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Review

Clinical applications of smart wearable sensors

Qingxiao Tao,[1,6] Suwen Liu,[1,6] Jingyu Zhang,[2,3,6] Jian Jiang,[1] Zilin Jin,[1] Yuqiong Huang,[1] Xin Liu,[1] Shiying Lin,[1] Xin Zeng,[2] Xuemei Li,[2] Guangming Tao,[4,5,*] and Hongxiang Chen[1,2,*]

SUMMARY

Smart wearable sensors are electronic devices worn on the body that collect, process, and transmit various physiological data. Compared to traditional devices, their advantages in terms of portability and comfort have made them increasingly important in the medical field. This review takes a unique clinical physician's standpoint, diverging from conventional sensor-type-based classifications, and provides a comprehensive overview of the diverse clinical applications of wearable sensors in recent years. In this review, we categorize these applications according to different diseases, encompassing skin diseases and injuries, cardiovascular diseases, abnormal human motion, as well as endocrine and metabolic disorders. Additionally, we discuss the challenges and perspectives hindering the development of sensors for clinical use, emphasizing the critical need for interdisciplinary collaboration between medical and engineering professionals. Overall, this review would serve as an important reference for the future direction of sensor devices in clinical use.

INTRODUCTION

Traditional healthcare systems encounter numerous barriers in chronic disease monitoring, personalized medicine, disease prevention, and early intervention. With the increasing prevalence of chronic diseases among the elderly, continuous monitoring and long-term care are necessary. However, hospitals in resource-limited areas struggle to provide long-term monitoring, which may result in disease progression and significantly impact the patients' quality of life.[1,2] For instance, in the case of diabetes, inadequate monitoring and control of blood sugar can eventually lead to chronic complications like atherosclerosis, diabetic nephropathy, diabetic retinopathy, and peripheral neuropathy.[3,4] Additionally, traditional healthcare systems tend to focus on diseases rather than recognizing the unique characteristics of individual patients. This may result in suboptimal treatment outcomes. Moreover, traditional healthcare systems often prioritize disease treatment over prevention, causing patients to delay seeking medical services until significant symptoms manifest. Consequently, opportunities for early treatment are missed. In contrast, real-time healthcare systems have gained considerable attention, aiming to offer immediate diagnostic and therapeutic services to patients.[5] Medical devices that facilitate timely diagnosis and disease monitoring are of great importance.

Smart wearable sensors are electronic devices worn on the body that can collect, process, and transmit various physiological data. Compared to traditional monitoring devices, these new wearable devices are continuously improving in portability, comfort, and detection accuracy.[6] On the one hand, through wearable sensors, healthcare professionals can track patients' abnormal conditions and receive alerts when medical attention are required. This facilitates early intervention and prevents disease deterioration.[7] On the other hand, wearable sensor devices can provide home-based monitoring solutions for chronic disease management, enabling patients to track and manage their own health status.[8] Wearable sensors are becoming increasingly important in the field of healthcare as they can improve patient care and outcomes.

In the era of Internet of Things (IoT) and fifth-generation (5G) wireless technology, data captured by wearable devices can be conveniently transmitted to the cloud. This enables healthcare professionals to gain insights into patients' health status and formulate diagnostic and treatment plans.[9,10] With the ongoing advancements in data processing technologies like cloud computing, machine learning, and artificial intelligence, the raw sensor data can be transformed into clinically interpretable information and the abnormal

[1]Department of Dermatology, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan 430022, China

[2]Department of Dermatology, Huazhong University of Science and Technology Union Shenzhen Hospital, Shenzhen 518052, China

[3]Shenzhen University Medical School, Shenzhen 518060, China

[4]Wuhan National Laboratory for Optoelectronics, Huazhong University of Science and Technology, Wuhan 430074, China

[5]State Key Laboratory of Material Processing and Die & Mould Technology, School of Materials Science and Engineering, Huazhong University of Science and Technology, Wuhan 430074, China

[6]These authors contributed equally

*Correspondence: tao@hust.edu.cn (G.T.), hongxiangchen@hotmail.com (H.C.)

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data can be identified. We believe that the integration of wearable sensor-based diagnosis, monitoring, and wireless communication may provide possibility to real-time medical services.[11,12]

This review summarizes the clinical applications of wearable sensor devices in various clinical scenarios, including skin diseases and injuries, cardiovascular diseases (CVDs), abnormal human motion, endocrine and metabolic disorders, drug concentration monitoring, and heavy metal toxicity detection. Although wearable sensors hold significant potential, challenges persist in their clinical implementation. Further research and collaboration between medical and engineering professionals are crucial to bridging this gap and deploying more sensor devices in clinical settings to serve patients. This will ultimately drive the transition of diagnosis and treatment from hospital-based to home-based, alleviating the burden on healthcare resources and illuminating the future of healthcare systems.

