European Society of Cardiology
European Heart Journal - Digital Health (2021) **2**, 494–510
doi:10.1093/ehjdh/ztab047

REVIEW

Ambulatory monitoring promises equitable personalized healthcare delivery in underrepresented patients

Kanchan Kulkarni[1], Rahul Kumar Sevakula[1], Mohamad B. Kassab[1], John Nichols[2], Jesse D. Roberts Jr.[1,2], Eric M. Isselbacher[3], and Antonis A. Armoundas[1,4]*

[1]Cardiovascular Research Center, Massachusetts General Hospital, 149 13th Street, Boston, MA 02129, USA; [2]Anesthesia, Critical Care and Pain Medicine, Massachusetts General Hospital, 55 Fruit Street, Boston, MA 02114, USA; [3]Healthcare Transformation Lab, Massachusetts General Hospital, 55 Fruit Street, Boston, MA 02114, USA; and [4]Institute for Medical Engineering and Science, Massachusetts Institute of Technology, Cambridge, MA 02139, USA

Received 6 February 2021; revised 28 March 2021; editorial decision 25 May 2021; online publish-ahead-of-print 28 June 2021

The pandemic has brought to everybody's attention the apparent need of remote monitoring, highlighting hitherto unseen challenges in healthcare. Today, mobile monitoring and real-time data collection, processing and decision-making, can drastically improve the cardio-respiratory–haemodynamic health diagnosis and care, not only in the rural communities, but urban ones with limited healthcare access as well. Disparities in socioeconomic status and geographic variances resulting in regional inequity in access to healthcare delivery, and significant differences in mortality rates between rural and urban communities have been a growing concern. Evolution of wireless devices and smartphones has initiated a new era in medicine. Mobile health technologies have a promising role in equitable delivery of personalized medicine and are becoming essential components in the delivery of healthcare to patients with limited access to in-hospital services. Yet, the utility of portable health monitoring devices has been suboptimal due to the lack of user-friendly and computationally efficient physiological data collection and analysis platforms. We present a comprehensive review of the current cardiac, pulmonary, and haemodynamic telemonitoring technologies. We also propose a novel low-cost smartphone-based system capable of providing complete cardiorespiratory assessment using a single platform for arrhythmia prediction along with detection of underlying ischaemia and sleep apnoea; we believe this system holds significant potential in aiding the diagnosis and treatment of cardiorespiratory diseases, particularly in underserved populations.

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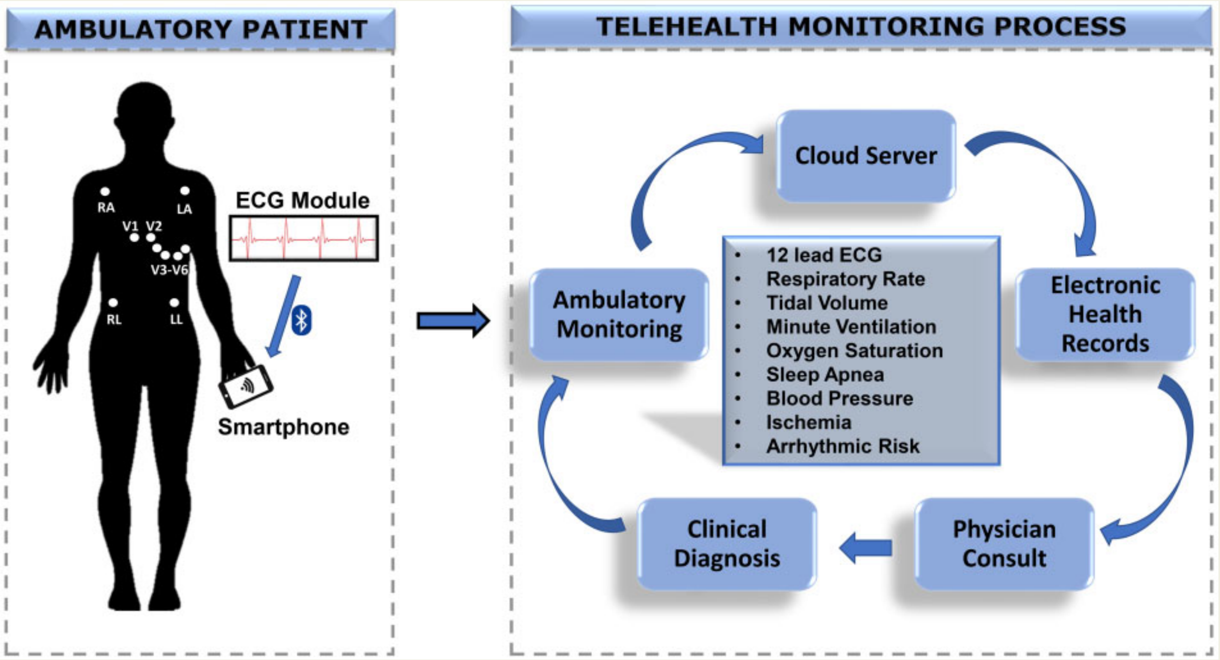
* Corresponding author. Tel: +617-726-0930, Email: armoundas.antonis@mgh.harvard.edu

Graphical Abstract



Keywords Telehealth • Cardiorespiratory • Haemodynamic • Smartphone • Personalized medicine • Monitoring

Introduction

Socioeconomic and geographic variances between rural and urban communities result in inequitable regional access to healthcare and disparities in mortality rates.[1] While there are multiple factors driving the community-based divide in healthcare outcomes,[2] the geographic inequality in the risk of death has shown to be higher among the elderly.[3] Hence, there is a growing need to develop and implement an accessible and affordable healthcare paradigm that provides a framework for equitable personalized medicine.

The ever-increasing availability of new technologies and an ever-improving health information technology infrastructure with >90% of American adults owning a cell phone, and 81% having a smartphone (elderly 53%, rural 71%, income < $30k 71%),[4] together with the evolution of wireless devices, has initiated a new era in medicine and a transition from population-level healthcare to personalized medicine. Therefore, mobile health technologies are expected to function not only as monitoring devices, but as essential components in the delivery of healthcare in patients with chronic diseases,[5] in underserved populations.[6] Furthermore, since a majority of medical consults today are accomplished through teleconference, with no access to vital sign data, the ability of a physician to have complete (medical grade) record of the cardiac–respiratory–haemodynamic state of patients with the help of mobile monitoring devices, has taken new, unforeseen significance.[7] *Figure 1* demonstrates a schematic of the telehealth paradigm offering remote medical monitoring and consultation to persons with limited access to in-hospital services.

Ambulatory monitoring devices and telemedicine offer a promising model to even disparities in healthcare and provide equitable delivery of clinical aid to patients who have limited access to in-hospital services. Telehealth aims to utilize new smartphone-based technologies to provide medical support to rural underserved populations, as well as patients across all age groups, thus paving the way towards personalized medicine.

However, despite the widespread use of smartphones across multiple age groups, utility of portable health monitoring devices has been limited due to the lack of user-friendly, non-intrusive, and computationally efficient physiological data collection and analysis platforms. Here, we present a review of the state-of-the-art of current wearable smart devices that enable cardiac, pulmonary, and haemodynamic telemonitoring and discuss the shortcomings, which highlight the need for novel tools to monitor the respiratory and cardiac state of ambulatory subjects with chronic diseases, that would aim to improve patient-provider communication, and adherence to treatment and self-management, in underserved populations.

In addition, we introduce a novel smartphone-based system capable of providing complete cardiac, respiratory, and haemodynamic monitoring in real-time by assessing various physiological parameters such as heart rate (HR), blood pressure (BP), pulse oximetry, respiration rate (RR), tidal volume (TV), minute ventilation (MV), underlying ischaemia, and arrhythmia susceptibility, in a single platform. The ability of this system to detect sleep apnoea, ischaemic events, and assess arrhythmia susceptibility make it a powerful tool that holds potential to aid diagnosis and treatment of cardiorespiratory diseases, particularly in underserved populations.

Search strategy

The Google Scholar database was manually searched without language or time restriction for articles published on wearable physiological monitors. Our search strategy focused on '[wearable devices OR smartphones AND (cardiac monitors OR respiratory monitors OR blood pressure monitors OR pulse oximetry monitors)]' and summarizes the current in-market, commercially available wearable monitoring technologies. Furthermore, to incorporate devices not covered in the Google Scholar academic search results, a manual search was performed for all commercial wearable products offering either cardiac, respiratory, blood pressure, or pulse oximetry monitoring. We present a list of wearables, capturing the most predominant vital sign monitors, currently used for fitness and healthcare assessment, covering devices with a broad range of utilities and form factors. From smart rings and watches primarily used for fitness tracking, to dedicated life vests for physician recommended life-saving medical-grade interventions, we provide an unbiased assessment of the advantages and pitfalls of using wearable devices for healthcare monitoring.

