PPG-based devices, a light source illuminates the tissue, and the photodetector measures the intensity of the reflected light from the artery over time, allowing the quantification of blood volume changes in the vascular tissue bed [13]. The reflective PPG uses green or yellow light, while in the transmissive configuration, infrared or red light is used. Thanks to the two components of the PPG waveform (DC and AC), both non-pulsatile (i.e. veins) and pulsatile (i.e. arteries) tissue can be detected. Notable examples of PPG-based non-invasive...
wearable devices in the market include the ViSi Mobile System by Sotera digital health (USA, launched in 2018) [14], the Aktiia 24/7 BP monitoring system by Aktiia (Switzerland, launched in January 2021) [15], the Biobeat 24BP wrist-worn and adhesive patch by Biobeat Medical Smartmonitoring (Israel, May 2021) [16] and the LiveOne device by LiveMetric S.A. (Luxembourg, FDA clearance received in June 2022) [8, 17].

PPG-based optical solutions offer two key advantages over ultrasound: low power consumption (50.58 mW in [18], in comparison to circa 4 W for ultrasound [19]) and higher compactness (module size: 3.8 mm x 7.1 mm x 0.6 mm [20]). However, clinical validation has revealed their subpar accuracy, with errors in systolic blood pressure (SBP) and diastolic blood pressure (DBP) reaching up to 15 mmHg and 10 mmHg, respectively [17]. Machine learning (ML) techniques can reduce the SBP and DBP mean errors of PPG solutions, as shown in Sun et al. [21] where the initial mean SBP error of 15.27 mmHg was reduced to 8.99 mmHg with a regression model. In Kilickaya et al. [22] ML is also applied, obtaining SBP and DBP errors of 13.57 mmHg and 8.30 mmHg, respectively.

The infrared signal of PPG sensors is influenced by factors such as heat, optical properties of near tissues and vessels, artery depth and movements, as well as external ambient light and motion artifacts. Due to the low penetration of PPG, this technology is very sensitive to body characteristics (skin temperature and tone, and body max index). That means that individual calibration for each person is required to obtain accurate measurements with PPG, which is tedious [23]. Another key limitation of PPG is the elimination of moving artifacts. Robust filtering techniques and detection algorithms need to be applied to detect feature points of the waveform. Moreover, PPG usually does not work properly for people with adiposity (due to the high attenuation of the signal) or with peripheral arterial disease (low peripheral perfusion) [24]. Hence, emerging sensing technologies require further investigation.

Vascular ultrasound stands out as device capable of directly measuring elastic properties of arterial walls (distensibility, stiffness index, Young’s modulus) and blood characteristics (blood speed, viscoelasticity), while also determining intima-media thickness (IMT) [25, 26]. It offers a safe and rapid technique for detecting plaques and stenosis in arteries with a sensitivity and specificity of 94% and 93%, respectively [27]. Additionally, echo tracking devices achieve precision up to 1 μm when determining diameter stroke variation [28]. Ultrasound’s high resolution in discerning arterial walls results in impressive and accurate BP measurements, with errors as low as ±0.78 mmHg and ±0.87 mmHg for mean SBP and DBP, respectively [29].

Ultrasound provides accurate BP measurements (errors smaller than 1 mmHg [27, 30]) and can penetrate deeper into tissues compared to PPG or optical coherence tomography (OCT). With OCT a tissue penetration of 1-3 mm can be achieved, compared with 4-8 mm in ultrasound.

Due to the use of multiple optical fibers, OCT has better axial and lateral resolution than invasive ultrasound applications (10-20 μm). However, due to its low penetration depth, non-invasive OCT can be only used to measure parameters on the human skin, such as the elastic properties [31]. Vascular measurements are only possible with invasive OCT and using contrast materials for blood clearance. Thus, due to its large penetration depth capabilities, ultrasound is a better technology to monitor vascular diseases in the body. Furthermore, ultrasound wearables are versatile, allowing placement on various arteries (e.g., radial, brachial, carotid), which is not feasible with PPG or OCT.

The proposed review aims to provide a deeper insight into wearable sensors based on ultrasound and their methods and use to continuously monitor vascular health, as illustrated in Fig. 1. First, ultrasound fundamentals related to the monitoring of cardiovascular parameters are explained in Section II. For device development, the transducer technology plays an important role in miniaturization, resolution, and portability. In Section III, a comparison of the three main ultrasound technologies (bulk piezoelectric, and piezoelectric and capacitive micromachined ultrasonic transducers) is discussed. Technical considerations are of high interest, such as how to reduce the size of the ultrasound wearable system by integrating it with new sensor approaches like patches, tattoos, and wristbands [32]. The trends in development of rigid and flexible transducers is described in detail in Section IV. Moreover, this article also encompasses the validation methods (in vitro, ex vivo, and in vivo) employed for new ultrasound devices intended for market entry (Section V). The future improvements of the ultrasonic wearable devices are included in Section VI and Section VII.

**Highlights of the review:**

- Underlines the potential of ultrasound for cardiovascular monitoring due to its deep penetration and vitality insights, despite challenges in integration.
- Reviews innovative solutions like silicone-embedded transducers and flexible patches for accurate and continuous cardiovascular health monitoring.
- While ultrasound shows promise for vascular parameter monitoring, challenges like high power consumption and compliance with BP estimation standards need resolution for widespread adoption.
- Comprehensive overview of sensor validation stages, spanning from lab testing to in vivo verification.
- Authors’ perspectives on future trends, technical demands, and challenges in the field.
II. ULTRASOUND FUNDAMENTALS

This section provides a comprehensive introduction to the principles of ultrasound propagation, fundamental instrumentation, and the diverse ultrasound modes employed in medical imaging. Moreover, it investigates the use of ultrasound techniques for assessing diameter and flow velocity, along with their applicability in estimating BP.

A. Ultrasound propagation

Ultrasound waves emitted by the transducer propagate through soft and hard tissues, being absorbed by the tissue, transmitted through the tissue, and reflected at material interfaces before detection at the transducer. In medical diagnostics, the appropriate ultrasonic frequency range is typically set between 2-30 MHz [33] (ultrasound range in the sound spectrum is illustrated in Fig. 2 (a)). Sound propagation in a medium involves the transmission of waves where rarefactions (regions of decreased pressure) and compressions (regions of increased pressure) propagate through the medium (see Fig. 2 (b)), carrying the sound energy forward. There are two types of transducer topologies, either two transducers are used independently as transmitter and receiver, or the same transducer is used for both tasks, which in this case is called a transceiver, as demonstrated in Fig. 2 (c-d), respectively. In the first configuration, the transmitter can emit a continuous wave, enabling continuous transmission and reception, whereas, in the transceiver configuration, only pulsed waves can be used since the transducer must alternate between transmitting and receiving. As sound waves propagate through tissue, their intensity diminishes due to circular wave nature, where intensity is inversely proportional to the square radius of the traveled distance from the source. Additionally, the vibration of sound waves generates heat dissipation in tissue or liquid (e.g., blood or serous fluids). This attenuation is directly proportional to the square of the ultrasound frequency [34], with an attenuation rate in body tissues ranging from 0.3-1.1 dB/(MHz·cm), with denser tissues experiencing greater impact [26]. Consequently, higher ultrasound frequencies lead to higher attenuation, and therefore, lower penetration depth (see Fig. 2 (f)). If the attenuation becomes too high, reflected waves are not captured by the transducer [35]. Hence, low-frequency transducers are used for visualizing deep organs or tissues (e.g., the heart), while high frequencies are employed for superficial tissues (e.g., radial or carotid artery). The relation

![Fig. 2. Fundamentals of ultrasound. (a) Ultrasound range in the sound spectrum. (b) Sound wave propagation through a medium. (c-d) Schematic of a transmitter-receiver (Tx and Rx) system, compared to a transceiver (Tx/Rx) and respected allowed types of transducer mode. (e) Doppler effect on everyday life, an ambulance seems to change sound pitch to two observers on the road while moving from left to right. The source frequency does not change, but due to the Doppler effect, the observer on the left experiences a low frequency, whilst the observer on the right experiences a high frequency. (f) The compromise between wavelength (resolution) and penetration depth to the frequency is depicted; the higher the frequency, the higher the resolution, but the lower the penetration depth. The influence of frequency on the resolution is shown by imaging two structures distanced at dx; at low frequency, the structures are overlapped (dx< \( \lambda /2 \)); at high frequency they are imaged as two separate structures (dx> \( \lambda /2 \)). (g) Different types of resolution shown in an ultrasound beam.]
between the wavelength \( \lambda \), speed of sound (medium dependent) \( c \), and the frequency (source dependent) \( f \), is given by
\[
\lambda = \frac{c}{f}.
\] (1)

In medical ultrasound applications, the sound velocity in soft tissues is commonly assumed constant and at 1540 m/s [36].

