Flexible Wearable Sensors in Medical Monitoring

Subjects: Health Care Sciences & Services
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Wearable devices for health monitoring are usually made into miniaturized rigid circuit boards and block power supplies placed on various parts of the human body, especially the wrist, to monitor body data in real-time.

Keywords: flexible wearable sensors ; physiological signal monitoring ; flexible substrates

1. Introduction

Since ancient times, people have struggled with diseases, so continuous innovation of medical equipment has always been the greatest goal of people's struggle. However, many efficient medical facilities are primarily concentrated in hospitals, which makes health care time-consuming and labor-intensive, and the high cost of maintaining and purchasing these facilities can also create barriers for patients, especially in developing countries [1]. Accordingly, scientists are motivated to develop emerging technologies to implement healthcare services in a convenient and low-cost way, free patients from tedious hospital diagnoses, and meet the concept of personalized medicine spreads [2]. In the context, wearable medical devices for health monitoring emerge as the times require, monitoring vital signs for the wearer, especially heart rate [3], body temperature [4], and blood pressure [5][6].

The development and integration of materials science, sensing techniques, wireless technologies, and the internet of things have greatly promoted the advancement of wearable devices [7][8]. Wearable devices have become a new way to maintain a healthy life [1][9]. According to the data from the International Data Corporation (IDC) [10], global shipments of wearable devices have gradually increased. In the past two years, it has shown explosive growth. In 2020, despite being affected by the epidemic, its shipments still increased by 32% to 444.7 million yuan. It can be seen that wearable devices are still hot, and the market demand is also increasing [10]. Wearable devices for health monitoring are usually made into miniaturized rigid circuit boards and block power supplies placed on various parts of the human body, especially the wrist, to monitor body data in real-time [11]. However, these sensors lack sufficient flexibility and adaptability. Thus, the properties related to long-term wear comfort, including biocompatibility, skin compactness, safety, and durability, remain important considerations [12][13][14]. For the above purposes, research focusing on "flexible wearable sensors" is increasing.

2. Application of Flexible Wearable Sensors for Health-Monitoring

Impelled by the increasing demand for the elderly and various patients, especially those with chronic diseases, a variety of sensors have been developed in recent years to meet the need for continuous medical monitoring. For the needs of continuous medical detection, highly flexible, stretchable, safe, and reliable wearable sensors have gradually become a hot topic. Wearable flexible sensors can detect and monitor biological signals, such as pulse rate, respiration rate, temperature, exercise, and blood pressure, for timely diagnosis of disease [15][16][17].

A series of recent reports have shown that various configurations of flexible sensors, including piezoresistive sensors, piezo-electromechanical devices, capacitive sensors, and transistor-transistor-based devices, have demonstrated high sensitivity capable of monitoring human physiological signals [18][19][19][20][21][22][23]. Roughly, the indicators detectable in medical monitoring are classified into two categories: (1) biophysical signals, including body temperature, heart rate, pulse, and body movement; (2) biochemical signals, such as blood, pH, and biomolecules [24][25]. Monitoring heart rate, temperature, and human movement play a vital role in assessing health [26]. A summary of flexible sensors for vital sign monitoring is shown in **Table 1**.

2.1. Temperature

Body temperature is one of the critical indicators of daily health status and clinical diagnosis and treatment, providing insight into the physiological state of the human body. For example, the plantar temperature rise has proven to be a measurable indicator of diabetic foot ulceration [27][28]. The normal range of body temperature regulation is 36.5–37.1 °C [29], and abnormal body temperature often indicates a threat to the patient's health. Maintaining body temperature within a healthy range is critical for blood circulation, the enzyme activity of the immune system, and physiological metabolism [30][31]. On the one hand, several diseases are characterized by irregular changes in body temperature [32] (physical activity and ambient temperature only cause slight changes in body temperature [33]). On the other hand, doctors can also accurately analyze the efficiency of treatment based on body temperature [34]. This indicator plays an integral role in medical health monitoring [35].

Changes in human body temperature are limited, so it is necessary to design flexible temperature sensors with high sensitivity and high accuracy to monitor the subtle changes in human body temperature. The traditional methods of measuring temperature include sticking temperature sensors and infrared digital cameras [36], but none of them can provide the function of continuous monitoring and cannot meet clinical needs. Therefore, many predecessors have devoted themselves to the development of new body temperature sensors. A flexible and stretchable temperature sensor array composed of single-walled carbon nanotubes was proposed, which can maintain stable mechanical properties under the external stain [37]. The flexible substrate of the sensor was polyaniline nanofiber, which can closely fit the skin. It adopted the embedded electrical connection method, with a precise response time of 1.8 s and high resistance sensitivity.