Telehealth systems for cardiac monitoring

Cardiovascular diseases are the leading cause of mortality worldwide.[8] Despite the availability of a multitude of evidence-based therapies for the treatment of heart failure (HF), the burden of this chronic disease on the US population remains unacceptably high, with an estimated 1 M admissions per year, primarily involving the elderly. HF readmission rates constitute a marker of worse prognosis and represent a significant healthcare expenditure and performance measure for payers,[9] while efforts to reduce the rehospitalization burden using conventional markers have been largely ineffective.[10]

A critical step to reducing HF hospitalizations is identifying which patients will imminently decompensate by evaluating their intravascular volume status. While physicians have traditionally relied on the bedside exam of the jugular venous pressure to assess volume status, this is impractical for ambulatory patients. Implantable haemodynamic monitors have shown promise as early warning systems in HF,[11] however, they are invasive and expensive, and their cost-effectiveness remains debatable.[12] A high proportion of deaths of HF patients,

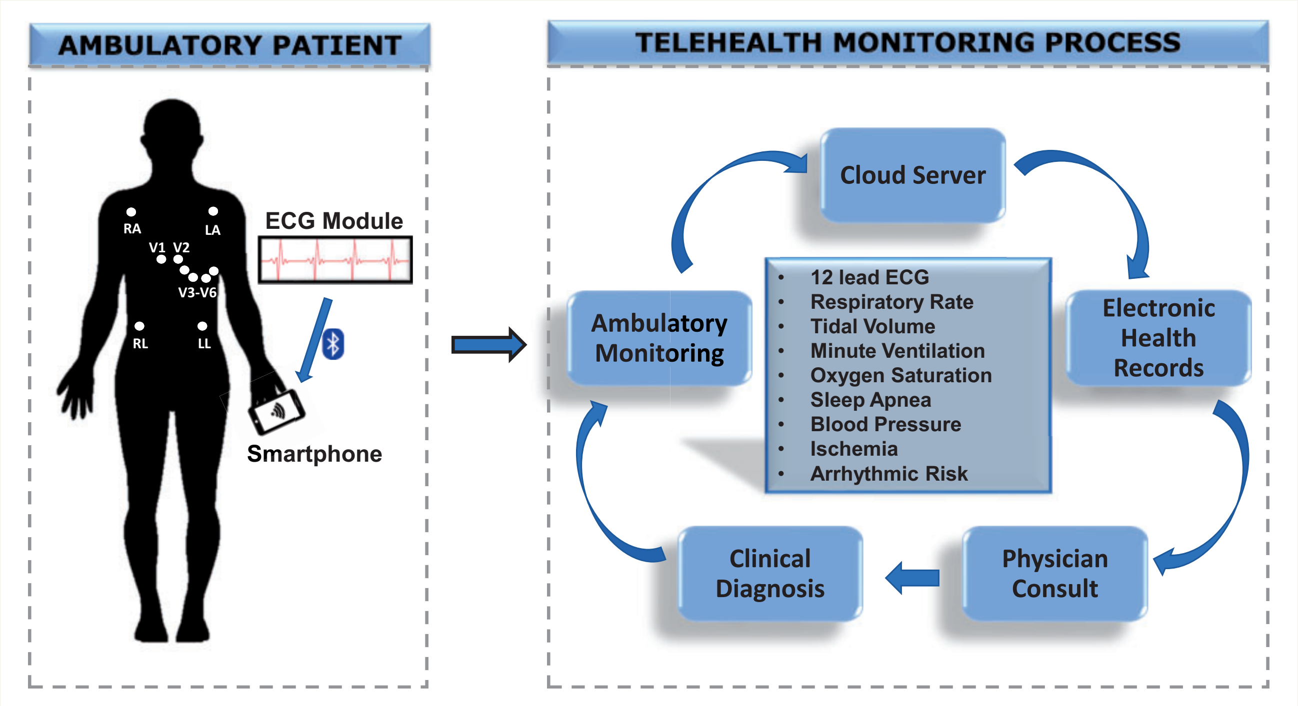


Figure 1 Schematic of a proposed telehealth monitoring system. Ambulatory monitoring of vital signals like the heart rate, blood pressure, oxygen saturation, respiratory rate, tidal volume, minute ventilation, sleep apnoea, and ischaemic or arrhythmic events is performed using a single platform telemonitoring device like the cvrPhone. Medical data are uploaded to cloud servers and transmitted to healthcare facilities as an electronic medical record. Healthcare professionals and physicians can access the data and provide clinical diagnosis along with necessary prescriptions for palliative care or recommendations for further treatments. The system provides a framework for remote monitoring and offers equitable personalized medical care for persons in rural communities and underrepresented areas. ECG, electrocardiograph; LA, left arm; LL, left leg; RA, right arm; RL, right leg.

especially those with milder symptoms, occur suddenly and unexpectedly. Many of these are due to abnormal heart rhythms, including ventricular arrhythmias, e.g. bradycardia and asystole.

An FDA-approved electrocardiographic (ECG) patch monitor named Zio Patch, which can be worn for up to 14 days has shown improved clinical event detection compared with the conventional 24 h Holter monitor.[13] However, it offers only one lead which explains its significantly lower sensitivity compared to the Holter monitor. The NUVANT, a wireless arrhythmia event monitor[14] consists of a wearable (patch) monitoring device and a portable data transmission device. Unlike the Zio Patch, which records and stores all ECG data for retrospective arrhythmia detection, the NUVANT performs real-time analysis and transmission.[14] The Bio patch Vitalerter[15] is designed for health monitoring in care homes; it generates the complete set of vital signs, including HR, and transmits them wirelessly, to alert the staff when a resident needs assistance. Multiple other smartwatches and wearable devices are available in the market (*Table 1*), which enable 24 h vital monitoring, namely the Apple watch, Motiv Ring, Oura Ring, Moov, and Fitbit, albeit without the specificity offered by the 12-lead ECG and hence, with limited ability to detect ischaemic events or life-threatening arrhythmias.[17] A smartphone-based, wireless, single-lead real-time ECG monitoring system (AliveCor Kardia) may accurately detect abnormal atrial rhythms.[18] However, the aforementioned devices[13,14,18] cannot provide an assessment of the patient's respiratory state, such as in-sleep disordered breathing (SDB). The Zephyr BioHarness and the Garmin Vivoactive can monitor both, pulmonary as well as cardiac activity, but they are primarily athletic performance monitoring systems, and provide limited assessment on patient deterioration by failing to identify dizziness signals, issue alerts in situations of hypoxaemia or hyper/hypothermia, or detect complex arrhythmias and ischaemic events. It may be noted that none of these devices (which determine HR and heart rhythm) provide medical-grade 12-lead ECGs. Since one cannot diagnose myocardial ischaemia (MI)-associated ST-elevation without 12-lead ECG, the US National Heart Attack Alert Program recommends that Emergency Medical Systems provide out-of-hospital 12-lead ECG to diagnose acute MI, and that all advanced life-saving vehicles be able to transmit the 12-lead ECG signal to the hospital.[19] It is therefore imperative that smartphone-based diagnostic devices, in the future, be capable of recording and transmitting 12-lead ECG to the treating medical team.