B. Spatial resolution vs. visualization depth

The ultrasound system's capability to differentiate between two points at a specific tissue depth is primarily governed by the transducer and is quantified through axial resolution, lateral resolution, and elevational resolution (see Fig. 2 (g)). The axial resolution, measured along the beam axis, is determined by half the product of wavelength and the number of waves sent per pulse [37, 38]. A compromise exists between wavelength (resolution) and penetration depth to the frequency; the higher the frequency, the higher the resolution, but the lower the penetration depth, as depicted in Fig. 2 (f). Conversely, lateral resolution, measured along the plane perpendicular to the sound wave's direction, is affected by the transmit frequency but is predominantly determined by the ultrasound system's focusing properties and resulting beam characteristics. Elevational resolution in ultrasound measures its ability to distinguish objects perpendicular to the axial and lateral dimensions.

C. Safety determination

Ultrasound absorption leads to a rise in tissue temperature, necessitating a regulation and control of energy levels in ultrasound devices to prevent cellular damage. The International Electrotechnical Commission (IEC) 60601-2-37 standard indicates a maximum temperature of 43°C or a temperature rise of 10°C when the probe is in contact with the skin [39, 40]. IEC 62359 regulates acoustic output exposure parameters, setting limits such as in situ spatial peak intensity lower than 720 mW/cm², the spatial pulse peak average intensity lower than 190 mW/cm² and the mechanical index and thermal index lower than 1.9 and 6.0, respectively [41–43]. The standard also outlines the methods to measure the exposure parameters, where a hydrophone is used in distilled water since performing these measurements in situ is impractical. The transferability of hydrophone measurements to in vivo values uses a derating process, with a \( \alpha \) factor of 0.3 dB/(MHz·cm) (represents minimum attenuation in tissues) [41].

D. Instrumentation

Signal bandwidth (BW) and transducer matching to the pulser/receiver circuitry are crucial parameters in developing transducer instrumentation [44]. Any mismatch between the transducer and the pulser/receiver system can lead to waveform degradation and signal loss. However, electrical impedance matching between the probe and receiving device can minimize the mismatch, resulting in increased energy transmission [45].

Ultrasound sensors can be single transducers (one-element transducers) or arrays. Single-transducer-based ultrasound requires only one single-channel interface circuitry, while array transducers use multiple channels integrated into a multiplexer. A typical commercial ultrasound system (i.e., conventional bulk piezoelectric transducers) consists of a pulser, transducer, receiver, scan converter, and display. The pulser drives the transducer at a pulse repetition frequency (PRF), defining temporal resolution. The transducer is driven by high voltage (e.g., ±100 Vpp) during transmission and receives low voltage (e.g., ±100 mVpp) signals from the body. The receiver amplifies and preprocesses the signal for memory/display processing, and the transmit/receive (T/R) switch isolates the receiver during transmission. Tissue depth attenuation is compensated by a time gain compensation (TGC) amplifier. Memory stores data and an analog-to-digital converter (ADC) facilitates digital display on a monitor, providing the image's location and strength.

E. Ultrasound imaging modes

The pulse-echo (transceiver configuration, see Fig. 2 (d)) approach is the fundamental methodology for most diagnostic ultrasound procedures. It involves applying pulsed excitation signals to the transducer. Reflected signals encounter acoustic mismatches, causing echoes that are converted into electrical signals at the transducer. The distance \( d \) to a reflecting surface is proportional to the speed of sound and time of flight \( TOF \) between the transmitted signal and detected echo. If the same transducer is used to send and receive the signal, then \( TOF \) includes the signal's round-trip time, needing to divide \( TOF \) by 2, as follows [33]:
\[
d = \frac{TOF \cdot c}{2}.
\] (2)

Ultrasound modes include Amplitude mode (A-Mode), providing one-dimensional information along one line of sight. Brightness mode (B-Mode) converts echo amplitudes into pixels/dots and with successive neighboring pulses generating scan lines, forms a 2D image. Motion mode (M-Mode) tracks the structures' movement along the beam path over time (e.g., arterial wall distension). The Doppler mode in diagnostic ultrasound relies on the Doppler effect, where an object's motion towards or away from a sound source causes a slight frequency shift in the received wave. This phenomenon is observed in everyday life, when, for example, an ambulance seems to change sound pitch when it passes observers on the road, as exemplified in Fig. 2 (e). In medical ultrasound, by analyzing backscattering signals of red blood cells in vessels, the Doppler effect can determine blood flow velocity, as it exhibits a frequency difference from the emitted wave. Doppler information is displayed through either a colorimetric map (Doppler overlaid on a B-Mode image) or spectral analysis.

1) Diameter calculation

The pulse-echo technique is employed for arterial diameter determination and distension waveform analysis. Commonly, vessel diameter is measured using calipers or edge-detecting software in B-Mode ultrasound images [46]. Naturally, by directly analyzing ultrasound echo signals in A-Mode, the distance between reflections of the vessel's anterior and posterior walls can be calculated for arterial diameter measurement [47]. Additionally, distances between inner and outer wall interfaces are measured to determine wall thickness (see Fig. 3). Various tracking algorithms can be used to determine the reference point, but their detailed discussion exceeds the scope of this work. For more comprehensive information, please refer to [47].

2) Flow velocity calculation

Blood flow velocity \( v \) is calculated in (3) using the Doppler shift equation, where the Doppler shift \( \Delta f \) is measured by
analyzing the difference in frequency between the transmitted and received ultrasound waves. The emitter frequency $f_0$ is known as it is set by the excitation signal of the ultrasound system. The angle of incidence $\theta$ is determined based on the direction of blood flow relative to the ultrasound probe.

$$v = \frac{df(t)}{2f_0 \cos \theta}$$

For accurate velocity estimation, it is crucial to use an angle $\theta$ less than $60^\circ$, as larger angles may lead to unacceptable errors in calculating flow velocity [33].

F. BP estimation

The underlying mechanism for the continuous estimation of BP through ultrasound entails the ongoing assessment and monitoring of the expanding arterial diameter and other pertinent hemodynamic characteristics. Subsequently, this dynamic assessment is algorithmically converted into BP waveforms, using mathematical equations. Typically, researchers have studied and used an exponential model (e.g., in [47, 48]), where a cuff pressure measurement is used as SBP and DBP calibration. It is assumed that the arteries are rotationally symmetrical due to the high transmural pressure, and thus the arterial vessel cross-section area $A(t)$ is obtained from $D(t)$, as in (4).

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

Consequently, the BP waveform $P(t)$ can be calculated through (5), where $\alpha$, calculated in (6), is the vessel rigidity coefficient, $A_D$ is the diastolic luminal area, and $A_S$ is the systolic luminal area.

$$P(t) = DBP \cdot e^{\alpha \left(\frac{A(t)}{A_D} - 1\right)}$$

$$\alpha = \frac{A_D \ln(\frac{DBP}{A_D})}{(A_S - A_D)}$$

While the exponential mathematical equation is commonly employed, numerous alternative models have been subject to investigation [49--52]. A comprehensive comparative analysis of these models was done for the first time in a study by Gonçalves Seabra et al. [53]. The study revealed that the optimal-performing model exhibits dependency on both arterial site and subject age. Interestingly, the most precise predictions for young simulated subjects (aged 25-35 years) were achieved using a simplistic linear model. Meuel et al. [54] compared the exponential model, as in (5), to the Moens–Korteweg algorithm, and similarly, both algorithms provide reproducible data with an accuracy that is superior to the validated commercial CNAP device (NSystems Medizintechnik GmbH, Austria). Both studies indicate ultrasonic BP measurement is a viable alternative for continuous hemodynamic monitoring.

G. Performance parameters in the transducer for specific target applications

The diameter, wall distension, position, and depth of the arteries and heart in the body need to be known a priori to determine the configuration and parameters of the ultrasound probes. A guide of performance and configuration parameters for small and large arteries, and deep organs is depicted in Table I [55--57]. In all cases, a beam bandwidth higher than 50% is required for image resolution and better interpretation of the acquisitions.