WEARABLE SENSOR APPLICATIONS IN HUMAN BODY SYSTEMS

Detection of skin diseases and injuries

The skin is the largest organ of the human body and serves as the primary interface for wearable sensor devices. It's a complex organ comprising the epidermis, dermis, and subcutaneous layers, interconnected by an intricate network of blood vessels and nerves.[13] The epidermis is mainly composed of keratinocytes and serves as a critical barrier. Its outermost layer acts as protection against mechanical stimulation, prevents cellular water loss, and helps maintain thermal homeostasis. The dermis, located between the epidermis and subcutaneous layers, is primarily comprised fibroblasts that synthesize and secrete collagen fibers, providing the skin with mechanical resistance and tensile strength. The dermis also houses numerous blood vessels that regulate heat loss by constricting or dilating. The subcutaneous layer consists mainly of connective tissues, adipose cells, and extensive blood vessels. This layer functions as a mechanical cushion that safeguards the skin from external impacts and aids in maintaining a consistent body temperature.[14]

Skin disorders can affect one or more layers of the skin, disrupting its essential functions. These conditions can be broadly classified as inflammatory skin diseases, skin tumors, and wound healing disorders. The assessment of skin diseases by visual inspection lacks objectivity and has limitations in providing information about the affected skin layers. Therefore, there is a need for precise and quantitative methods to detect and monitor skin diseases and injuries. The applications of wearable sensor devices in the field of skin detection are discussed in separate sections in the following text.

Inflammatory skin diseases

Inflammatory skin diseases such as atopic dermatitis (AD) and psoriasis have different underlying causes, including genetic predisposition, immune dysfunction, and environmental factors. These diseases can affect different skin layers and lead to symptoms like itching, redness, and rash, significantly impacting patients' quality of life.[15] Wearable sensor devices offer potential assistance in diagnosing and monitoring of inflammatory skin diseases by providing objective and quantitative data on skin parameters.

Pruritus, or itching, is a typical characteristic of AD and can impose a significant burden on patients with moderate to severe AD.[16] However, quantifying itchiness poses challenges due to its subjective nature. While direct visual inspection of scratching in video recordings is considered the gold standard, it is labor-intensive and impractical for clinical use. To address this, Chun et al. developed the advanced acoustomechanic (ADAM), a wearable sensor device that accurately detected scratching signals produced by fingers or wrist movements (Figure 1A). The device has been clinically validated in both children and adults, providing a highly accurate approach for the objective assessment of pruritus.[17,18]

Accurate measurement of skin hydration is crucial for both dermatological research and clinical practice. Skin hydration is considered a valuable surrogate marker for skin barrier function and overall skin health. Madhvapathy et al. have presented a soft, reusable, battery-free, and noninvasive skin hydration sensor (SHS) that could accurately measure skin water content irrespective of body location or environmental factors. The researchers utilized SHS to detect differences in skin hydration at lesional sites of patients with AD or psoriasis and monitored the efficacy of moisturizer treatment.[19] In 2022, Shin et al. optimized the SHS to enhance its sensitivity and accuracy (Figure 1B).[20] This innovative approach assists in the diagnosis and monitoring of treatment for patients with inflammatory skin diseases.

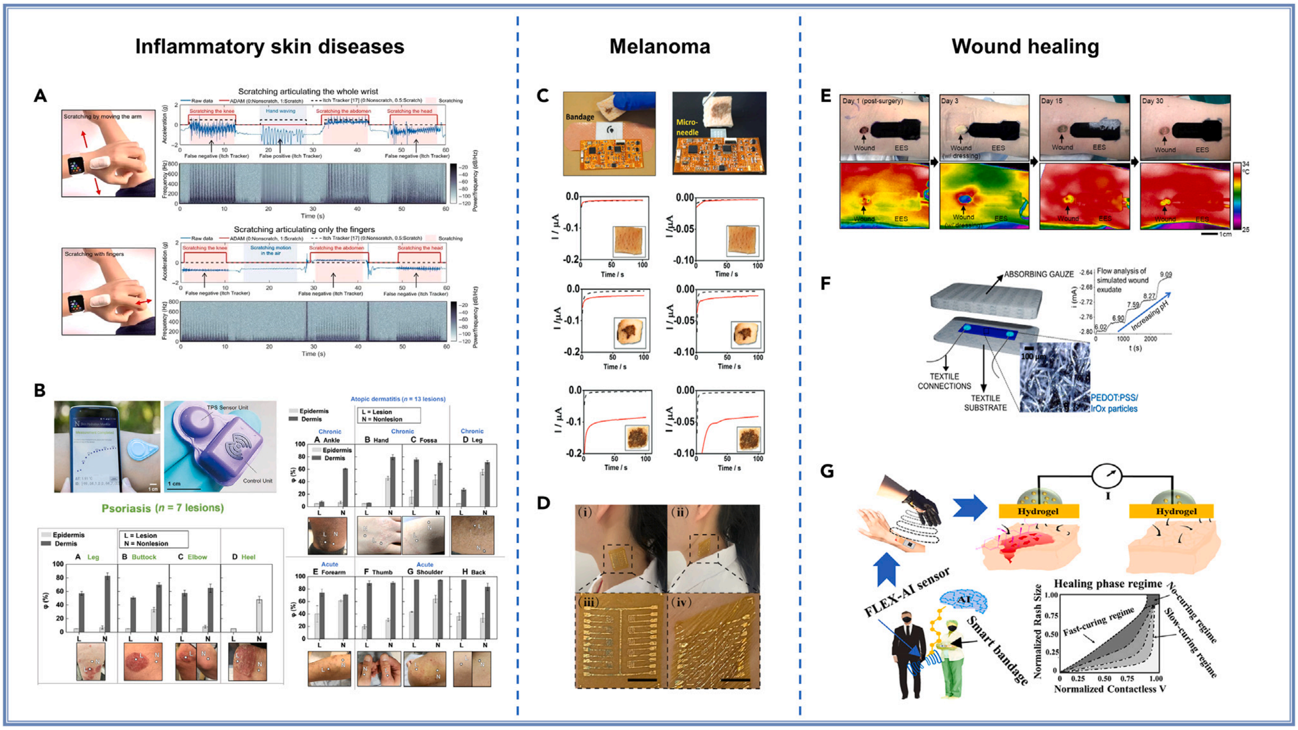

Figure 1. Wearable sensor detection of skin diseases and injuries

(A) Comparison of results obtained with an advanced acoustomechanic (ADAM) device on the hand and an Apple Watch with the Itch Tracker mobile application. Reproduced with permission, from Chun et al.,[17] Copyright 2021, AAAS.