We have recently developed a novel smartphone-based ambulatory monitoring system, cvrPhone, with the capability to perform complete cardiorespiratory assessment based on 12-lead body surface ECG.[20–22] *Figure 2A* demonstrates the ability of the cvrPhone to detect the onset of ventricular tachycardia (VT).[20] It has been suggested that repolarization alternans (RA), an alternation in the T-wave morphology and/or duration, may be a precursor to VT and serve as a short-term[23,24] and long-term[25] predictor of susceptibility to ventricular tachyarrhythmias. Our smartphone-based system can detect and quantify the onset of RA and the corresponding K_{score} (a statistical measure of alternans, accounting for the backgrounding noise levels),[24] as depicted in *Figure 2B*, where a significant rise in RA levels is observed in all leads, just prior to the onset of VT.[20] These results demonstrate the ability of cvrPhone to accurately detect the onset of RA, demonstrated by a significant rise in RA in each lead ($P < 0.05$) within 1 min of occlusion compared to baseline ($n = 29$ swine).[26] In addition, we tested the utility of the cvrPhone in detecting the onset of ischaemia using an MI swine model. *Figure 3A* depicts the instantaneous beat-to-beat change in ischaemic index over time, with $t = 0$ marking the time of MI induction by coronary artery occlusion. Summary results depicted in *Figure 3B* show a significant rise in ischaemic index across all leads after MI induction.[22] Similarly, the ischaemic index which significantly increases following myocardial infarction ($P < 0.05$) and preceding a tachyarrhythmic event, can also be successfully captured by cvrPhone. Hence, cvrPhone enables the continuous monitoring of ST-segment changes underlying acute closure of a coronary artery, which has been shown to be essential in reducing symptom-to-door time and improve outcomes.[26]

Telehealth systems for respiratory monitoring

Assessment of the RR and TV are integral components of patient monitoring in chronic disease management, and especially in monitoring of patients with Cheyne–Stokes respiration,[27] a form of SDB. SDB is probably the most common respiratory disorder, with recent data from the USA and Europe suggesting that between 14% and 49% of middle-aged men have clinically significant sleep apnoea.[28] Sleep apnoea has been associated with the prognosis of many diseases including HF,[27] obstructive pulmonary disease,[29] sudden infant death syndrome,[30] atrial fibrillation,[31] chronic kidney disease,[5] diabetes,[32] hypertension,[33] and obesity.[34]

The need for medical-grade real-time mobile respiratory monitoring is not limited to the adult population. Premature infants routinely remain hospitalized overnight for clinical apnoea monitoring after receiving general anaesthesia for procedures that would otherwise not require hospitalization. Additionally, 2.25 million children in the USA suffer from obstructive sleep apnoea (OSA) and the gold standard remains overnight polysomnography.[35] Unfortunately, only 50% of children who snore actually suffer from OSA, and thus more effective screening tools could be invaluable. A mobile, real-time apnoea monitoring device could provide significant cost savings in the paediatric population by potentially reducing both the number of post-anaesthesia hospital admissions in infants and in-hospital sleep studies in children.

In a hospital setting, measurement of RR/TV can be accomplished either directly or indirectly,[36] using specialized hardware with features that are not often practical and convenient for ambulatory subjects, especially those with chronic conditions that live in underserved areas. Traditional TV estimation methods incorporate a spirometer or pneumotachometer that is physically attached to the mouth or nose of the patient, making it highly inconvenient for ambulatory measurement. While newer techniques for TV measurement including pitot tubes,[39] ultrasonic airflow meters,[38] respiratory inductance plethysmography,[39] electrical impedance tomography,[40] differential pressure pneumatachographs,[41] and impedance pneumography[42] have been suggested, these techniques require specialized hardware and have restricted telehealth application. Furthermore, the accuracy of pneumotachographs in TV estimation is limited[43] and most of these techniques are inadequate in detecting

Table 1 Summary of commercially available wearable devices for cardiac, respiratory, pulse oximetry, and haemodynamic monitoring along with their cost, indication, primary features, strengths, shortcomings, and reference website

Devices	Cost	Indication	Technical features	Strengths	Shortcomings	Website
Cardiac monitors						
Holter[16]	∼$600	Arrhythmia detection	24–48 h clinical 3–12 lead cardiac monitor, event recorder	Medical-grade ECG	Physician guided	
ZioPatch[13]	∼$330	Detect arrhythmias	Continuous (14 days) cardiac monitor, water resistant, leadless, manual event recorder	Long duration, leadless patch ECG	Low-resolution single-lead HR monitoring	
NUVANT[16]	∼$700	Detect arrhythmias	Leadless, continuous (∼7 days) patch monitor, wireless data transmission	Leadless patch ECG	Low-resolution single-lead HR monitoring	
Kardia Mobile	∼$80	Detect arrhythmias	Event recorder, wireless transmission, smartphone compatible, voice memo recorder	Leadless mobile medical-grade ECG in 30 s	Low-resolution single-lead HR monitoring	https://www.alivecor.com/kardiamobile
Applewatch	∼$499	Detect slow or fast HRs and atrial fibrillation	GPS, water resistant, optical HR sensor, gyroscope, accelerometer	Leadless, wristwatch-based ECG for general fitness tracking	Low-resolution single-lead HR monitoring, cannot detect complex arrhythmias or ischaemic events, not intended for medical diagnosis	https://www.apple.com/watch
Fitbit	∼$149	Detect slow or fast HRs and atrial fibrillation	GPS, temperature sensor, water resistant, optical HR sensor, multi-purpose electrical sensors, red and infrared sensors, gyroscope, accelerometer	Leadless, wristwatch-based ECG	Low-resolution single-lead HR monitoring, cannot detect complex arrhythmias or ischaemic events, not intended for medical diagnosis	https://www.fitbit.com/global/us/products/smartwatches
Motiv Ring	∼$200	HR, sleep, and fitness tracker	Bluetooth, accelerometer, optical HR sensor, waterproof, 3 days continuous monitoring battery life	User-friendly smart finger ring design	Leadless optical HR sensor, cannot detect ischaemia or arrhythmias, no haemodynamic monitoring	https://mymotiv.com/
Oura Ring	∼$299	HR, sleep, and fitness tracker	LED sensors, temperature sensor, accelerometer, gyroscope, memory storage of 6 weeks, water resistant, battery life of upto 1 week	User-friendly smart finger ring design	Leadless optical HR sensor, cannot detect ischaemia or arrhythmias, no haemodynamic monitoring	https://ouraring.com/
Moov	∼$30	Sports tracker for HR	Motion sensor, battery life of 6 months, water proof, Bluetooth	Motion-based fitness coach that enables exercise with audio guidance		https://welcome.moov.cc/

Continued

Table 1 *Continued*

Devices	Cost	Indication	Technical features	Strengths	Shortcomings	Website
Zoll LifeVest	—	Wearable cardioverter defibrillator	Continuous monitoring, automatic delivery of electrical therapy on event detection	Only available wearable life-saving device for patients at risk of sudden cardiac death	Physician guided	https://lifevest.zoll.com/
Kenzen Patch	~$300	Body heat, HR, and activity monitor	Compact, waterproof, multi LED PPG sensor, temperature sensor, sweat rate, bioimpedance, 6 axis inertial measurement unit	Designed for continuous worker safety monitoring		https://kenzen.com/end-to-end-health-and-safety-monitoring/
Biopatch vitalerter	—	Hypoxaemia, hyper/hypothermia, and acute irregular HR incidents, fall prevention	Bluetooth, waterproof, HR, motion, temperature and SpO_2 sensors	Designed for monitoring health in care homes		https://www.vitalerter.com/biopatch-sensor/
Zephyr BioHarness	~$700	Physiological data tracker for sports, combat, emergencies/safety, research, or fitness training	Bluetooth, accelerometer, HR, HRV, respiration, core temperature, posture and activity sensors	Wireless chest-based device, capable of real-time and long-distance recording of various physiological parameters		https://www.zephyranywhere.com/
Garmin Vivoactive	~$250	Sports and fitness/activity tracker, abnormally high or low HR alerts	GPS, smartphone compatible, accelerometer, HR, sleep, SpO_2, RR, hydration and activity sensors	Smart watch, easy to use, daily continuous monitoring	Low-resolution single-lead HR monitoring, cannot detect complex arrhythmias or ischaemic events	https://buy.garmin.com/en-US/US/c10002-p1.html
Respiratory monitors						
Bodyguardian heart	—	Detect and capture irregular heartbeats	Wireless, accelerometer, 24 h continuous ECG, periodic data transmission, strip electrodes for HR, RR, and activity monitoring	Small, leadless chest patch	By physician prescription	https://www.preventicesolutions.com/patients/body-guardian-heart.html
Somaxis Cricket	~$225	Physiological monitoring for research, ergonomics, physical therapy/rehabilitation, and fitness/wellness	Accelerometer, gyroscope, muscles, heart, brain, posture, breath, and movement sensors, Bluetooth	Multiple onboard sensors for wireless real-time data collection from different locations		https://www.somaxis.com/
Hexoskin	~$169–$579	Physiological assessment for research, first responders, stress monitoring, or other clinical applications	Single-lead ECG, RR, MV, VO2max, and activity monitor, continuous, battery life of 12–30 h, Bluetooth, respiratory inductance plethysmography sensors, accelerometer	Machine washable advanced smart clothing for continuous monitoring		https://www.hexoskin.com/