III. ULTRASOUND TRANSDUCER TECHNOLOGIES

Ultrasound wearables are being developed these days using either bulk piezoelectric, piezoelectric micromachined ultrasound transducers (PMUTs), or capacitive micromachined ultrasound transducers (CMUTs) [58--60]. The choice of a certain technology over the other for a specific cardiovascular application requires a deep knowledge of each technology itself, as well as the working principle, advantages, and constraints. In Section III-A and Section III-B, a description of the bulk PZTs, PMUTs, and CMUTs technologies and an overview of their parameters and performance are included. In Section III-C, a direct comparison of those three technologies,
with application to CVD assessment, and focus on integration, BW, and power consumption is discussed.

A. Bulk and 1-3 composite PZT

The emergence of new compact wearable devices calls for high-efficiency transducer technologies, with high acoustic coupling, low energy consumption, high SNR, and ultra-broad BWs at high ultrasonic frequencies. A major step forward in the ultrasonic field came from the discovery of lead zirconate titanate (PbZr$_{0.52}$Ti$_{0.48}$O$_3$, PZT) in the 1950s [61]. PZT is characterized by its high Curie temperature of $\sim$350°C, and high dielectric and piezoelectric properties. Bulk PZT ceramics are up to now a highly robust and established technology, and they are used for the fabrication of most medical ultrasonic imaging systems. The combination of flexible 1-3 composite ultrasound transducers with stretchable electrodes offers several advantages for wearable devices to measure BP: robust mechanical flexibility, relatively high $\sim$6 dB fractional BW of up to 49%, and transmitting sensitivity of 107 mV/V [62]. Due to their conformability and stretchable properties, these skin-worn sensors offer promising characteristics for the continuous monitoring of multiple biomarkers [63, 64].

The working principle of bulk PZT is based on an alternate tension-compression effect of the PZT material, as depicted in Fig. 4 (a). When an electrical source applies a high AC voltage on the two conductive plates of the transducer (made of chromium, gold, or platin, Cr/Au/Pt), the PZT crystal in between vibrate in a “thickness-mode” and produces the acoustic wave. Due to the high acoustic impedance difference between the PZT material and the skin, an acoustic matching layer needs to be introduced [65]. Otherwise, a high amount of the energy produced by the PZT will be lost or reflected, instead of being transmitted to the tissue.

Usually, multiple mechanical vibrations appear in the transmitted pulse, which strongly affects the final resolution of the acquired signals, particularly the axial resolution. Thus, “damping” of these undesired vibrations is necessary so that the transmitted pulse is shortened; this can be achieved by attaching a backing layer at the back of the ceramic [55, 66]. The backing layer also reflects the energy back to the front surface. In addition to the matching and backing layer, acoustical lenses can be attached to the front of the probe so that the signal is focused to a certain depth. Otherwise, it would be an unfocused ultrasound transducer, which is mainly used for attenuation measurements of materials such as tissue, liquids, and medical phantoms [67, 68]. When fabricating PZT transducers, the thickness of the PZT crystal and the matching layer is directly proportional to the wavelength of the operating ultrasonic frequency ($\lambda$/2 and $\lambda$/4, respectively) [65]. Thus, for wearables operating at extremely high frequencies, it is imperative to fabricate exceptionally thin layers, which makes the transducers highly fragile.

Furthermore, the European Union has raised significant concerns regarding the toxicity levels associated with the use of lead oxide in patient contact, considering the resulting contamination. Specifically, in invasive applications like intravascular ultrasound, lead is forbidden due to its direct contact with the patient’s body [69, 70]. As alternative materials must be used for the fabrication of ultrasound transducers, numerous researchers have explored lead-free materials that exhibit comparable properties to PZT.

B. Micromachined ultrasonic transducers

Micromachined ultrasonic transducers (MUTs) offer many new possibilities to ultrasonic technology. Since they are fabricated using microelectromechanical systems (MEMS), they can be easily integrated on-wafer with complementary-oxide-semiconductor process (CMOS) devices that will act as the transceivers of the signal that goes through the tissue. Thus,
parasitic effects due to connectors or interfaces between the transducer and the instrumentation circuit are highly reduced.

Furthermore, MUTs offer levels of flexibility in the design that are not possible to achieve with bulk PZTs. This is because the resonance frequency of the transducer does not depend only on the material thickness but on the whole geometry of the MUTs. On top of that, as MUT membranes vibrate in flexural mode, they have a much lower mechanical impedance and are better acoustically matched to biological tissue than ceramic PZT transducers [71]. This means that MUTs can be fabricated without any matching layer, reducing fabrication costs and time and improving the final performance of the wearable device.

1) Piezoelectric micromachined ultrasound transducers

With a similar working principle to the PZT, PMUTs are a promising type of MUTs. The structure sketch of PMUTs is shown in Fig. 4 (b). PMUTs are micro membrane ultrasound transducers that are backed by an acoustic cavity. The substrate is made of highly doped silicon and a protective insulator layer of silicon oxide is deposited over the cavity, to protect the bottom electrode [72]. The membrane of a PMUT is a multilayer structure formed by a piezoelectric active layer, that is stacked between two electrodes. This membrane is driven under an AC voltage that is applied between the bottom and top electrode, typically with values lower than 40 V. An electric field appears due to the AC voltage applied in the membrane, creating also a transversal displacement of the PZT-active layer. This PZT flexural movement creates pressure acoustic waves that is transmitted through the medium [70].

One important parameter to consider in PMUT fabrication is the thickness of the piezoelectric active layer. As the deflection of the membrane is due to the lateral strain produced by the piezoelectric effect, transverse dynamic strain should be avoided, and this is guaranteed when the PZT has a thickness under 3 µm [73]. Thus, thin-film-based devices are preferred over thick-film PMUTs, as they present better performance (they easily deform with low amounts of stress), better temperature coefficient, and more stability.

A scanning electron microscope (SEM) photograph of the layer-stacked cross-section of a PMUT is visualized in Fig. 4 (d) [58, 59]. The etched PZT/Pt/SiO2 layer-stacked is appreciated in the figure, as well as the Si membrane.

2) Capacitive micromachined ultrasound transducers

In contrast to PMUTs, the operation of CMUTs needs the initial application of a DC voltage between the top electrode and the substrate, as illustrated in Fig. 4 (c) [60, 74]. The DC voltage must always remain below the collapse mode, which occurs when the membrane comes into contact with the cavity bottom. The applied electric field subsequently propels the membrane downward, towards the bottom of the cavity. However, the induced stress within the membrane counteracts this attraction. Subsequently, an AC voltage is introduced, resulting in the generation of an AC current due to the membrane's flexural movement and associated capacitance variation. This phenomenon is responsible for producing the ultrasound signal. Similar to PMUTs, the substrate in CMUTs consists of a highly doped silicon substrate, whereas the cavity is formed by an oxide layer deposited on the substrate. The vibrating layer made of silicon is positioned atop the cavity, and the contact electrodes, typically composed of aluminum, are where the AC and radiofrequency (RF) signals are applied.

In Fig. 4 (e) the SEM image of the cross-sectional layers of a typical CMUT is depicted [59]. The cross-sectional view of the CMUT shows how the vacuum cavity, silicon plate, and aluminum layers are deposited on top of the substrate and the insulator oxide material.

C. Integration, assessment, and comparison of the properties of ultrasound technologies for CVD applications

The choice of ultrasound technology is determined by the depth of the biomarker or vital parameter that the wearable will acquire, as well as resolution, BW, SNR parameters, portability, and costs.