(B) Image of noninvasive skin hydration sensors and evaluation of the hydration levels in atopic dermatitis and psoriasis. Reproduced with permission, from Madhvapathy et al. and Shin et al.,[19,20] Copyright 2020, AAAS.

(C) Screening of tyrosinase in porcine skin using the wearable bandage and microneedle electrochemical sensors. Reproduced with permission, from Ciui et al.,[25] Copyright 2018, Wiley-VCH.

(D) Photographs of field-effect transistor-based biosensor (bio-FET) arrays that are flexible and conformably attached to the skin on the human neck in both the flat and stretched states. Reproduced with permission, from Ren et al.,[26] Copyright 2022, Elsevier.

(E) Quantitative monitoring of wound healing progress over the course of 30 days using an epidermal electronics system (EES). Reproduced with permission, from Hattori et al.,[29] Copyright 2014, Wiley-VCH.

(F) Wound dressing for real-time pH monitoring. Reproduced with permission, from Mariani et al,[31] Copyright 2021, American Chemical Society.

(G) A conceptual diagram of binary wearable system and prediction of inflamed wound healing stages using AI. Reproduced with permission, from Kalasin et al.,[32] Copyright 2022, American Chemical Society.

Melanoma

Melanoma originates from melanocytes and is the most common type of skin tumors. It displays aggressive behavior and undergoes malignant transformation throughout the epidermis and superficial dermis via blood and lymphatic vessels.[21] Dermoscopy is a widely used noninvasive technique for the early detection of melanoma, while heavily relying on dermatologists' expertise.[22] In addition to noninvasive morphological examinations, researchers are also exploring the detection of melanoma biomarkers. Immunohistochemistry can be used to stain multiple biomarkers, with lactate dehydrogenase (LDH) in serum being the most specific biomarker.[23] However, these techniques remain complex and time-consuming.

Recent researches have focused on faster and simpler methods for detecting other melanoma biomarkers, such as the enzyme tyrosinase (TYR). TYR is a polyphenol oxidase involved in melanin synthesis and its overexpression and accumulation in skin cells associates with melanoma development.[24] Ciui et al. have introduced novel integrated wearable bandage and microneedle electrochemical sensing platforms for detecting TYR on both the skin surface and subcutaneously. They validated their approach by using a porcine skin melanoma model and obtained accurate screening results (Figure 1C).[25] In another study, Ren et al. reported the use of wearable field-effect transistor-based biosensors (bio-FETs) for tyrosinase sensing in melanoma screening (Figure 1D).[26] This sensor device exhibited excellent mechanical flexibility to conform well to the skin. These studies presented wearable sensors capable of screening for TYR in both skin and deep tissues, providing a promising, rapid, and convenient tool for future melanoma tissue screening.

Wound healing

For dermatological surgery, monitoring wound healing is crucial for evaluating treatment effectiveness and ensuring optimal healing outcomes. Accurate and timely assessment of wound healing is essential for preventing complications like infections, delayed healing, and scarring. However, traditional methods such as visual inspection and manual measurements can be subjective, time-consuming, and may not capture changes in the wound over time. Confocal laser scanning microscopy and spectroscopy are quantitative imaging techniques that can detect microscopic changes of the epidermis and dermis morphology. However, these methods often require patient's immobilization during testing.[27,28]

To address these limitations, sensor devices for wound monitoring have emerged as a promising approach. These devices provide objective, real-time, and continuous data on wound healing parameters like temperature, pH, and so on. Hattori et al. introduced an innovative epidermal electronics system (EES) that recorded time-dynamic temperature and thermal conductivity of the skin tissue, providing valuable insights into the healing process (Figure 1E).[29] Noninvasive assessment of wound pH is also useful in determining wound status and evaluating the effectiveness of therapeutic interventions, as a slightly acidic pH promotes optimal healing by controlling collagen formation, increasing fibroblast activity, and inhibiting bacterial proliferation.[30] Mariani et al. developed a smart dressing that enabled real-time monitoring of wound pH, which assessed wound status without disturbing the wound bed (Figure 1F).[31] Additionally, Kalasin et al. introduced a wearable system for non-contact monitoring of wounds. This binary system comprised a flexible artificial intelligence (FLEX-AI) wearable sensor and a smart bandage that communicated via radio frequency identification (RFID) technology. This contactless healthcare technology utilized AI to determine the recovery stage of inflammatory skin disease lesions, whether they were in inflammation, proliferation, or remodeling. This provides objective parameters for evaluating treatment effectiveness and guiding medication plans for dermatologists (Figure 1G).[32]

Detection of Cardiovascular Diseases

CVDs encompass a range of conditions that affect the heart and blood vessels, contributing to reduced quality of life and high mortality rates. CVDs account for approximately 17 million deaths annually, which represent 31% of total global deaths.[33] Urgent attention is needed for effective monitoring and management of these diseases. Heart rate and rhythm, blood pressure, and blood oxygen saturation are crucial parameters for CVD diagnosis and monitoring. However, traditional measurement methods lack real-time monitoring capabilities and can be challenging to operate without professional guidance. Fortunately, advancements in sensor technology have yielded portable, high-precision, real-time, and noninvasive devices for monitoring these parameters.