Continued

Table 1 ***Continued***

Devices	Cost	Indication	Technical features	Strengths	Shortcomings	Website
BioStamp	—	Data monitoring by healthcare professionals and researchers	Wireless, surface biopotential data for sleep, posture, activity, HR and RR sensing	Soft, flexible, conformal biosensors for multi-modal, multi-location sensing		https://www.mc10inc.com/
Ava Science wristband	~$249	Women's health monitor	Temperature sensors, accelerometer, PPG, HR, RR, activity and skin perfusion monitor	Bracelet shaped, designed for women to monitor fertility		https://www.avawomen.com/how-ava-works/healthcare/technology/
Sensium	—	Vital sign monitor for patients, early detection of sepsis, cardiac arrest, respiratory depression	Wireless, single-lead ECG, impedance pneumography, temperature sensor, 5-day battery life, shower-proof, standard ECG electrodes	Chest patch-based monitor used as an early warning system to detect remote patient deterioration		https://www.sensium.co.uk/us/
Intelesens Zensor		Detect arrhythmias, atrial fibrillation	3-lead 14-day continuous ECG, remote event detection, WiFi enabled	Long duration continuous monitoring of HR and RR		http://www.zensordevice.com/
Pulse oximetry monitors						
Everion	—	Vital sign monitor for adults, HR, SpO_2, RR, and activity monitor	PPG, Bluetooth, galvanic skin response electrodes for electrodermal sensing, photosensor	22 vital sign monitoring	Pending FDA approval, not intended for medical diagnosis	https://support.biofourmis.com/hc/en-us/categories/201377109-Everion-Device-
VinCense WHMS	~$200	Health monitoring for senior citizens and at home patients	Wireless, water resistant, PPG, Pulse rate, RR, temperature and SpO_2 sensors	Continuous 24 h clinical grade monitoring		https://www.vincense.com/
Spryhealth Loop	—	Health monitoring for patients with chronic conditions, chronic obstructive pulmonary disease	Optical sensors for monitoring HR, respiration and SpO_2	Wristband designed for seniors, easy to use		https://spryhealth.com/the-loop-monitoring-solution/
Current Health (Snap40)	—	Detects warning signs of health deterioration	Wireless, continuous SpO_2, HR, RR, temperature, movement, posture monitoring	Can improve patient outcomes by early detection of vitals		https://currenthealth.com/
EQ02+ Lifemonitor	—	Physiological data monitor for first responders, researchers, military personnel, or industry workers	Accelerometer, 48 h battery life and 8 GB memory for up to 50 days of continuous monitoring, 2 lead ECG, RR, temperature, SpO_2, motion and BP monitor	Light weight chest belt, clinical-grade vital signs monitoring sensor		https://www.equivital.com/products/eq02-lifemonitor

Continued

Table 1 *Continued*

Devices	Cost	Indication	Technical features	Strengths	Shortcomings	Website
VitalPatch	—	Detect arrhythmias, real-time patient monitoring	Single-lead ECG, RR, thermistors, accelerometer, 168 h battery life, BP and SpO_2 sensors, water resistant	Small, elegant, biosensor for continuous real-time clinical grade monitoring		https://vitalconnect.com/solutions/vitalpatch/
Masimo MightySat	~$299	RR and SpO_2 monitoring in clinics, emergencies, medical services, and at-home	Optional Bluetooth, PPG-based SpO_2, pulse rate, perfusion index and RR sensing	Fingertip-based user-friendly measurement		https://www.masimo.com/products/monitors/spot-check/mightysatrx/
Smartphone camera (eg. iPhone, iPad, Samsung Galaxy)	—	General health monitoring, fitness tracking	Bluetooth, camera lens-based PPG sensor for HR, RR and SpO_2 assessment	Simple, fingertip-based measurement, easy data transfer, wide availability	Not recommended for medical diagnosis	
Haemodynamic monitors						
ViSi Mobile	—	Continuous adult patient monitoring, fall prevention, detect patient deterioration	Wrist worn monitor, optical thumb sensor for SpO_2 and pulse rate, 3–5 lead chest sensor for ECG RR and temperature, cuff module for BP	Continuous vital sign monitoring		https://www.soterawireless.com
BPM Connect Withings	~$100	Hypertension, BP monitor	WiFi and Bluetooth enabled, cuff-based BP and HR sensor	Easy to use, leadless cuff-based smart monitor	Not continuous monitoring	https://www.withings.com/it/en/bpm-connect
Care Touch	~$26	BP monitor	Wrist-based BP and HR sensor, irregular heartbeat indicator	Fully automatic wrist-based cuff monitor	Not continuous monitoring	https://caretouchusa.com/product/fully-automatic-wrist-blood-pressure-monitor-classic-edition/
Accurate 24	—	Hypertension, BP, and HR monitor	Pulse, BP, pulse wave velocity and blood vessel parameter sensors	Cuffless continuous monitoring		http://accurate-meditech.com/
Biobeat wrist monitor	~$1500	Hypertension	PPG sensor, wireless and continuous monitoring, battery life of 3 days	Cuffless wrist band-based monitor, 13 vital signs measured	Awaiting mass production	https://www.bio-beat.com/copy-of-clinical-trials-and-researc-1
Omron HeartGuide	~$499	Hypertension, BP monitor	Oscillometric measurement using an inflatable cuff within the watch band, BP, pulse rate, sleep and activity sensing, Bluetooth	Miniaturized wristwatch-based monitor		https://omronhealthcare.com/products/heartguide-wearable-blood-pressure-monitor-bp8000m/

BP, blood pressure; ECG, electrocardiograph; GPS, Global positioning system respectively; HR, heart rate; HRV, heart rate variability; LED, Light emitting diode; MV, minute ventilation; PPG, photoplethysmographic; RR, respiration rate; SpO_2, oxygen saturation.

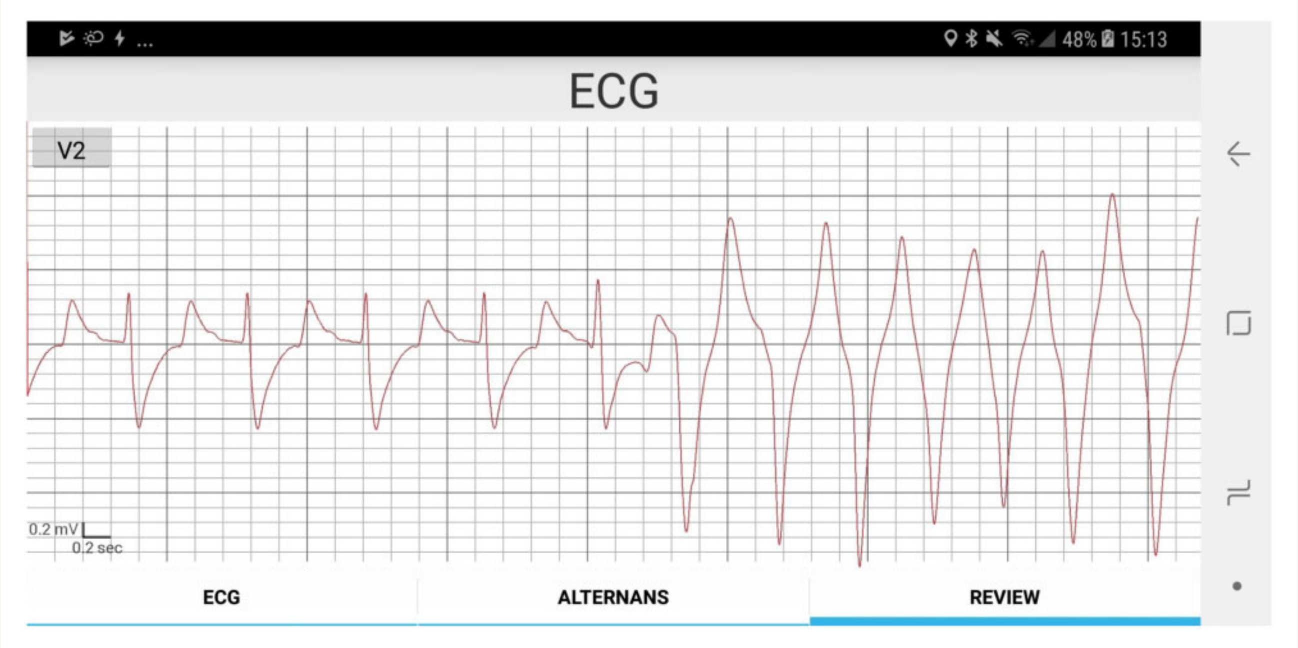


Figure 2 Telehealth system for cardiac monitoring.[20] (*A*) Representative electrocardiographic tracing acquired by the cvrPhone, using the precordial lead V2 depicting onset of ventricular tachycardia. (*B*) Summary results ($n = 4$) of minute wise change in alternans voltage and K_{score} across all 12 body surface electrocardiographic leads, preceding the onset of spontaneous ventricular tachycardia or fibrillation. $t = 0$ corresponds to the induction of myocardial infarction by coronary artery occlusion. Significant rise in alternans voltage and K_{score} is observed in all leads just after onset of ischaemia post-occlusion.