Regarding the application of both MUTs and bulk PZTs for portable devices, each exhibits distinct advantages and disadvantages, as outlined in Table II. Obtaining high resolutions at high operation frequencies is still the main challenge. CMUTs provide wide bandwidth [75] while still operating at high frequencies, which makes them suitable for applications where high axial and spatial resolution is required (for example catheters in intravascular ultrasound [70]). CMUTs have high power consumption, whereas PMUTs are attractive for portable devices due to low voltage requirements, high sensitivity, potential CMOS integration, and broad BWs [76–79]. Thus PMUTs, and concretely Aluminum Nitride PMUTs (low coupling coefficient), are promising technologies for hand-held and wearable ultrasound systems. However, PMUTs require further research for wearable applications as

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<th>Tech</th>
<th>Advantage</th>
<th>Disadvantage</th>
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<tr>
<td>Bulk PZTs</td>
<td>- Very robust and established technology.</td>
<td>- High power requirement.</td>
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<tr>
<td></td>
<td>- No DC bias required.</td>
<td>AC voltage of 100-200 V is required.</td>
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<td></td>
<td>- Highest transmit (Tx) sensitivity.</td>
<td>- Low receive (Rx) sensitivity.</td>
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<td></td>
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<td>- Lack of MUT: multiple chips cannot be produced in a single wafer. No mass production.</td>
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<tr>
<td>PMUTs</td>
<td>- Low power consumption (only AC voltage required).</td>
<td>- Reduced BW in comparison to CMUTs.</td>
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<td></td>
<td>- Possible integration with CMOS chips.</td>
<td>(However, a -3 dB BW of 118% was achieved in [55] and a -3 dB BW of 87% in [67] at a 1.5 MHz and 4 MHz center frequency, respectively.)</td>
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<td>- No acoustic matching layer is required.</td>
<td>- High frequencies limited by membrane thickness.</td>
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<td>- Fabrication design flexibility and portability.</td>
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<td>- Free choice of membrane geometry.</td>
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<td>- High Tx and middle Rx sensitivity.</td>
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<tr>
<td>CMUTs</td>
<td>- High integration with CMOS: less parasitic effects due to interconnections or cables to the front end, low weight, very compact devices.</td>
<td>- High power requirement (AC and DC voltage required). DC bias voltage of 30–100 V is required.</td>
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<td>- High BW (more than 100% at -6 dB BW): enhanced resolution and accuracy.</td>
<td>- Increment of BW with membrane thickness, but decrease of Tx (output) acoustic pressure and sensitivity [69].</td>
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<td>- Highest Rx sensitivity.</td>
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they are less established than CMUTs. In summary, CMUTs and PMUTs offer advantages over bulk PZTs, including miniaturization, integration, and low-cost high-volume production. Still, bulk PZTs remain widely used for portable cardiovascular monitoring [29, 48, 70, 80–82] due to their mature and well-known technology.

IV. TRENDS IN DEVICE DEVELOPMENT

The evolution of portable devices for non-invasively measuring vital parameters is shown in Fig. 5. The first portable method developed to acquire BP at the wrist employs oscillometric measurement [83]. The cuff, shown in Fig. 5 (a) [84], is inflated to the point of completely obstructing the blood flow in the radial/ulnar artery. Subsequently, a valve opens to gradually release the pressure within the cuff, resulting in its deflation. As a result, blood flow resumes, and the oscillatory sounds generated by turbulent flow in the artery are captured. By analyzing the temporal amplitude of these oscillations, the SBP and DBP can be determined [85]. The obstructive method used with the cuff is highly uncomfortable for patients due to wrist compression and is prone to errors such as incorrect cuff position or size, improper alignment of the measuring artery at heart level, and psychological factors, e.g., anxiety induced by cuff pressure or the white coat syndrome (elevated BP values when measured by a doctor). Even though the BP cuff remains accessible to the general public, is commercial and cost-effective for at-home monitoring, there is a growing trend in developing comfortable and miniaturized ultrasound wearables, including neck-brace-like structures, patches, tattoos, armbands, and watches [48, 82, 86, 87].

Envisioned by Shomaji et al. [82], the carotid IMT, lumen diameter, and abnormalities such as atherosclerosis and plaque formations could be detected by measuring the two carotid arteries on either side of the neck with CMUTs, as depicted in Fig. 5 (b). Since the carotid artery is connected directly to the left ventricle of the heart through the aorta, and also is the main supply (together with the vertebral arteries) of blood to the brain, it is a key vessel for the monitoring and prevention of several cardiovascular diseases. To guarantee good contact between the skin and the sensor, two nozzles automatically administrate acoustic gel before performing a measurement. The wearable concept in Shomaji et al. (2016) [82] remains theoretical and was not built. In Shomaji et al. (2019) [26], the project advanced using commercial PZTs instead of CMUTs, to eventually realize the envisioned project.

The relationship between stroke volume change and preload in the heart can also be effectively measured at the carotid artery by Doppler ultrasound. For this purpose, Kenny et al. [87] developed an easy-to-use, hands-free and commercial Doppler patch, depicted in Fig. 5 (c). For the use of the Doppler device, an acoustic coupling is required to ensure a good acoustic matching between the wearable and skin. The use of acoustic coupling can be avoided by creating conformable, flexible ultrasonic patches, such as the ones illustrated in Fig. 5 (d) [48, 88].

In Fig. 6, prototypes and commercial cardiovascular monitoring devices are illustrated. They are categorized into two main groups: rigid and full-integrable devices [87, 89]; and stretchable-conformable patches [63, 90].

The devices from Fig. 6 (d-l) are compared in detail with other recent ultrasound wearable systems in Table III. The table includes the integration’s level, PRF, excitation signal, transceiver system, data acquisition system (DAQ), as well as the algorithms used [29, 55, 62, 63, 76, 87, 90–92]. The design characteristics of the same devices are depicted in Table IV, which summarizes important factors to consider for the transducer design and performance, such as the technology used, resonance frequency, transducer configuration, BW, penetration depth, and axial resolution.

Most of the recent work on wearables ultrasound has focused on the integration of the transmitter/receiving ultrasonic system with the transducer array into a single device, as appreciated in Table III. However, this is not always possible, and it mainly depends on the excitation voltage that the transducer requires to operate and on the receiving system and signal-processing requirements to obtain high-quality read-outs.

A. Hardware integration and stable placement

While this manuscript focuses on ultrasound wearable technology, it is important to recognize the broader landscape of smart devices for cardiovascular health monitoring. Within this context, and although the gold standard is the cuff BP measurements at the brachial artery, BP can be also measured at the fingertip, at the transverse palmar arch artery [89]. Fig. 6 (a) illustrates an integrated mobile phone solution based on the combination of force transducers, PPG, and the oscillometric principle.

Moreover, in the scope of this review, it is noteworthy that novel integrated ultrasound-based wearable devices have been successfully developed. The primary challenge lies in optimizing the trade-off between compactness and data quality.

---

The figure shows a comparison of different wearable devices. The legend indicates the types of devices, including oscillometric, ultrasound, and other related technologies. The devices are categorized into different groups, such as commercially available and research prototypes. The figure highlights the evolution towards more flexible and comfortable designs, with examples of integrated mobile phone solutions and ultrasonic patches. The text accompanying the figure provides a detailed explanation of the various technologies and their applications in cardiovascular monitoring.
Beyond that, the systems are also expensive due to the circuit and signal processing complexity. As seen in Table III, in most of the ultrasound wearable approaches the transducer is not fully integrated with the ultrasonic transceiver system. That means that ultrasonic systems, such as the Vantage 64, pulser-receiver systems like the 5900PR, and 5077PR, or evaluation boards such as the VCA5807 are externally connected to the transducer. Later on, the signals are digitalized with a DAQ (in most cases with Picoscopes) and the images and physiological signals are constructed and post-processed through an external computer. This is always the case for flexible and stretchable patches as the ones illustrated in Fig. 6 (g, j). Thus, the devices shown in Table III (except the Doppler patch from Kenny et al. [87]) are still in the prototype or research phase, where further integration research on the external devices will move these devices from the benchtop to the bedside. Fully integrated wearables in the market are available only for Doppler ultrasound. The wearable Doppler patch by Flosonics Medical (Sudbury, ON, Canada) [87], shown in Fig. 6 (d), provides direct readings of stroke volume and estimates cardiac output. Moreover, it remains attached to the neck during the duration of the measurement, avoiding errors due to “skill-dependent” positioning of the probe [93] and the angle of insonation remains uniform throughout the measurement. Hence, temporal velocity variations remain unaffected by erroneous nominal angle of insonation values. The only trade-off arises from the device’s packaging in a rigid gasket, which renders it unusable at any other arterial site. Flexible, bioadhesive, and comfortable ultrasound patches, as illustrated in Fig. 5 (d) and Fig. 6 (g, j), overcome the rigidity issues [48]. These devices can monitor vital parameters even on curved and irregular surfaces, where the linear ultrasonic probes will lose contact at the edges (e.g., elbow, knuckle, wrist, neck, and joints). Due to the fixed attachment of these patches to the