Heart rate and rhythm

Cardiac arrhythmias are abnormalities in the frequency, rhythm, origin site, conduction speed, or excitation sequence of cardiac impulses. They include atrial fibrillation, ventricular fibrillation, and supraventricular tachycardia, which can lead to serious consequences such as heart failure or even death. The frequency of cardiac impulses is known as heart rate (HR), typically ranging between 60 and 100 beats per minute in healthy adults at rest.[34] Electrocardiogram (ECG) electrodes are commonly used to record heart activity signals, with traditional gel-assisted Ag/AgCl wet electrodes applied to limb and chest areas. However, such electrodes may not be suitable for long-term wear due to the poor gel adhesion and water evaporation. The Holter monitor can capture ECG changes over 24 h but requires multiple electrodes affixed to the patient's chest, resulting in complex wiring, lack of portability, and potential disconnection risks.

Advances in technology have led to the development of skin-adhesive dry electrodes for ECG measurements. Zhang et al. have fabricated a fully organic, self-adhesive, and stretchable dry electrode with excellent skin compliance and high conductivity. It maintained its conductive properties even when stretched and adhered well to dry and wet skin conditions. Compared to standard Ag/AgCl gel electrodes, it exhibited lower contact impedance when applied to the skin, resulting in significantly reduced noise levels during static and dynamic detection (Figure 2A).[35] Furthermore, electronic textiles, like sewable electrodes and signal transmission wires made of carbon nanotube threads (CNTT), offered comfort in wearable

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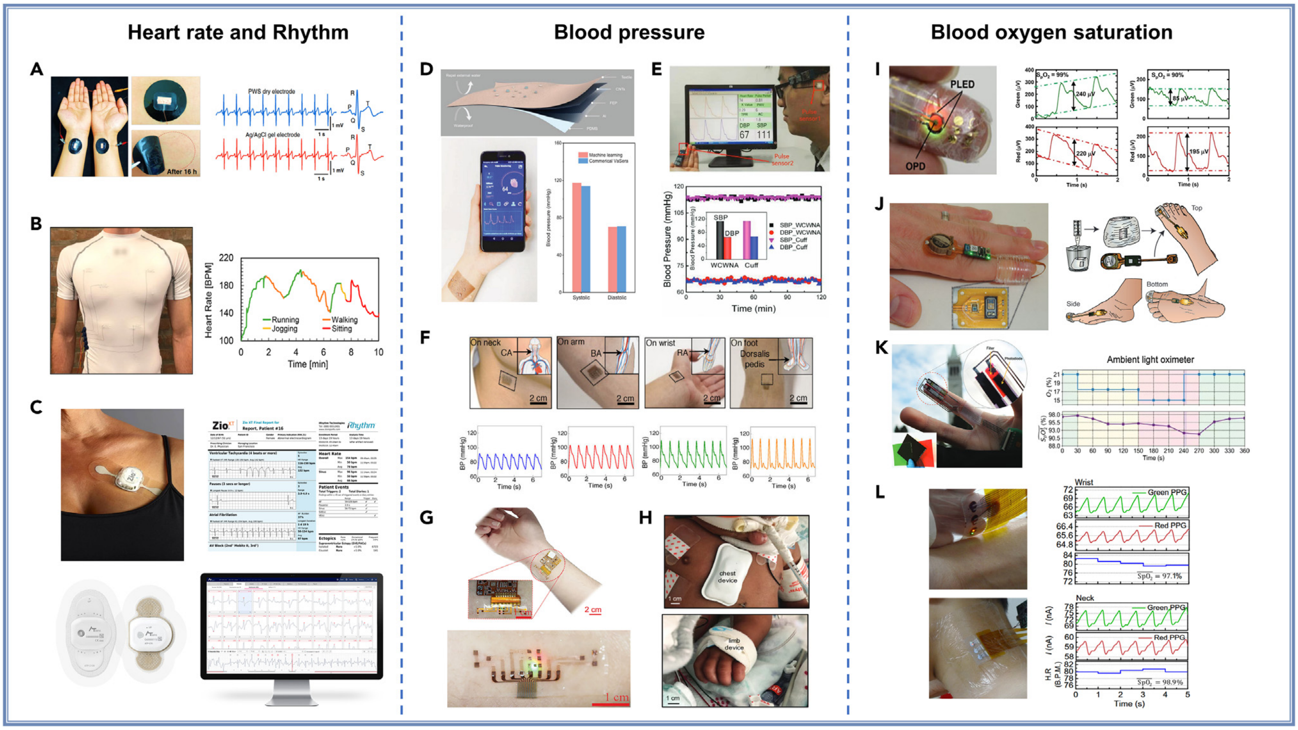

Figure 2. Wearable sensor detection of CVDs

(A) ECG detection using dry electrodes. Reproduced with permission, from Zhang et al.,[35] Copyright 2020, Nature Publishing Group.

(B) Heart rate monitoring with carbon nanotube threads (CNTT) textile. Reproduced with permission, from Taylor et al.,[36] Copyright 2021, American Chemical Society.