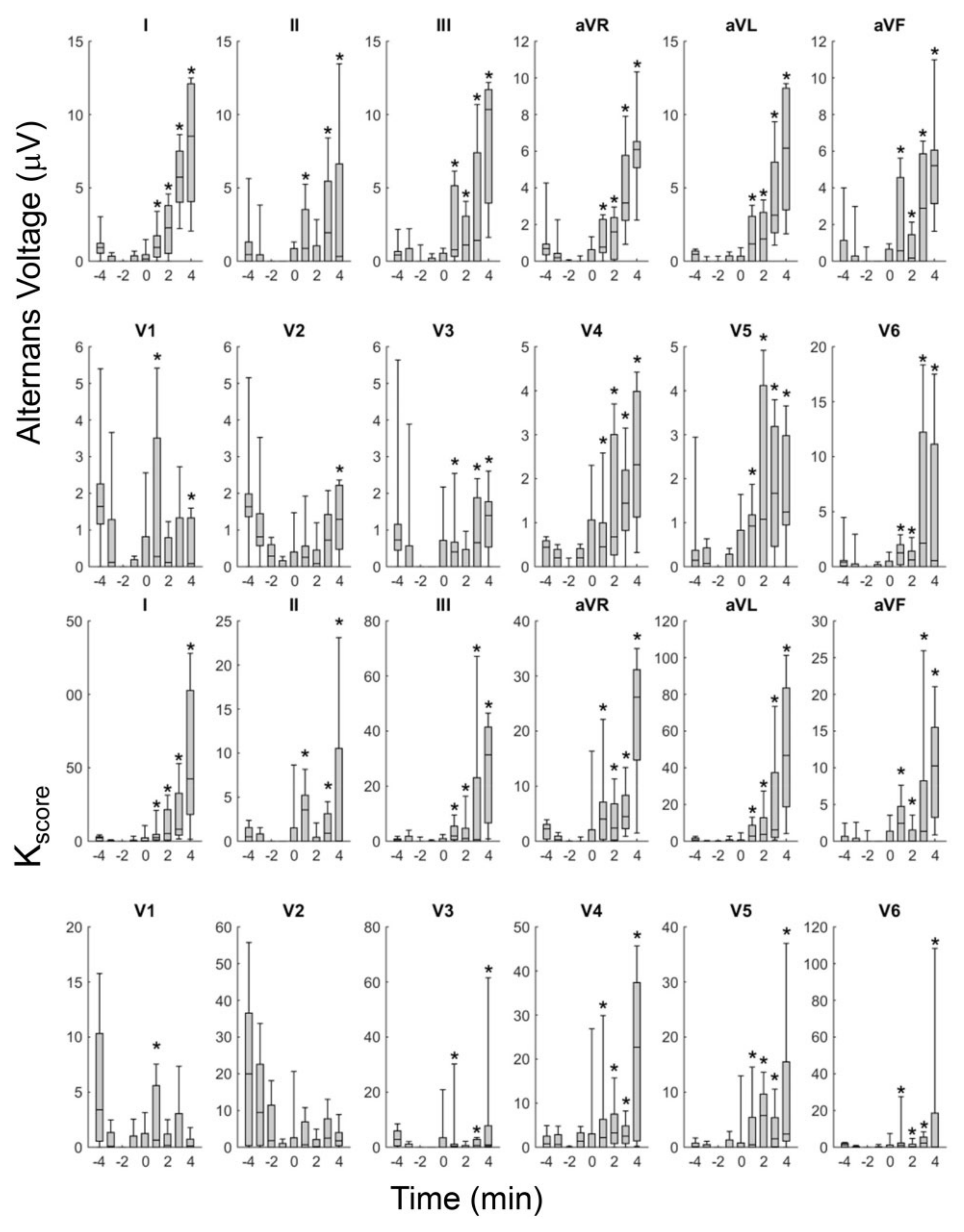
dynamic respiratory events such as apnoeas.[44] MV is another important respiratory parameter that plays an important role in the assessment of a patient's pulmonary activity. The most direct method of MV estimation has been from regression analysis of the HR[45] or correlations of the HR with oxygen consumption.[46] Yet these models perform poorly with patient-to-patient variability, leading to large errors, limited clinical utility,[47] and have little applicability in the ambulatory setting.

We tested the utility of our smartphone-based system, cvrPhone, in performing pulmonary assessment by estimating the RR, TV, MV, and onset of apnoeic events in real-time ($n = 9$ swine).[21] *Figure 4* depicts a representative plot of RR, TV, and MV estimation as the true RR was varied from 6 to 0 to 6 to 0 to 6 to 0 to 6 breaths/min, TV was varied from 250 to 0 to 750 to 0 to 500 to 0 to 750 mL, and MV was varied from 1500 to 0 to 4500 to 0 to 3000 to 0 to 4500 breaths*mL/min ($n = 9$ swine). The smartphone-based system accurately estimated TV at different settings (0, 250, 500, and 750 mL) with statistically significant difference ($P < 0.01$) between any two different settings regardless of the RR (6 or 14 b.p.m.).[21] During apnoea, the estimated TV and RR values were 11.7 ± 54.9 mL and 0.0 ± 3.5 breaths/min, which were significantly different ($P < 0.05$) than TV and RR values during non-apnoea breathing. In addition, the time delay from the apnoea onset to the first apnoea detection was 8.6 ± 6.7 and 7.0 ± 3.2 s for TV and RR, respectively.[21] Furthermore, the cvrPhone was also accurately able to determine MV at varying TVs and RRs with median relative estimation errors of 17%, -4%, 35%, -3%, -9%, and 1%, for true MVs of 1500, 3000, 3500, 4500, 7000, and 10 500 breaths*mL/min, respectively ($n = 9$ swine).[48] These studies provide proof-of-concept of the utility of cvrPhone to detect multiple cardiorespiratory parameters from 12-lead surface ECG in real-time with high accuracy and relatively low error, compared to the gold standard mechanical ventilator (Ohmeda-GE, Madison, WI, USA).

Telehealth systems for pulse oximetry monitoring

Use of pulse oximetry is a clinically standardized method for non-invasively assessing the pulse oxygen saturation levels, SpO_2. Based on changes in the optical absorption properties of haemoglobin, non-invasive SpO_2 measurements are typically spectrophotometric and performed in the visible and near-infrared spectral regions.[49] Pulse oximetry uses photoplethysmographic (PPG) signals detecting volumetric changes in blood flow that correlate with cardiac contraction and relaxation. Multiple techniques for monitoring PPG-based SpO_2 have been suggested, utilizing either finger-based[50] or forehead oximeters,[51] offering wireless[52] monitoring of SpO_2 levels. Furthermore, smartphones with optical sensors have now enabled instantaneous detection of SpO_2 in conjunction with other vital physiological parameters in mobile and remote settings.[53]

The use of smartphone sensors and in particular the camera function for health monitoring has gained considerable popularity over the past few years. Multiple studies have shown the utility of acquiring a PPG like pulsatile signal from a fingertip placed in contact with a