![Fig. 6. Latest wearable devices to measure blood pressure, blood flow, stiffness, monitor organs, and other biomarkers. The wearables are divided into two categories: rigid, full-integrated devices; and flexible, conformal patches. (a) Wearable solution of the oscillometric method using a mobile phone and the fingertip. (b) Results from the applied finger pressure. (c) Oscillometric measurements of the BP, including SBP, DBP, and MAP. (d) Device to measure the stroke volume variations at the carotid artery from Flosonics Medical. (e) Internal visualisation of the device. (f) Acquisitions of the pulse wave Doppler measurements. (g) Ultrasound wearable patch array that maintains the adhesion to the skin over 48 hours. (h) Rigid ultrasound probe attached to the curved skin through a bioadhesive, soft and antidehydrating hydrogel elastomer couplant. Color flow doppler imaging obtained from the patch in (h). (i) Multimodal patch to monitor blood pressure and biomarkers from the sweat and the derma in the skin, such as glucose, caffeine, and interstitial fluid (ISF). (j) Working principle of the cathodes, anodes, and ultrasound transducers for the acquisition of the vital parameters. (k) Examples of physiological signals measured. Images adapted from [89, 78, 88] and reused with permissions. All images are produced with the license Creative Commons Attribution 4.0 (CC BY 4.0 DEED) [74].]
### TABLE III

<table>
<thead>
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<tbody>
<tr>
<td>Fully integrated</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Mechanical property</td>
<td>Rigid</td>
<td>Strechable patch</td>
<td>Rigid patch</td>
<td>Strechable patch</td>
<td>Rigid</td>
<td>Flexible</td>
<td>Rigid</td>
</tr>
<tr>
<td>Contact gel</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No, bioadhesive hydrogel elastomer couplant</td>
<td>Yes</td>
</tr>
<tr>
<td>Excitation signal</td>
<td>One pulse Vpp=10 V</td>
<td>Pulses</td>
<td>CW (Carotid) PW (Aorta)</td>
<td>Pulse Vpp=100-200 V</td>
<td>Pulse Vpp=90 V</td>
<td>Pulse 4 µJ</td>
<td>Four pulses Vpp=40 V</td>
</tr>
<tr>
<td>PRE (kHz)</td>
<td>0.2</td>
<td>NA</td>
<td>Continuous</td>
<td>5</td>
<td>NA</td>
<td>200</td>
<td>1</td>
</tr>
</tbody>
</table>

### Transceiver system

- **ArbStudio 1102 waveform generator** (Teledyne, Inc., Chesnut Ridge, NY, USA), VCA 5807 evaluation board (Texas Instruments, Dallas, TX, USA), Gain=42 dB
- **Costumed PCB paired wirelessly with tablet**
- **Vantage 64** (Verasonics, Kirkland, WA, USA)
- **Vantage 64** (Verasonics, Kirkland, WA, USA)
- **5900PR** (Panametrics Inc., Waltham, MA), BPF=1-20 MHz
- **Costumed PCB paired wirelessly with tablet**
- **Picoscope443B** (Pico Technology, Cambridgeshire, UK), Sampling frequency, F<sub>s</sub>=31.2 MSPS
- **Picoscope6000** (Pico Technology, Cambridgeshire, UK), Vantage 64, FIR filter added to improve image quality
- **Vantage 64** (Verasonics, Kirkland, WA, USA)
- **Picoscope6000** (Pico Technology, Cambridgeshire, UK), Vantage 64
- **Picoscope6000** (Pico Technology, Cambridgeshire, UK), F<sub>s</sub>=80 MHz
- **Picoscope6000** (Pico Technology, Cambridgeshire, UK), F<sub>s</sub>=80 MHz (12-bit)
- **Microcontroller**
- **NXP M4 microcontroller**, F<sub>s</sub>=80 MHz
- **STMicroelectronics**, Geneva, Switzerland
- **LFP=8 MHz**, Gain=40 dB
- **LPF=8 MHz**, Gain=40 dB
- **DAQ**

### Algoithms

- **Velocity**: autocorrelation
- **Arterial motion**: integration of filtered (BPF 0.3-11 Hz) velocity
- **HR**: FFT of arterial motion waveform
- **T0F**: signal of best transducer, BP: exponential equation (5)
- **Flow velocity**: FFT
- **BP**: exponential equation (5)
- **T0F**: peak detection
- **BP**: exponential equation (5)
- **Raw signal**: Butterworth
- **BPF=1-8 MHz**, TGC
- **T0F**: covariance and correlation method
- **BP**: novel algorithm [91]

*Fs*: sampling frequency; **NA**: not available; **CW**: continuous wave; **PW**: pulsed wave; **LPF**: lowpass filter; **BPF**: bandpass filter; **HR**: heart rate; **FFT**: fast Fourier transform.

In contrast, with PZTs, the typical voltages begin at around 90 V, with 100 V for high SNR [48, 90], with a power density in human tissue (derived from hydrophone measurements) of 0.47 W/cm² in [90]. However, in the PZT-based system ARTSENS [91], the AC voltage was kept to a minimum of 40 Vpp (average power consumption of 410 mW), granting a feasible integration of the circuit (sender/receiver) with the transducer. The DBP root-mean-square error (RMSE) of ARTSENS was 8.3 mmHg.

### C. Technologies and working frequencies

The first and second rows of Table IV present information regarding the material composition and operational frequencies of ultrasound wearables. As depicted in the first row, piezoelectric transducers remain the predominant technology for vital parameter acquisition, owing to their established maturity and high piezoelectric coupling coefficients. Additionally, the manufacturing costs associated with piezoelectric transducers are lower, and the fabrication process is more straightforward and robust when compared to CMUTs [43]. CMUTs pose processing challenges due to their low Curie

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skin, not only “skill-dependent” errors but even involuntary movements of the user do not introduce significant errors during continuous monitoring. The patch is simply attached to the skin during the measurement and, in some of the cases, as shown in the “Contact gel” category in Table III, it does not require an external ultrasonic coupling agent, such as an acoustic gel. For example, as depicted in Fig. 6 (g-h), a thin layer of silicone elastomer (also used for encapsulation) may act as the coupling layer, and, due to its adhesive behavior, it also guarantees intimate contact even from a rigid probe with the epidermis [58].

### B. Power requirements according to technologies

Unlike CMUTs, PMUTs require low AC voltage, which is an important advantage as it leads to a decrease in energy consumption, and reduces the size and weight of the final wearable device. As seen in Table III, Jiang et al. [76] present a PMUTs’ stretchable approach. One pulse of 10 Vpp is enough to excite the sender transducer and to get reliable and high-quality readings with a spatial resolution of up to 5 µm for arterial tracking and standard deviations (SD) of only 0.35 µm.
point, while piezoelectric ceramics exhibit superior electromechanical performance and ease of processing. Nonetheless, some approaches employ PMUTs [76], primarily for their low operating voltage requirements. Consequently, power consumption is minimized, and PMUTs can be seamlessly integrated into a single wearable device.

The choice of the working frequency is mainly determined by the desired penetration depth, as the resonance frequency of the transducer is inversely proportional to the penetration depth. Wearables for monitoring peripheral vessels, such as the carotid artery, radial, and ulnar artery should operate at frequencies above 4 MHz. However, if the wearable is to monitor internal organs, frequencies of around 2 MHz should be chosen, with a consequent resolution reduction.

D. Advantages of multi-modal devices

In Tables III-V, bi-modal (P M et al. [91]) and multimodal devices (Sempionatto et al. [63]) are shown. With multimodal approaches, the wearable contains various sensor technologies that are used to monitor vascular signals or diseases that the other sensor technology cannot.

The standout feature of the P M et al. [91] wearable lies in its pioneering use of a bi-modal methodology, combining optical devices (PPG) with ultrasound technology. The added advantage of the bi-modal approach is the complete elimination of the cuff and the achievement of continuous BP measurements. Without using the cuff, patient comfort and reliable measurements without changing the physiology of the artery are guaranteed. To our knowledge, up to date, this is the only multimodal device based on ultrasound and PPG for cuffless BP measurements.