(C) Portable ECG monitoring with Zio Patch (iRhythm Technologies, Inc, San Francisco, Calif) and AT-Patch (ATsens, Seongnam, Korea).

(D) Machine learning-enabled textile triboelectric sensor for estimating systolic and diastolic blood pressure. Reproduced with permission, from Fang et al.,[41] Copyright 2021, Wiley-VCH.

(E) Weaving constructed self-powered pressure sensor (WCSPS) for blood pressure measurement. Reproduced with permission, from Meng et al.,[42] Copyright 2018, Wiley-VCH.

(F) Wearable ultrasonic device for blood pressure monitoring across central and peripheral arteries. Reproduced with permission, from Wang et al,[44] Copyright 2018, Nature Publishing Group.

(G) Optoelectronic system with skin-like properties. Reproduced with permission, from Li et al.,[45] Copyright 2020, Oxford Univ Press.

(H) Wireless blood pressure monitoring in PICU patients with soft, skin-interfaced devices. Reproduced with permission, from Liu et al.,[46] Copyright 2021, Wiley-VCH.

(I) SpO_2 measurement using organic pulse oximeter with exceptional flexibility. Reproduced with permission, from Yokota et al.,[48] Copyright 2016, AAAS.

(J) Wearable pulse oximeter for finger and toe, fabricated by 3D printing technology. Reproduced with permission, from Abdollahi et al.,[49] Copyright 2020, Wiley-VCH.

(K) Comparison of SpO_2 measurement using ambient light oximeter (ALO) and commercial oximeter. Reproduced with permission, from Han et al.,[50] Copyright 2020, Wiley-VCH.

(L) Organic pulse oximeter (OPO) sensor measurements at wrist and neck. Reproduced with permission, from Lee et al.,[51] Copyright 2018, AAAS.

electronic products due to their softness, light weight, and breathability. They could withstand repeated stretching and machine-washing without compromising signal quality (Figure 2B).[36] Besides sensors that are still in the experimental phase, wearable patch devices such as the Zio Patch from iRhythm Technologies and AT-Patch from ATsens, have received FDA clearance and are commercially accessible (Figure 2C). Zio Patch has advanced algorithms for accurate arrhythmia detection and can store up to two weeks of data. AT-Patch shows high performance in gathering ECG signals from the heart, and its short-length electrode within the patch effectively reduces noise caused by body movement.[37,38]

Blood pressure

Hypertension is characterized by elevated blood pressure, typically measured in systolic and diastolic values. Uncontrolled blood pressure can result in severe medical complications including congestive heart failure, myocardial infarction, cerebrovascular accidents, retinopathy, and renal dysfunction.[39] Continuous monitoring of blood pressure is essential because traditional cuff-based measurements only provide a snapshot of pressure. Thanks to technological advancements, there is a growing availability of sensor devices for continuous blood pressure monitoring, which are beneficial for the prevention and management of hypertension.

The arterial pulse wave is a crucial biological signal used for monitoring and diagnosing arterial stiffness and hypertension-related CVDs. It provides valuable information on arterial elasticity, peripheral resistance, and left ventricular contractility.[40] By utilizing machine learning algorithms, a textile triboelectric sensor device could provide continuous and accurate measurements of systolic and diastolic blood pressure (Figure 2D). The device's accuracy has been validated against a commercial blood pressure cuff. The textile triboelectric sensor enabled the creation of a wireless biomonitoring system, offering a practical solution for continuous and personalized characterization of the cardiovascular system in the era of IoT.[41] Additionally, Meng et al. reported a flexible weaving constructed self-powered pressure sensor (WCSPS) for noninvasive measurement of the pulse wave and blood pressure. The WCSPS demonstrated a difference in recorded blood pressure values of approximately 0.87–3.65% compared to a commercial cuff-based device (Figure 2E).[42]

Central blood pressure (CBP) waveforms are more informative to CVDs than peripheral blood pressure (PBP) waveforms, as the central arteries directly supply blood to vital organs such as the heart, brain, and kidneys.[43] Wang et al. developed a flexible ultrasonic device (240 μm thickness) that could noninvasively and continuously monitor blood pressure waveforms from deeply embedded arterial and venous sites, including the carotid artery, brachial artery, radial artery, and dorsalis pedis artery (Figure 2F).[44] To monitor arterial pressure, Li et al. introduced a high-performance, skin-like optoelectronic system integrated with ultra-thin flexible circuits, providing a more convenient method for blood pressure measurement (Figure 2G).[45] For newborns, Claire et al. reported the development of soft, skin-interfaced, and wireless devices for accurate and continuous blood pressure monitoring in pediatric intensive care unit (PICU) patients. This noninvasive, wireless alternative could greatly improve the quality of patient care (Figure 2H).[46]

Blood oxygen saturation

Oxygen saturation is a crucial indicator of human physiological status, and it is determined by the proportion of oxyhemoglobin (HbO_2) among the total hemoglobin in the blood. In healthy adults, normal arterial oxygen saturation (SaO_2) levels typically range from 96% to 98%. For sensor devices such as pulse oximeters, peripheral oxygen saturation (SpO_2) is measured in a noninvasive and continuous manner as an estimation of SaO_2.[47]