Temperature sensors can not only monitor changes in human body temperature but also monitor changes in external ambient temperature [38]. An ultra-thin, lightweight, multi-function sensor was proposed for continuously monitoring light intensity and ambient temperature to avoid excessive or low ambient temperature hindering the healing of certain diseases and wounds [39]. The photodetectors and temperature sensors were integrated on the polyetherimide (PEI) soft substrate by lithography and etching techniques. The overall thickness of the sensor is within 20 μm, and is compliant with any part of the body without discomfort to wearers. All of the above innovations in temperature sensors for various applications demonstrate the extreme interest of the entire community of researchers.

2.2. Heart Rate and Pulse

Continuous monitoring of heart rate and pulse is essential for the prevention and diagnosis of cardiovascular disease. The main function of the human heart is to pump blood to the tissues and organs of the whole body while recycling venous blood and completing the exchange of substances [8]. Heart rate is the frequency of the cardiac cycle. In clinical practice, heart rate and pulse are the two most basic indicators of the heart [4][40]. Cardiovascular disease is one of the leading causes of human death, with cardiovascular disease (CVD) accounting for more than 17 million deaths annually, accounting for 31% of global deaths [41], and this number is expected to increase to 23.6 million by 2030 [42]. Despite high mortality, 90% of CVD can be prevented with early detection [43]. However, heart rate and pulse provide necessary information for timely prevention and treatment of cardiovascular disease [44].

At very early stages, cardiovascular disease is asymptomatic but causes arterial pulse pathology, affects arterial blood pressure, and causes changes in the pulse waveform at the wrist [45]. At present, traditional cuff sphygmomanometers are still used in the clinic to monitor blood pressure by measuring systolic and diastolic blood pressure [46][47], which is an indirect monitoring method and cannot meet the need for continuous monitoring.

Often, the activity of the heart can be represented by the electrocardiogram (ECG) signal, which provides general information about the cardiovascular system. Since the ECG is periodic, the heart rate can be obtained from the R wave-to-R wave (RR) interval of the ECG signal [8]. Traditional monitoring methods generally use gel-assisted Ag/AgCl, but this method is still relatively cumbersome to use [48]. The skin-contactable ECG sensor allows users to easily identify their cardiac condition and diagnose critical cardiac problems early, such as cardiomyopathy and arrhythmia, and high blood pressure [49][50]. The ECG electrodes are the key to monitoring ECG signals in flexible wearable devices. Traditional monitoring electrodes generally use gel-assisted Ag/AgCl electrodes, but there are still some troubles in using this method, such as causing skin problems [48][51]. With further research, flexible dry electrodes have gradually attracted extensive attention of researchers due to their soft and non-invasive characteristics. A flexible and wearable electrode was reported for ECG signal monitoring [52]. Through plasma sputtering technology, silver with excellent electrical conductivity was made on the substrate made of cowhide as a flexible material. In this work, the researchers performed ECG tests on six subjects and demonstrated that the monitored ECG signal quality was comparable to that of conventional Ag/AgCl electrodes. It is worth mentioning that this kind of cowhide material is easier to make clothes with integrated flexible sensors, and it is more easily accepted by people.

Plethysmography and ultrasound are commonly used methods for monitoring pulse and heart rate [53]. However, the bulky monitoring equipment and the accuracy of long-term monitoring prevent these two methods from becoming the best choice for wearable pulse sensors [54][55]. Recently, a flexible strain sensor for real-time pulse monitoring has been proposed, which can be easily attached to the skin [56]. The sensing element of this patch-type sensor adopted polyaniline with high sensitivity and excellent flexibility. Through the pressure changes caused by blood flow, the signal characteristics monitored by the pulse sensor were analyzed for clinical analysis. With more in-depth research, a flexible pressure sensor that can monitor three pulse positions simultaneously was designed [57]. This design combined traditional Chinese pulse theory with modern sensor technology to achieve innovation. Ionogel-based pressure sensor arrays were fabricated on polyethylene terephthalate (PET) flexible substrates to convert pressure changes brought about by arterial flow into resistance changes. The special feature of this research is that three-dimensional pulse mapping can be formed. The key information, including the strength and waveform of the pulse, is displayed on maps, perfectly simulating the sensation of a doctor touching the pulse on the skin. Another successful example of flexible sensors for monitoring pulse rate is based on poly(vinylidenefluoride-co-trifluoroethylene) (PVDF-TrFE) [58]. The device integrated analog amplification circuitry and detector elements on the flexible material that was capable of detecting weak pressures (10 kPa) and amplified electrical signals by a factor of 10. Therefore, the performance of the sensor is excellent for monitoring the pulse of the human body.