Another multimodal approach is the one depicted in Sempionatto et al. [63]. An epidermal patch that combines PZT transducers with biosensors is enabled for the simultaneous monitoring of BP, heart rate, and various metabolic biomarkers. The difference to the previous bi-modal approach is that this wearable is stretchable, flexible, and can acquire multiple numbers of physiological parameters so that a better diagnosis of the health status of the patient can be made. However, the only inconvenience is that the BP measurement needs to be calibrated with another extra device.

E. Factors influencing measurement accuracy and resolution

The conformable, flexible, and light patches produced by Peng et al. and Wang et al achieve an impressive accuracy for in vivo BP acquisition of under 2 mmHg [29,48]. The flexible 80-element piezoelectric array obtained a biased error of 0.004 m/s and a precision error of 0.0047 m/s for end-diastolic velocity (EDV) measurements at the carotid artery. In all these three cases, the patches are fabricated in an array configuration of various PZTs that are connected throughout stretchable electrodes and filled with either polydimethylsiloxane (PDMS) or other silicones (see encapsulation in Table IV). The main reason for these highly accurate readings lies in the comfortable and conformable properties of these patches that ensure full contact even on curvilinear and round skin surfaces.

Furthermore, as the spatial and temporal resolution are determined by the sampling frequency $Fs$ and by the PRF, respectively, elevated values of $Fs$ and PRF increase the accuracy of the vascular readings. The effective spatial

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**TABLE IV**

<table>
<thead>
<tr>
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<tbody>
<tr>
<td>Ultrasound frequency (MHz)</td>
<td>5</td>
<td>7</td>
<td>4</td>
<td>2</td>
<td>3, 7, 10</td>
<td>5</td>
</tr>
<tr>
<td>Phased array</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes, No, No</td>
<td>Yes</td>
</tr>
<tr>
<td>Number of elements</td>
<td>12 x 12</td>
<td>1 x 8</td>
<td>2</td>
<td>12 x 12</td>
<td>40 x 2, 40 x 2, 40 x 2</td>
<td>14 x 12</td>
</tr>
<tr>
<td>Pitch (mm²)</td>
<td>0.0085 x 0.0085</td>
<td>1.1 x 4</td>
<td>NA</td>
<td>0.55 x 0.55</td>
<td>0.5 x 0.5, 0.55 x 0.5</td>
<td>0.35 x 0.35</td>
</tr>
<tr>
<td>Active aperture (mm)</td>
<td>1.5</td>
<td>9.4</td>
<td>23</td>
<td>6.6</td>
<td>20, 20, 20</td>
<td>6</td>
</tr>
<tr>
<td>BW (%)</td>
<td>20</td>
<td>NA</td>
<td>NA</td>
<td>24.58</td>
<td>68, 75, 78</td>
<td>47.60</td>
</tr>
<tr>
<td>Encapsulation</td>
<td>PDMS</td>
<td>SEBS (1645: Kraton Corporation, Texas, USA), Ecoflex 00-30 (Smooth-on Inc, USA)</td>
<td>Non-conductive epoxy</td>
<td>Ecoflex silicone</td>
<td>Epoxy layer</td>
<td>PDMS</td>
</tr>
<tr>
<td>Focal depth (mm)</td>
<td>60</td>
<td>NA</td>
<td>23</td>
<td>14</td>
<td>60, 30, 20</td>
<td>20</td>
</tr>
<tr>
<td>Axial resolution (mm)</td>
<td>0.005</td>
<td>NA</td>
<td>NA</td>
<td>2.5-2.7</td>
<td>0.77, 0.225, 0.193</td>
<td>NA</td>
</tr>
</tbody>
</table>

NA: not available; PDMS: Polydimethylsiloxane.
CV: cardiovascular

For arbitrary values $F_S=50$ MHz and speed of sound $c=1540$ m/s, a maximum effective resolution of 30.8 $\mu m$ ($d_{y\text{min}}$) can be achieved. The results of [29] demonstrated a resolution of 45 $\mu m$ in arterial diameter, which is very close to the calculated theoretical value. In [48], as the sampling frequency is increased to 2 GHz, precise vessel wall tracking with a spatial resolution of 0.77 $\mu m$ can be theoretically achieved.

The temporal resolution ($d_{x\text{min}}$) is determined as follows:

$$d_{x\text{min}} = \frac{1}{PRF}.$$ (8)

For $PRF=200$ Hz, a temporal resolution of 5 ms can be obtained, as in [29]. A high $PRF$ of 2 kHz increases the ultrasound temporal resolution to 0.5 ms, i.e. 2000 ultrasound pulses are launched in one second, and 2000 points of the diameter waveform can be recorded in one heart cycle (for subjects with 60 bpm) [48].

Spatial and temporal resolution, together with the sensitivity of the system (given by the SNR) and the transducer frequency, are relevant for the accuracy of A-Mode ultrasound. For B-Mode, the beamwidth at the measured depth and the spatial pulse length (SPL) are other additional factors that determine the spatial resolution. B-Mode’s spatial resolution can be categorized into axial, lateral, and elevational resolution. The axial resolution increases when a shorter excitation pulse is applied to the transducer (lower SPL), calculated as [94]:

$$d_{x\text{min array}} = \frac{SPL}{2}.$$ (9)
The axial resolution also increases with the working frequency, as seen in Table IV. In Wang et al. [58], three kinds of transducer arrays have been developed, the transducers operating at 2 MHz presents an SPL of 1.54 mm, i.e. an axial resolution of 0.77 mm, while the transducer operating at 7 MHz has an SPL of 0.385 mm, i.e. an axial resolution of 0.193 mm. However, as previously mentioned, when increasing the frequency, the penetration depth decreases as well. Lateral resolution is determined by the active aperture diameter of the array, while the elevational resolution is determined by the passive aperture of the array.

F. Constraints to achieve reliable measurements

When working with stretchable devices, it is vital to report mechanical deformation testing, as exceeding deformation limits can compromise sensor measurements due to track breakage, track deformation, or transducer element misalignment. Table V (last row) highlights the conducted tests on stretchable sensors under review. Sempionatto et al. [63] demonstrated their sensor’s resilience through 200 cycles at 20% strain, enduring various deformations including neck movement. They noted stretching as the most stressful, mitigating electrode abrasion with hydrogels. Wang et al. [90] addressed accurate beamforming challenges under various strain scenarios, ensuring reliable performance at 20% strain. Additionally, Peng et al. [29] observed minimal changes in sensor properties after 10 bending cycles at a ~10 mm radius.

Although the stretchable patches in Table V achieve the highest accuracy in BP and blood flow readings, they are not “fully” wearable ultrasound devices. These patches need to be externally connected to commercial pulse/receiver systems through flexible flat cable (FFC). In addition, the signal processing is not real-time but relies on additional post-processing systems (e.g., Picoscope, LabView, or Matlab) for the conversion of the ultrasound echoes into hemodynamic signals. The lack of integration lies in the compromise between accuracy and processing speed. High accuracy needs high SNR (determined also by the amplitude of the sent signal), high processing speeds and computational resources, and bulky batteries for the transducers’ activation. Thus, the accuracy needs to be reduced to achieve light and highly integrated wearable devices.

V. VALIDATION OF SENSORS

Section V provides a comprehensive overview of the Technology Readiness Level (TRL) progression for novel ultrasound wearable technology for cardiovascular monitoring. The TRL assesses technology maturity from concept (TRL 1) to full deployment (TRL 9), guiding development and testing stages [96], as depicted in Fig. 7. Since conducting human clinical trials is neither feasible nor ethically acceptable during the initial proof-of-concept studies (TRL 3), it is recommended to perform experimental calibration and validation of novel systems within a laboratory environment (TRL 4). Once high fidelity is attained, the technology can advance toward clinical trials (TRL 6-8). This section navigates through laboratory studies, culminating in in vivo validation protocols. Exemplary studies of emerging devices are presented, contributing to the manuscript’s clarity and consolidation.

A. Types of laboratory studies

The validation and testing of sensors can occur at various levels of environment specificity, depending on the type of study and the device’s development phase. Nowadays, computer simulations, also known as in silico studies, often serve as the initial validation phase. For instance, in the case of ultrasound sensors, simulations can involve analyzing the acoustic field of a piezoelectric sensor using MATLAB (MathWorks, Massachusetts, USA) [90]. Similarly, for proof-of-concept studies on BP devices, simulated hemodynamic pulse waves may be processed to estimate BP [53, 97]. These examples showcase the capabilities of in silico studies, with the only limitation being the scientist’s creativity and ingenuity.