In clinical applications, commercial pulse oximeters traditionally use rigid materials, which negatively impact the size of the sensor. Yokota et al. created an ultra-flexible reflective pulse oximeter which discreetly attached to a finger and measures blood oxygen concentration. The device included digital displays with seven-segment characters and color indicators applied directly to the skin for data visualization (Figure 2I).[48] To overcome poor fit and mechanical mismatch for continuous monitoring, Abdollahi et al. combined 3D printing of polydimethylsiloxane (PDMS) with flexible electronics to create a patient-specific pulse oximeter, known as P3-wearable (Figure 2J). This small-sized device (approximately 8 cm) composed of soft materials provided continuous, real-time feedback on a tablet. Other than used on fingers and toes, this approach has the potential to be locating sensors on other parts of the body.[49]

Traditional pulse oximetry sensors consume significant power, making them unsuitable as stand-alone continuous monitoring systems. To address this limitation, Han et al. developed an ambient light oximeter (ALO) that utilized various types of ambient light to measure photoplethysmography signals and SpO_2, eliminating the need for LEDs and reducing power consumption (Figure 2K).[50] Additionally, Lee et al. created an ultralow power consumption, reflective patch-style pulse oximetry sensor known as organic pulse oximeters (OPOs). These devices require only a few tens of microwatts of power, indicating great potential for power efficiency. OPOs are an attractive option for stand-alone wearable devices capable of continuous all-day monitoring (Figure 2L).[51]

Detection of abnormal human motion

Human motion disorders can be caused by various factors such as musculoskeletal injuries, neurological disorders, and cerebrovascular accidents. The abnormal motion patterns can occur at different body regions, including the neck, shoulders, fingers, and limbs. On-site wearable sensors offer a reliable means of detecting these abnormal patterns. The use of the sensor devices provides an energy-efficient and cost-effective solution for motion tracking, opening up the possibility for early diagnosis, disease progression monitoring, and improvement of rehabilitation outcomes.

Motion tracking of neck, shoulders, and fingers

The head and neck play an important role in human posture and motion. Cervical spine problems including forward head posture and chronic neck pain are prevalent in the modern world.[52,53] From a clinical standpoint, evaluating the range of motion in the head and neck can provide valuable insights into cervical spine problems. Sensor-based monitoring of the neck motion can facilitate neck posture adjustment and consequently prevent cervical spine disorders. In 2022, a neck motion detector demonstrated promising applications in neck monitoring, control, and rehabilitation. This detector consisted of a self-sufficient triboelectric sensor group integrated onto a neck collar, along with a convolutional neural network-based deep learning block. The sensors generated voltage signals that varied in amplitude and direction, effectively representing different motion states during neck movements. The deep learning model accurately recognized eleven classes of neck motion with an average accuracy of over 90% (Figure 3A).[54]

Shoulder disorders are also highly prevalent and a significant source of morbidity. Physical workplace strains like overhead work, heavy lifting, forceful exertion, as well as working in awkward postures are established risk factors for shoulder disorders including frozen shoulder (adhesive capsulitis), rotator cuff, and so on.[55] For individuals with frozen shoulder or rotator cuff disease, physical exercise therapy has been found efficacious in enhancing the range of motion, function, and reducing pain.[56,57] However, shoulder activity after the early postoperative phase is linked with a heightened risk of rotator cuff retears among patients receiving surgical repair.[58] In 2020, a flexible resistive sensor network was reported to provide robust shoulder tracking. Through principal component analysis and neural network algorithms, the device mapped the obtained data onto shoulder posture and achieved optimal accuracy requirements. The sensor could also be easily embedded into fabrics or wearable devices without hindering the user's movement (Figure 3B).[59]

In addition to neck and shoulder, accurate and objective monitoring is also crucial for finger rehabilitation. In 2020, a novel measuring system successfully integrated electronic skin with a deep neural network to capture distant dynamic motions. The skin sensor could decode five finger movements in real time when placed on the wrist (Figure 3C).[60]

Motion tracking of the upper limb (UL) and lower limb (LL)

Neurological disorders have become the leading cause of disability worldwide, with Parkinson's disease (PD) being the fastest-growing disorder among them. PD is a neurodegenerative disorder that affects the nigrostriatal system, resulting in distinct motor symptoms including tremor, bradykinesia, and rigidity.[61] The diagnosis of PD currently relies on clinical evaluation, including the Unified Parkinson's Disease Rating Scale (UPDRS), which heavily depends on the clinician's experience and expertise. Nowadays, wearable sensor devices are increasingly recognized for their potential to improve the accuracy and objectivity of PD diagnosis via movement monitoring.[62] Stroke is also a leading cause of long-term disability.[63] For numerous stroke survivors and their families, the disease leads to a life which encompasses physical disability, cognitive dysfunction, exhaustion, and psychological issues including depression and anxiety.[64] The rehabilitation process for stroke patients entails tailored exercises, which are frequently constrained by healthcare resource availability. Wearable technology has shown potential in providing objective assessment and monitoring of patients in both clinical and non-clinical settings, enabling a detailed evaluation of impairments and personalized rehabilitation therapies. Several technological aids have been developed to monitor post-stroke impairments of both upper limb (UL)[65] and lower limb (LL)[66] movements.