2.3. Human Motion

Correct exercise and fitness, medical rehabilitation training, and daily healthy life are inseparable from accurate and timely monitoring of human body movement signals. In daily life, detecting physical activity and exercise habits can provide useful information for fitness and maintaining correct posture. In the field of medicine, continuous monitoring and regular analysis of body movements will help doctors timely detect abnormalities in the patient's body, thereby improving the efficiency of treatment. For example, abnormal posture and tremors in the hands are symptoms of some deadly diseases such as diabetes [59], Alzheimer's [60], and Parkinson's [61][62]. Wearable medical devices are essential in detecting sudden tremors and abnormal movements. Therefore, designing continuous monitoring sensors will help detect symptoms in time and treat them accurately and efficiently [63]. The normal movement of hands and limbs can ensure a high quality of life and efficient work, among which gestures are also vital and often serve as a range of signs to transmit information [64]. Given that the feet of the body bear most of the pressure of the body, especially for manual workers or athletes, monitoring the pressure changes on the soles of the feet can effectively prevent injuries [65][66][67].

To date, many efforts and achievements have been reported on flexible sensors for continuous monitoring of human motion. Wearable motion detection is mostly based on strain sensors, whereby the change in the base resistance is correlated with motion-related activities [68]. Strain sensors were developed using metal embedded into an elastomer and placed onto the hip, knee, and ankle joints to monitor their bending angles. A flexible strain sensor integrating sensing elements into textiles was proposed, which can effectively monitor the movement of the knee joint [69]. This research analyzed and guided sensor design based on the biomechanics of knee motion deformation. The sensing elements that monitor movement were encapsulated to avoid errors in measurement results. In addition, another special feature of this work was that they designed the sensor to be personalized, designed in different sizes and shapes to meet the comfort needs of different wearers. Long-term use of metals as electrodes may cause skin problems. A human motion detection device was developed using triboelectric nanogenerator (TENG) yarn, which has good skin compatibility and can be washed [70]. The device monitored body movement by attaching highly flexible and stretchable TENG fabric to different parts of the body, such as arms and knees. The TENG fabric was designed as a five-layer structure, of which the innermost layer was a coil spring. Since both ends of the coil spring are hook-shaped, they can be connected to each other to form an 11 × 11 array sensing fabric for multi-channel sensing. Surface-parallel TENG fabricated polytetrafluoroethylene yarns for large-scale energy harvesting. These works provide strong support for continuous monitoring of body movement, which should be widely used in the field of medical monitoring in the future. Recently, a magnetic tactile sensor was developed that distinguishes stretching and bending stimuli accordingly by opposite electrical signals [71]. The sensor used PDMS as the flexible substrate and mask-patterning and spin-coating technology to design a sandwich structure thin film sensor. The sandwich structure sensor attached to the surface of the skin was converted into the electrical signal output by feeling the pull force when the joint was bent. Since the sandwich structure sensor contained magnetic nanoparticles and the ability of self-sensing, it can be used as a non-contact magnetic sensor to effectively prevent the spread of bacteria in medical environments.

2.4. Respiratory Rate

Monitoring respiratory rate has always been an important indicator of concern for doctors, patients, and those who care about their own physical health. With the outbreak of COVID-19 in recent years, people are paying more attention to monitoring respiratory rates. Therefore, the respiratory rate should be given more attention as a key aspect of vital signs because an abnormal respiratory rate is often a symptom of many diseases, such as sleep apnea, asthma, chronic obstructive pulmonary disease, anemia, nasal and sinus blockage, cough, and mild fever [72][73].