The subsequent phase of testing typically involves an in vitro study, and optionally, an ex vivo study. In the field of non-invasive BP devices, in vitro studies pertain to device tests using a technical model of the cardiovascular system (CVS), where centrifugal pumps and silicone tubes are used to simulate hearts and arteries, respectively [97]. These in vitro studies aim to replicate in vivo conditions using non-biological materials, offering a controlled environment for tuning different (patho-) physiological cardiovascular conditions to specific validation requirements. The exciting potential lies in the creation of patient-specific models, enabling the replication of diverse arteries characterized by numerous bifurcations, varying thicknesses, and distinct stiffness profiles [98, 99]. Moreover, the precise simulation of tissue thickness variations can be achieved through the use of biocompatible hydrogel phantoms.

The phantoms, employing flexible materials like polyvinyl alcohol cryogel (PVA-C), offer reliable means to assess arterial and tissue stiffness with accuracy [100]. On the other hand, ex vivo studies employ similar in vitro CVS models, but they integrate tissues or organs from an organism (e.g., porcine arteries instead of silicone tubes) that have been extracted post-mortem, thus creating an environment with minimal alteration of natural conditions [101].

Table V showcases a myriad of validation studies, summarizing the validation procedures conducted on state-of-the-art ultrasound wearable devices. For instance, Jiang et al. [76] employ in vitro validation by demonstrating the PMUT’s ability to track a mounted rigid target that models the radial artery movements. The device achieved 0.35 µm SD of the extracted full displacement, comparing well with the programmed motion profile. Similarly, Kenny et al. [87] validated their CW Doppler sensor using a tissue-mimicking flow phantom, and blood-mimicking fluid, obtaining excellent absolute measurement accuracy after implementing a small correction (≤2°) in the insonation angle.

Fig. 7. Technology Readiness Levels according to Horizon 2020 showcasing validation types at different development stages [96].
B. In vivo validation protocols

The final validation of the sensor before it can be used commercially is done through in vivo studies, which should go in hand with a standardized protocol. Standards for the validation of BP devices have existed since 1987 when the Advancement of Medical Instrumentation (AAMI) created its first protocol for cuff sphygmomanometers [102]. During the next two and a half decades, the standard was followed by the British Hypertension Society (BHS) protocol in 1990 [103], the German Hypertension League protocol in 1999, the International Protocol by the European Society of Hypertension (ESH) in 2002 [104], the International Organization for Standardization (ISO) protocol in 2009, and the Universal Protocol (ISO 81060-2:2018) [105] by AAMI/ESH/ISO in 2018, all with associated revisions and amendments [106].

Most of the standards, such as the Universal Standard, indicate a minimum of three tests with non-invasive BP devices and 85 subjects, with multiple pairs of measurements (more than 255) to a reference device. Validation is conducted against the mean readings of two trained observers from a mercury sphygmomanometer, or, in the later standards, an aneroid one. Apart from the BHS standard, all other standards consider a BP device approved if its Mean Absolute Error (MAE) and SD are less than or equal to 5 mmHg and 8 mmHg, respectively. The BHS introduced a grading system from Grade A to Grade D based on the percentage of test measurements deviating from the reference by 5 mmHg, 10 mmHg, and 15 mmHg. Grade C represents deviations of 40%, 65%, and 85% for 5 mmHg, 10 mmHg, and 15 mmHg, respectively, whereas Grade D indicates worse performance than Grade C (Supplementary Information, Table S11) [103]. According to BHS guidelines, devices rated as Grade C and Grade D are not recommended for use. Note that the pass/fail assessment is unique to SBP, DBP, or MAP. The standards might differ in subject criteria (e.g., age, sex, arm circumference, entry BP ranges), or the validation procedure (e.g., sample size, number of tests, recommendation of special groups), but all are to be applied only in cuff devices [107].

Cuffless BP monitoring surged in 2005 [108], researchers applied the above-mentioned standards to validate the cuff-free non-invasive BP devices, even if the procedure was aimed at cuff-based devices [109]. Long overdue, in 2018 there was a consensus from the AAMI/ESH/ISO stating the need for separate validation protocols for continuous, cuffless, and central BP monitors [110], and whilst the majority of articles claim to have validated their novel device, too often no appropriate protocol has been followed. It was only in 2014 that the Institute of Electrical and Electronics Engineers (IEEE) released the first protocol for, as the name implies, “Wearable, Cuffless Blood Pressure Measuring Devices” [111]. Even with its amendment in 2019 [112], the standard hasn’t been widely used in research, perhaps because the standard has practical difficulties, such as a lack of protocol details to ensure standardization, and does not cover continuous BP measurement [108, 113]. Regardless, the validation process is divided into two phases to avoid unnecessary waste of time and money, as only when the test device passes the first phase with more than 20 subjects, does the second phase start with more than 65 subjects. Therefore, the total of subjects from the previous standards is maintained (at least 85 subjects), as in ISO 81060-2 standard, for example [112]. To pass, the mean absolute deviation (MAD) should be lower than 6 mmHg for SBP and DBP, separately. Furthermore, IEEE 1708 closely follows the Universal Standard (ISO 81060-2) on general and special population descriptions required for testing (Supplementary Information, Table S12).

In December 2022, ISO released a protocol for continuous, non-invasive BP sphygmomanometers’ validation (ISO 81060-3:2022), which controversially features the validation of the novel device with a simultaneous reference for invasive BP measurement [114]. The reasoning behind it is that a cuff-based reference is not quick enough to track and measure continuous, per heartbeat, quick BP changes, and therefore is not suitable to validate continuous BP monitoring. Applying the standard, where invasive BP serves as a reference, for devices designed for hospital use is logical, as demonstrated by Livemeterics’ LiveOne watch [17]. Yet, this approach becomes challenging for everyday smart wearables outside hospitals. ISO regulations limit using invasive BP measurements alone for validation due to the significant risks involved in invasive methods [113]. In addition, the goals of antihypertensive therapy are defined from cuff measurement values, and, as it is known that BP values have substantial differences between invasive and upper arm cuffs (direct and indirect measurement methods), the comparison of an invasively validated novel device to the reference hypertension values would be at fault [108].

Most cuffless devices are calibration-based, and for accurate use, the device needs a periodic recalibration disclosed by the manufacturer (e.g., every day, week, or month). Due to this constraint, where the calibration greatly impacts the accuracy of the device, the validation procedure for each subject should start with a static test, followed by a test with BP change from the calibration point, and a test after a certain period from calibration (stability test) [112, 113]. Another issue often ignored is the study of intraindividual correlation, because whereas the overall pool of measurements might show a strong correlation between test and reference, the intraindividual correlation may be close to zero [108]. A lack of adherence to standardized protocols is evident in all examined studies (Table V) related to BP assessment, often referring to compliance with protocols established by the respective research institutions. Sempionatto et al. [63] validate BP estimation using a cuff measurement but lack detailed subject information and error analysis. Peng et al. [29] validate their novel device using two methods: comparing the distension waveform with a commercial ultrasound probe and estimating BP against a commercial cuff. However, their validation is rudimentary, involving only one participant and 5 seconds of data, compared to 40 consecutive cuff measurements. Lastly, P M et al. [91] validate BP estimation with 83 participants (both normo- and hypertensive, 76% male and 24% female), nearing the sample size and sex distribution required for the Universal Standard (at least 85 participants, and least 30% male and 30% female, respectively). Despite not citing a standard, the validation to a reference BP cuff is comprehensive and well-executed. Wang et al. [48] claim their patch meets Grade A criteria from the BHS protocol, as 100% of their measurements are within 5 mmHg (for Grade A, ≥60% of test measurements need to be below 5 mmHg, ≥85% below 10 mmHg and ≥95%
below 15 mmHg; see Supplementary Information, Table SI1). However, they tested only three subjects instead of the required minimum of 85 participants to comply with the protocol. This further underscores the imperfect adherence to protocols, even when standards are referenced.

To the best of our knowledge, there are presently no standards for the validation of other cardiovascular parameters, such as flow velocity. Usually, researchers must abide by in vivo protocols approved by the respective research institutions, but the description of these documents is often omitted in research papers and the validation results are either shallow, with a qualitative assessment instead of a quantitative, or altogether missing. Wang et al. [90] validate the developed stretchable sensor by calculating the biased and precision error of peak systolic velocity (PSV) and EDV and revealing them comparable to the commercial device. Whereas Wang et al. [55] developed a rigid adhesive patch that successfully tracks cardiovascular parameters for up to 48 hours in vivo, yet, they did not validate it to a reference device.