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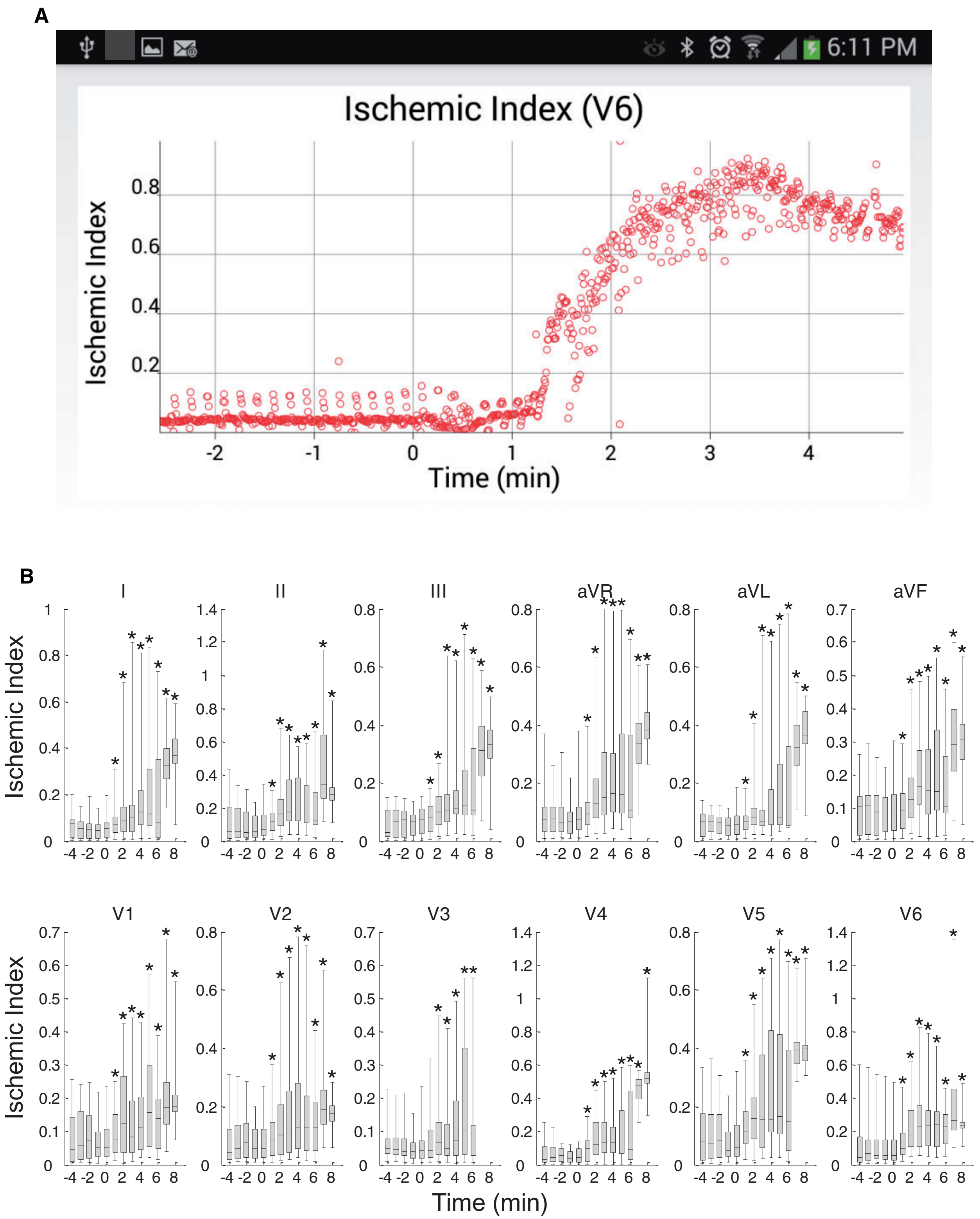


Figure 3 Detection of myocardial ischaemia.[22] (*A*) Instantaneous beat-to-beat change in ischaemic index acquired by the cvrPhone using precordial lead V6, quantifying the changes in ST-segment elevation. $t = 0$ corresponds to the induction of myocardial infarction by coronary artery occlusion. (*B*) Summary results ($n = 9$ records, 6 swine) of minute wise change in ischaemic index across all 12 body surface electrocardiograph leads. $t = 0$ corresponds to the induction of myocardial ischaemia by coronary artery occlusion. Significant rise in ischaemic index is observed in all leads within a minute of myocardial ischaemia induction.

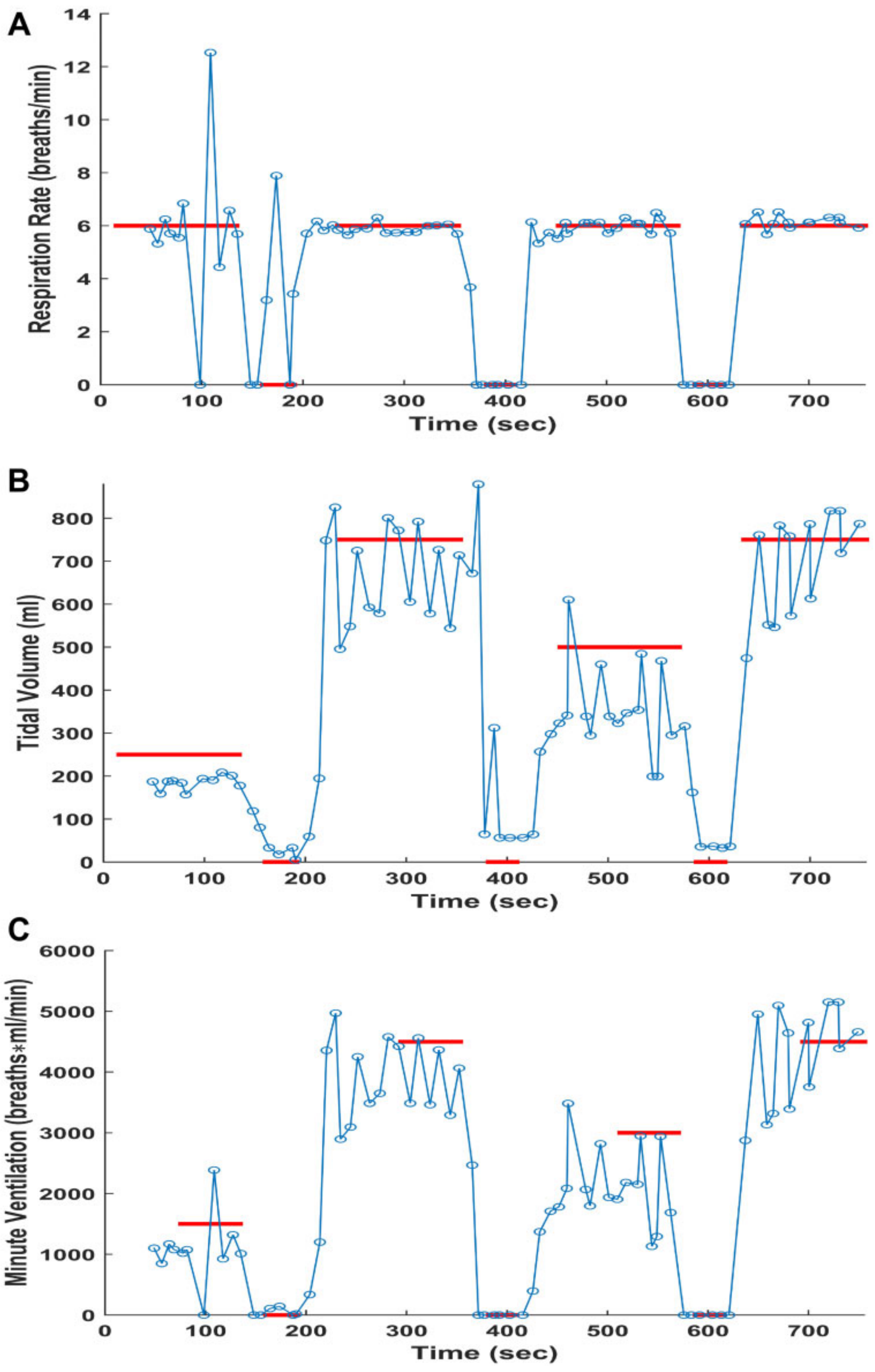
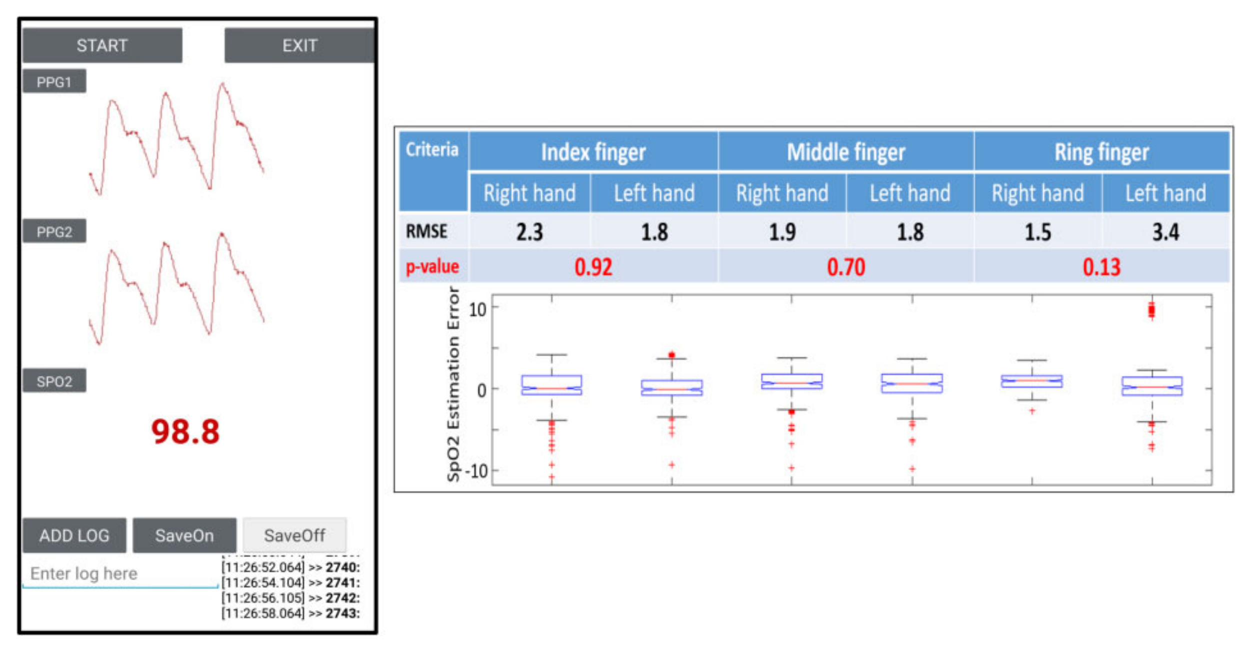