The commonly used respiratory rate monitoring technology is mainly the chest impedance method. In impedance plethysmography, electrodes are placed onto the body, and the change in impedance between them reflects the change in lung volume during inhalation and exhalation [74]. However, long-term attachment to the skin can cause discomfort. Due to their simplicity, stretchability, small size, and immunity to electromagnetic interference, fiber Bragg grating (FBG) sensors are widely used in respiratory rate monitoring applications [75][76]. When the FBG sensor monitors the respiratory rate, it is usually based on two methods. First, the FBG sensor records the respiratory rate by monitoring the change in the chest volume during the breathing process. Another way is to monitor respiration rate by differences in temperature and humidity during respiration [77]. A sensor designed to monitor the breathing rate of workers working under high pressure was proposed, which equipped the FBG to the clothing to form a smart clothing system [78]. The polyimide (PI) was used as a fiber coating, and then the FBG was encapsulated in a flexible matrix, which can improve the performance of the sensor and accommodate people of different body sizes.

2.5. Glucose

Blood glucose concentration is an essential indicator of the management of certain diseases, such as diabetes. According to the World Health Organization, 9% of adults worldwide have diabetes [79], so it is crucial to continuously monitor glucose to keep people with diabetes on track. Although routine blood glucose testing is done by sampling blood, this invasive method is uncomfortable and does not allow continuous monitoring. According to research, glucose levels in the blood correlate with biological fluids such as sweat, saliva, and tears [80][81][82]. Then, compared to the other two liquids, sweat extraction is obviously more convenient and hygienic. Therefore, sweat can be monitored by stretchable electrochemical sensors, providing important information related to blood glucose in time [80][83]. A device for the extraction and analysis of sweat was reported based on agarose hydrogels [84]. In this research, an L-lactic acid biosensor using potentiometric detection technology enabled in situ sweat extraction when the skin of the finger came into contact with the hydrogel.

2.6. pH

pH is another critical parameter to maintain physiological homeostasis and assess physical conditions because it is closely related to the wound-healing of human skin. Moreover, the activity of most enzymatic reactions also depends on pH, which can prompt much information about physiological conditions [85][86]. Therefore, continuous monitoring of pH also makes sense to maintain a healthy state. With the gradual popularization of pH sensor applications in various industries, especially in the field of healthcare, traditional electrodes (such as glass electrodes) can no longer meet the new needs of personalized healthcare [87]. Traditional electrodes often have shortcomings due to the lack of bending ability, difficulty in miniaturization, and brittleness during movement [88]. Flexible, wearable, low-cost, and biocompatible pH sensors have attracted considerable interest from researchers [89].

Table 1. Summary of flexible sensors for vital sign monitoring.

Biological Signals	Sensors	Flexible Materials	Features	Refs
Temperature	temperature sensor array	PANI, Ecoflex	precise response time, high resistance sensitivity	[37]
	temperature sensor array	PI, PDMS	excellent mechanical flexibility, visible transparency, self-power	[90]
	temperature sensors	PEI	ultrathin, flexible, lightweight	[39]
Blood pressure	graphene electronic tattoos	graphene	self-adhesive, low-impedance, lightweight	[91]
	piezo-composite ultrasonic sensor	PDMS	noninvasive, nonocclusive, calibration-free	[92]
ECG	ECG electrode	natural leather	convenient, comfortable, flexible, wearable	[52]
Pulse	strain sensor	PANI	flexible, low cost, wearable, simple manufacturing process	[56]
	pressure sensor arrays	PDMS, PET	flexible, wearable, multichannel	[57]

Biological Signals	Sensors	Flexible Materials	Features	Refs
Human motion	strain sensor	conductive textile	washable, lightweight, flexible, reusable wearable	[69]
	triboelectric nanogenerator fabric sensor arrays	PDMS	flexible, stretchable, self-power	[70]
	eye-movement sensor	PDMS	highly-sensitive, skin-attachable, noninvasive	[93]
Respiratory rate	fiber Bragg gratings sensors	PI, silicone	wearable, flexible	[78]
	fiber Bragg gratings sensors	textiles	Wearable, multi-point sensing,	[94]
Glucose	sweat sensor	agarose hydrogel	noninvasive, simple, in-situ analysis	[84]
	iontophoresis integrated microfluidic epidermal biosensor	PDMS	soft, flexible, wearable, skin-mounted, non-invasive,	[95]
pH	pH sensor	composite silk fibroin film	high flexibility, biocompatibility, air permeability, biodegradability	[96]
	electrochemical pH Sensor	PET, PANI	skin-attachable, wearable, flexible	[97]

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