VI. DISCUSSION

This article provides a tailored review of ultrasound technologies for cardiovascular health monitoring, specifically BP estimation. Whereas other techniques, such as PPG, electrocardiogram, or a combination of modalities, are more established and researched, ultrasound could provide a more robust usage due to its configurable wide and deeper beam field, providing vitality insights to inner structures and arteries. However, the integration of ultrasound in a wearable device is challenging, namely due to the high voltage needed to drive the sensors. This problem can be reduced through newer and less power-consuming transducers such as PMUTs. However, CMUTs are preferred for imaging due to their higher BW, even if the sender/receiver system is not fully integrated but externally connected to them through FFC [55]. Fig. 8 provide a comprehensive parameters comparison of the technologies, based on the information provided in this manuscript and the authors’ perspectives (Supplementary Information, Table SI3). It indicates both the advantages and disadvantages of each technology, while also recommending the characteristics of an ideal ultrasound technology suitable for wearable applications.

Ultrasound sensors are also characterized by low impedance matching to the skin surface, usually demanding the use of acoustic gel to minimize impedance mismatch and, consequently, produce less signal attenuation. Researchers have developed patches with the transducer incorporated into a silicone that acts as the impedance-matching layer, rendering the acoustic gel unnecessary.

Attaining and maintaining the correct sensor position is a key challenge, as the focus zone can be small, and the structure might not be easy to locate. When using a matrix of sensors, it is possible to choose the sensor best aligned to the vessel through signal analysis and use it as the sole data-acquiring transducer [115]. Moreover, novel flexible, stretchable, and skin-worn patches maintain the ultrasound wearable at the same position. The conformal device in Baek et al. [115] enables continuous BP monitoring at the radial artery with small uncertainty (1%) even while bending the wrist.

Usually, multiple sensors are used, with the possibility of integrating different technologies, combining the modalities of PPG and electrocardiogram, or ultrasound. Whilst the discussion of such pairings is outside the range of this review, as we provide a review of solely ultrasound-based wearables, it is worth mentioning that one of the goals of these multimodal sensors is to calculate regional PWV and determine its power as an indicator and predictor of vascular health. Another application of single and multiple-modal modalities is the extraction of features from the biosignals to be input parameters into ML and deep learning models used to estimate BP waveforms, which have been reviewed in [116, 117]. Whereas various techniques have been suggested as alternatives to the invasive process of measuring BP waveforms, a dependable commercial device remains unavailable at present. International validation protocols for continuous BP assessment have recently been created, but their use is either inadequate or arduous, even if essential. It is up to researchers and manufacturers to create a diligent stature on systems validation in the years to come. A multitude of research questions remain open and are summarized in the ESH 2022 statement which emphasizes the need to develop an internationally accepted standard specific to cuff-free non-invasive BP devices. Until all points have been addressed and devices are appropriately tested, the ESH does not recommend the use of continuous or intermittent cuffless devices for the diagnosis and management of hypertension [108].

Continuous monitoring is advantageous with unobtrusive devices and with approaches that do not disturb natural behavior and sleeping conditions. This minimizes disruptions and ensures more accurate measurements compared to methods that alter normal behavior. In summary, ultrasound offers insights into pressure and blood flow dynamics with the possibility of portability and miniaturization, making its role in cardiovascular health remarkable. Wearable ultrasound devices become feasible with the advancements in miniaturization technology addressing the power requirements of ultrasound. Imagine the potential of continuous monitoring providing a deeper understanding of our bodies’ rhythms throughout the day.
and night. It is not just about data; it is about the prospect of improved quality of life. These developments are not just scientific breakthroughs; they are steps towards a healthier future for all.

VII. FUTURE DEVELOPMENT: CHALLENGES AND TRENDS

Ultrasound shows promising advances for non-invasive, wearable cardiovascular monitoring. However, there are still some challenges that researchers, engineers, and clinicians need to address for successful translational adoption and global acceptance of wearable ultrasound. The most critical technical demands and challenges are the following:

1) Safety and comfort

As ultrasound wearable devices should perform continuous measurements for long periods (in-home monitoring), the comfort and safety of the patient are non-negotiable. Stretchable and conformal patches are more comfortable for the user than rigid devices. However flexible devices are less robust and reliable than rigid ultrasound devices. In terms of safety, the thermal index in phantoms can be validated in vitro with phantoms, and the temperature absorbed by the skin should be continuously measured in vivo (for example with thermo patches [118]).

2) Standardization

This is only possible when society is aware of the potential of ultrasound, people know how to use it, and easy methods to interpret the vascular images are implemented for in-home monitoring (for example with ML). Moreover, well-designed and large clinical trials are required for standardization. Physicians and engineers should promote awareness of ultrasound wearables through dissemination and offering workshops to the employees.

3) Power requirements

Batteries are the main constraint for a wearable, lightweight, and comfortable device to be produced. Technologies that require low power consumption (such as PMUTs) should be further developed and used. Moreover, methods to save energy such as duty cycles (turn on and turn off the device every minute for example), multiplexing, modulating the signal to reduce the sampling rate, and post-processing data in the cloud can save huge amounts of energy demands. Power harvesting produced by multiple sources may extend the battery life of wearable devices. Piezoelectric sensors can store the energy produced by movements in the joints and deliver it to the wearable ultrasound patch [119]. The integration of microgrid harvesters into e-textile platforms shows also promising results for power harvesting [120].

Energy harvesters might need to be combined with energy storage devices such as rechargeable batteries or supercapacitors to result in fully standalone platforms. Stretchable supercapacitors greatly increase the energy density in comparison to lithium-ion batteries and offer an elastic modulus closer to the skin and tissues than rigid supercapacitors. Thus, flexible supercapacitors are promising power storage units for future technological generations of bioelectronics [121].

4) Wireless communication

Most of the emerging devices reviewed in this article are still wired for power supply and data transmission. Solving the issue with the power supply will also make possible a wearable and wireless ultrasound device. For a more practical use at home, the data measured by the wearable can be sent to the personal phone via Bluetooth or the Internet. Methods to reduce the data transmission rates are required to not exponentially increase the power demands due to wireless communication.

5) Privacy and security

Wireless communications, save the data on the cloud, share your data with the hospitals. All of those steps should go through strong protocols of privacy and security. The user should be aware of the importance of privacy and what happens when the data is transmitted between devices, saved, and stored in the cloud. Bluetooth and other wireless communication methods are not encrypted, but encryption of the data should always be implemented. The use of processing techniques, such as Federated Learning, Homomorphic Encryption, and TinyML, strengthens security and privacy [122].

6) Materials for wearable devices

The use of biomaterials (such as silicone encapsulation, silicone elastomers, and polyurethane) for the contact between the ultrasound and the skin is a must, as any kind of irritation or allergies in the skin should be avoided. Moreover, the creation of couplings based on hydrogel encapsulated by elastomer membranes and coated by thin bioadhesive layers makes possible robust adherence of rigid probes to the curvature of the skin [55]. Three-dimensional printing, photolithography, and laser techniques promote the fabrication of flexible and 3D freeform surfaces that offer promising conformability to the skin [55, 123, 124].

VIII. CONCLUSION

In this review, we surveyed the outcomes, innovations, and limitations of stretchable and wearable devices based on ultrasound to continuously monitor vascular parameters. For a better understanding, a deep analysis of the various technologies (piezoelectric, PMUTs, and CMUTs), hardware, signal processing and algorithms, design parameters and resolution, and validation protocols required to validate proof-of-concept wearable devices is included. Comparative assessments have been conducted between ultrasound and alternative wearable sensor modalities, such as PPG and oscillometric cuffs. Ultrasound offers multiple advantages in terms of accuracy, portability, and penetration depth, with high potential in the monitoring of diverse vascular parameters. However, its integration into a wearable is limited, due to its high-power consumption, hardware complexity, and lack of compliance with international standards for BP estimation. Although there has been an impressive development in ultrasound sensors during the last decade, the technology, as well as societal paradigms, such as more suitable validation protocols, need to be further established to investigate the key hypothesis: Can ultrasound-based wearable sensors replace the cuff sphygmomanometer as the gold standard for blood pressure estimation?