Figure 4 Telehealth system for respiratory monitoring.[49] (*A*) Representative plot of respiration rate estimates acquired using cvrPhone, as true respiration rate was varied between 0 and 6 breaths/min. (*B*) Representative plot of tidal volume estimates acquired using cvrPhone, as true tidal volume was varied from 250 to 0 to 750 to 0 to 500 to 0 to 750 mL. (*C*) Representative plot of minute ventilation estimates as true minute ventilation was varied from 1500 to 0 to 4500 to 0 to 3000 to 0 to 4500 breaths/min. Red lines denote true respiration rate, tidal volume, or minute ventilation values.

smartphone camera for assessing the HR, HR variability, RR, and SpO_2 levels.[54–58] Also, various signal processing algorithms and mobile apps are being developed to extract health parameters from smartphone camera signals and test its utility in medical diagnosis.[21,48,59,60] For example, Lagido *et al.*[60] demonstrated that HR can be accurately estimated using the PPG signal acquired from a smartphone camera and in addition atrial fibrillation can be detected with a specificity of 97% and sensitivity of 75%, in patients with HF. Similarly, a recent prospective clinical study (DETECT AF PRO), on detection of atrial fibrillation using smartphone cameras demonstrated high specificity (99.6%) and sensitivity (91.5%).[61] However, while such modalities promised to provide basic cardiac assessment, the utility of smartphone camera-based apps for comprehensive clinical diagnosis has not yet been established. For instance, while smartphone pulse oximetry was shown to not be inferior to traditional probe-based oximetry in healthy children,[53] SpO_2 measurement has been shown to be less reliable in hypoxaemia patients.[62] Similarly, many smartphone apps have been shown to be less accurate and thus provide less reliable estimates,[63] questioning the clinical utility of these approaches.[64,65]

Commercially available wearable measurement devices like the Masimo MightySat offer user-friendly fingertip-based monitoring of SpO_2 and the pulse rate (*Table 1*). However, they lack comprehensive cardiac monitoring to detect abnormal rhythms and ischaemic events. The VitalPatch, EQ02+ Lifemonitor, and VinCense WHMS devices offer continuous 24 h clinical-grade pulse oximetry monitoring, but with similar limitations of low-resolution ECG measurements, making them insufficient to assist at-risk cardiovascular patients and detect early warning signs of cardiopulmonary events. The Everion system promises a more complete physiological assessment by monitoring 22 vital signs, but is currently pending FDA approval. A convenient wristband-based SpO_2 monitoring device, Spryhealth Loop, has been designed for use by seniors, offering easy assessment of HR and respiration in addition to pulse SpO_2 levels. Finally, Current Health has designed a mobile monitoring device for continuous SpO_2, temperature, HR, respiration, and movement measurements, for detection of warning signs of health deterioration.

Despite the surge in pulse oximetry devices for mobile monitoring, there is yet an unmet need for implementing a unified solution that provides comprehensive cardiorespiratory monitoring, in addition to pulse oximetry measurements using a single low-cost platform to aid remote patient surveillance. cvrPhone, in addition to cardiac and respiratory monitoring, offers the capability of continuous SpO_2 estimation using two-channel PPG signals.[50] We evaluated the feasibility of the system to record continuous, instantaneous changes in SpO_2 in healthy humans ($n = 11$).[50] *Figure 5* demonstrates summary results of SpO_2 estimation using different fingers with the corresponding root mean square error values, indicating efficient detection of SpO_2 using either the index, middle, or ring fingers with no significant differences between fingers,[50] albeit the right hand ring finger exhibited the smallest error.



```
[11:26:52.064] >> 2740:
[11:26:54.104] >> 2741:
[11:26:56.105] >> 2742:
[11:26:58.064] >> 2743:
```

Criteria	Index finger		Middle finger		Ring finger	
	Right hand	Left hand	Right hand	Left hand	Right hand	Left hand
RMSE	2.3	1.8	1.9	1.8	1.5	3.4
p-value	0.92		0.70		0.13	

Figure 5 Instantaneous blood oxygen saturation estimation.[51] Representative photoplethysmography and oxygen saturation signals acquired by the cvrPhone. Quantification of oxygen saturation estimation error ($n = 11$), acquired using different fingers (index, middle, and ring fingers), demonstrating no significant difference among fingers/hands. *P*-value is calculated using Wilcoxon signed-rank test. Data are presented as bar graphs denoting 10, 25, 50, 75, and 90 percentiles of oxygen saturation estimation error. PPG, photoplethysmographic; RMSE, root mean square error (%); SpO_2, oxygen saturation.

Telehealth systems for haemodynamic monitoring

Regular monitoring and analysis of the historical patterns of BP is essential for the detection and prediction of hypertension and subsequent cardiac arrhythmias. Portable/wearable health monitoring equipment unequivocally strikes a good balance between recording accuracy and user comfort. Notable examples for portable, continuous non-invasive BP monitoring include (i) automated oscillometric methods,[66] (ii) ultrasonic device-based methods,[67] and (iii) software-based BP estimation methods.[68] Oscillometric methods which use cuffs are the most commonly used devices; the difficulty with them, however, is that (i) they are uncomfortable to wear and (ii) they have an inherent error with respect to their ability in representing the arterial BP values.[69] The feasibility in estimating BP from the SpO_2 and ECG signals has been previously explored with little success[70] and ultrasonic devices are yet to become mainstream in continuous BP monitoring.

The Omron HeartGuide is a commercially available wristwatch-based BP monitor with miniaturized components for oscillometric measurement using an inflatable cuff within the watch band. It also tracks sleep and activity in real-time, offering a portable user-friendly solution for BP sensing, albeit on the costlier side. *Table 1* lists some of the other currently available commercial wearable BP monitoring