In UL rehabilitation, ad hoc contraptions incorporating inertial measurement units and accelerometers are frequently utilized to enhance the range of motion and movement performance. There is also an emerging trend toward incorporating sensors within wearable garments or appliances.[65] In 2018, a garment equipped with posture-monitoring sensors was developed for upper extremity rehabilitation training. Patients undertook four guided training tasks on a tablet, receiving feedback from the Zishi system's inertial sensors located in the scapula and thoracic spine region. The participants exhibited strong motivation to engage in training via the Zishi system, which received favorable ratings for usability

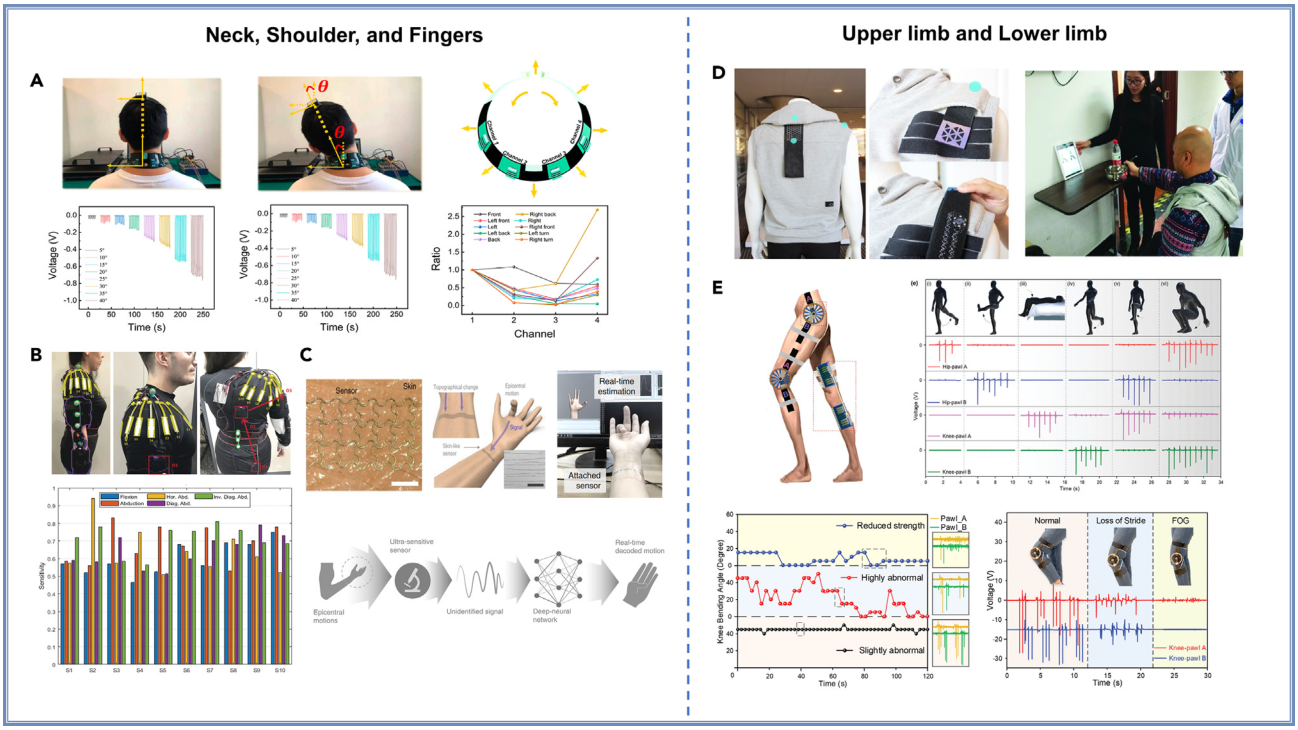

Figure 3. Wearable sensor detection of abnormal human motion

(A) Picture of the neck motion sensor. Schematic diagram of bending/twisting directions and the channels of the sensor. Channel 1 and 4 generate voltage signals that reflect the neck bending to the left and right at various angles (θ). Ratio of output voltage of the 4 channels during 10 types of neck motions. Reproduced with permission, from An et al.,[54] Copyright 2022, American Chemical Society.

(B) Shoulder motion tracking systems, including the orthesis blocking the elbow (purple), flexible resistive sensors (yellow), OptiTrack markers (green), and the inertial measurement units embedded in fabric (red). Detection of shoulder motions by each flexible resistive sensor. Reproduced with permission, from Samper-Escudero et al.,[59] Copyright 2020, Mary Ann Liebert, Inc.

(C) Image of the finger motion sensor attached to the skin. Illustration depicting the measurement of the epicentral motions of fingers. Photo of actual finger motion generation. Design of the proposed sensory system. Reproduced with permission, from Kim et al.,[60] Copyright 2020, Nature Publishing Group.

(D) Back view of the sensor-embedded garment and the adjustable design. A subject is instructed of performing a training task. Reproduced with permission, from Wang et al.,[67] Copyright 2018, IEEE.

(E) Configuration of the motion-capturing and energy-harvesting hybridized lower-limb (MC-EH-HL) system mainly consisting of two components: ratchet-based triboelectric nanogenerator (R-TENG) and sliding block-rail piezoelectric generator (S-PEG). Output voltages of the hip- and knee-located R-TENGs on the left leg of the user under distinct lower-limb motions. The detected knee angles during motions, with three gait features including reduced strength, highly abnormal, and slightly abnormal. Voltage of the R-TENG on the knee during stepping to detect typical parkinsonian gait patterns such as normal gait, loss of stride, and freezing of gait period. Reproduced with permission, from Gao et al.,[69] Copyright 2021, Wiley-VCH.