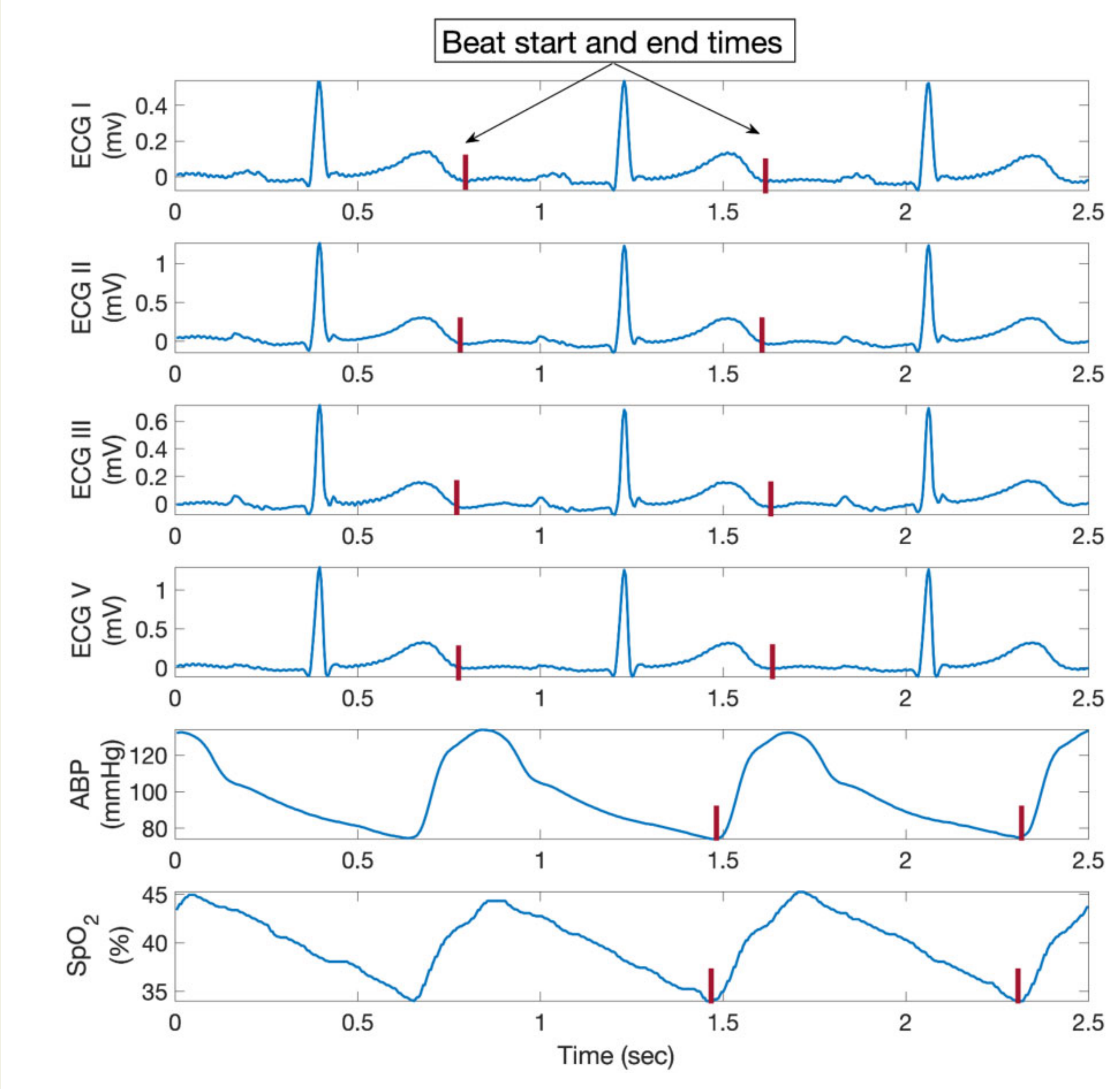


Figure 6 Beat-to-beat real-time blood pressure estimation. Representative, noise-free signals. A beat here corresponds to: (i) end of prior beat's T-wave to the end of current beat's T-wave, (ii) diastolic to diastolic, for blood pressure, and (iii) minimum to the next beat's minimum value for oxygen saturation. ABP, arterial blood pressure; ECG, electrocardiogram; SpO_2, oxygen saturation.

devices. A new cuffless wristband-based BP monitor developed by Biobeat is still awaiting mass production, while BPM Connect Withings offers a leadless cuff-based, smart, WiFi-enabled device but without the ability for continuous monitoring. Similarly, Care Touch offers a fully automatic wristband-based cuff monitor for intermittent tracking of BP and pulse rate, unlike the VisiMobile or Accurate 24, which provide continuous monitoring of vital signs.

We developed a BP estimation method that uses ECG and SpO_2 signals to estimate in real-time, the systolic and diastolic BP values on an almost beat-to-beat basis. Following selection of noise or artefact-free four-lead ECG, SpO_2, and arterial BP signals from 281 intensive care unit patients, R-wave peak detection, and application of ECG waveform delineation methods, individual heartbeats and their corresponding span (*Figure 6*) were obtained, resulting in ∼22 M beats, i.e. 4.52 M five-beat sequences. The age and body mass index, obtained from the electronic medical records, were used as features, together with features extracted from the SpO_2 and four-lead ECG signals. These additional futures include, features characterizing the HR and its variability, the morphology of ECG signals, the duration of the QT interval, the amplitude of the T-wave, the pulse arrival time, the power spectral distribution of SpO_2, and statistical measures over the Kaiser–Teager energy of SpO_2 signal, across windows of five consecutive beats.

With these features as the input, and the corresponding arterial waveform systolic/diastolic BP values as gold standard output, a random forest model with 400 trees was used to fit a regression model for future BP estimation. The performance of the method was assessed using five-fold cross-validation, and resulted in a mean absolute error of 4.37/2.49 mmHg, respectively, in estimating the systolic/diastolic BP. We therefore believe that this technology can be generalized and likely enable the BP monitoring of ambulatory patients.

Discussion and future perspectives

In a hospital setting, measurement of RR, TV, MV, SpO_2, BP, assessment of sleep apnoea, ischaemia, and the risk of abnormal heart rhythms is accomplished either directly or indirectly, using specialized hardware and procedures with features that are often impractical and inconvenient for free-moving, ambulatory subjects, especially those with chronic conditions that live in the underserved areas. cvrPhone, encompasses critical and essential features for cardiorespiratory assessment that can drive medical decision-making, offering an alternative, efficient modality for mobile monitoring. Using the cvrPhone (Galaxy S8, 6 GB RAM, 64 GB expandable memory) we have been able to estimate the RR, TV, MV; detect ischaemia and apnoeic events; and predict cardiac arrhythmias, in real-time. The choice of the Android was made to enhance cost efficiency with the first prototype built with over-the-shelf parts at a cost of <$100. Furthermore, we believe that since an ever-increasing percentage of the population worldwide will be using smartphones or tablets in the near future, even in rural and underserved areas, cvrPhone has the potential to be an affordable, medical-grade cardiac, pulmonary, and haemodynamic monitoring solution for a wide section of the population. A further comprehensive clinical assessment of this novel system holds promise for aiding telehealth and providing personalized medicine in underrepresented populations.

The successful implementation of a telehealth paradigm involves addressing multiple shortcomings in the current telemonitoring modalities: (i) reliability—construction of efficient, accurate, real-time algorithms that are constantly refined with new data and signal processing techniques; (ii) accountability—while developers are responsible for the quality and performance of any device or algorithm, adequate training for physicians and personnel handling the data streams from the devices are warranted for accurate diagnosis; (iii) legislation and liability—involvement of all stakeholders from developers, clinicians, researchers to participant population is necessary for the successful and safe translation of a product from development, testing, FDA approval, and mass production to end consumer marketing; and (iv) data security—protection of personal patient data recorded on cloud servers and transferred via various IoT platforms needs to be ensured.

Conclusion

Despite evidence that remote patient monitoring and telehealth can improve patient-provider communication in remote residential populations[71] and rural healthcare settings,[72] there is a paucity of medical grade, affordable tools to monitor the respiratory and cardiac state of ambulatory patients with chronic conditions in such communities, and thus provide equitable patient-specific healthcare. Successful implementation of a telehealth paradigm requires reliable, accountable, secure, and accurate real-time remote monitoring devices. In the long term, precision medicine that employs artificial intelligence to provide clinicians with tools to enable best treatment predictions,[73] when applied to streaming vital sign-signals, is expected to impact positively all population groups, and eliminate disparities in such populations as racial/ethnic minorities, structurally disadvantaged population subgroups, sex, and sexual identity minorities, people with different levels of functional ability, rural residents, as well as other marginalized groups.[74]

Funding

This work was supported by a Grant-in-Aid [#15GRNT23070001] from the American Heart Association (AHA), the Institute of Precision Medicine [17UNPG33840017] from the AHA, and the RICBAC Foundation, NIH grants [1 R01 HL135335-01, 1 R21 HL137870-01, 1 R21EB026164-01, and 3R21EB026164-02S1]. This work was conducted with support from Harvard Catalyst, The Harvard Clinical and Translational Science Center (National Center for Research Resources and the National Center for Advancing Translational Sciences, National Institutes of Health Award 8UL1TR000170-05 and financial contributions from Harvard University and its affiliated academic healthcare centres). The content is solely the responsibility of the authors and does not necessarily represent the official views of Harvard Catalyst, Harvard University and its affiliated academic healthcare centres, or the National Institutes of Health.

Conflict of interest: none declared.

Data availability

Data will be available to any investigator upon request.

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