(Figure 3D).[67] Furthermore, a systematic review also highlighted the potential of wearable technology for UL rehabilitation in motivating stroke survivors to engage in more exercises independently. This can further lead to improved recovery outcomes in the absence of a therapist.[68] On the other hand, a motion-capturing and energy-harvesting hybridized lower-limb (MC-EH-HL) system with 3D printing has been developed in 2021. This system incorporated a sliding block-rail piezoelectric generator (S-PEG) for low-frequency energy harvesting and a ratchet-based triboelectric nanogenerator (R-TENG) for LL motion sensing. The R-TENGs located at the hip and knee on user's left leg outputs voltages under LL motions, and the knee angles could be detected with three imitated gait features, including reduced strength, highly abnormal, and slightly abnormal. Additionally, the voltage output of the knee-mounted R-TENG during stepping could serve as an indicator of typical Parkinsonian gait patterns, including normal gait, loss of stride, and freezing of gait (Figure 3E).[69]

Detection of endocrine and metabolic abnormalities

Endocrine disorders refer to diseases caused by insufficient or excessive secretion of hormones, or hormone resistance in target tissues, including diabetes, hypothyroidism, hypopituitarism, and so on. Endocrine disorders can further affect human metabolic processes and lead to a series of complications.[70,71]

Metabolic diseases are often resulted from the abnormal accumulation or degradation of metabolisms. Nowadays, endocrine and metabolic diseases are prevalent and impose a significant burden on public health, and the long-term monitoring of these diseases is necessary.

Blood is typically considered the gold standard for the diagnosis and monitoring of endocrine and metabolic conditions, but invasive blood collection has limitations for daily monitoring. Nowadays, noninvasive sensors through monitoring sweat, urine, tears, and saliva, have emerged as promising alternatives.[72] These sensing methods are painless, infection-free, and easy-to-use, among which sweat sensors are the most common and advantageous.

Metabolism of organic matter

There is a strong correlation between the concentration of glucose in sweat and blood.[73] Researchers have developed an all-printed temporary tattoo-based sensor that combined reverse iontophoretic extraction of interstitial glucose with an enzyme-based amperometric biosensor to detect glucose levels in sweat. This sensor, worn conveniently on the skin, could withstand repeated mechanical deformation. It provided accurate detection results and showed a strong correlation with commercial glucose meters, holding great promise for noninvasive diabetes management (Figure 4A).[74] Sweat-based glucose sensors could also be used to estimate blood glucose changes before and after exercise to prevent hypoglycemic shock caused by intense exercise.[75] Additionally, microfluidic contact lens sensors have been developed for the detection of glucose,[76] pH, protein, and nitrite levels through tears (Figure 4B).[77]

In our body, ammonia can be produced during protein metabolism. The ammonia accumulation in blood can serve as a biomarker to monitor the metabolic changes during the transition from aerobic to anaerobic exercise, and abnormally high blood ammonia levels may be associated with hepatic cirrhosis, diabetes, and chronic kidney disease.[78,79] In sweat, most of the ammonia (NH_3) molecules separated from the blood will get protonated into ammonium ions (NH_4^+) due to the relatively low pH value. This protonation of ammonia increases the concentration of NH_4^+ in sweat, which simplifies the detection methods of sensors.[80] In 2013, a tattoo-based potentiometric sensor was designed to monitor ammonium levels in sweat, providing promising prospects for exercise performance monitoring and metabolic disorder detection (Figure 4C).[81] In addition, a thread-based multiplexed sensor patch that could be directly woven or sewn onto clothing managed to keep in close contact with the skin and performed a real-time measurement of important biomarkers in sweat, including NH_4^+, sodium ions (Na^+), lactate, and pH. Extensive *in vitro* validation and human testing studies have demonstrated the potential of this sensor for health monitoring and diagnosis through sweat analysis.[82]

Tyrosinaemia type 1 (TYR1) is a rare genetic disorder with abnormal accumulation of tyrosine in the body, leading to liver, kidney, and nervous system damage. Recently, screening for TYR1 in infants has been recommended as part of England's newborn screening program.[83] Gout, a common metabolic disease characterized by a high level of uric acid (UA) in blood, can lead to painful inflammatory arthritis and a high burden of comorbidities, including hypertension, diabetes, hyperlipidemia, myocardial infarction, stroke, and chronic kidney disease.[84] In 2020, Yiran Yang et al. developed a highly sensitive laser-engraved graphene-based chemical sensor by utilizing differential pulse voltammetry (DPV), which showed rapid and accurate on-site detection of low concentrations of UA and tyrosine in human sweat (Figure 4D).[85]

Electrolyte metabolism

In clinical scenarios, the abnormal metabolism of water and sodium are common among electrolyte imbalance. Adrenal insufficiency, an endocrine disorder, can cause decreased aldosterone secretion and reduced reabsorption of sodium, which may finally contribute to hypovolemic hyponatremia and even hypovolemic shock in severe cases.[86] Central diabetes insipidus often leads to inadequate production and release of antidiuretic hormone, which results in excessive excretion of low-solute urine. In severe cases, this can cause hypernatremia and dysfunction of the central nervous system.[87] Excessive physical activity and sweating can also lead to water and electrolyte loss. In 2014, a tattoo-based potentiometric sodium sensor was developed. This sensor, when coupled with a miniature wireless transceiver, enabled real-time monitoring of sodium levels in perspiration. The data collected by the tattoo sensor could be wirelessly transmitted to a laptop for analysis.[88] In 2015, an adhesive band-aid-like sensor patch was reported. This patch adhered closely to human skin, and the paper microfluidics integrated within it absorbed sweat

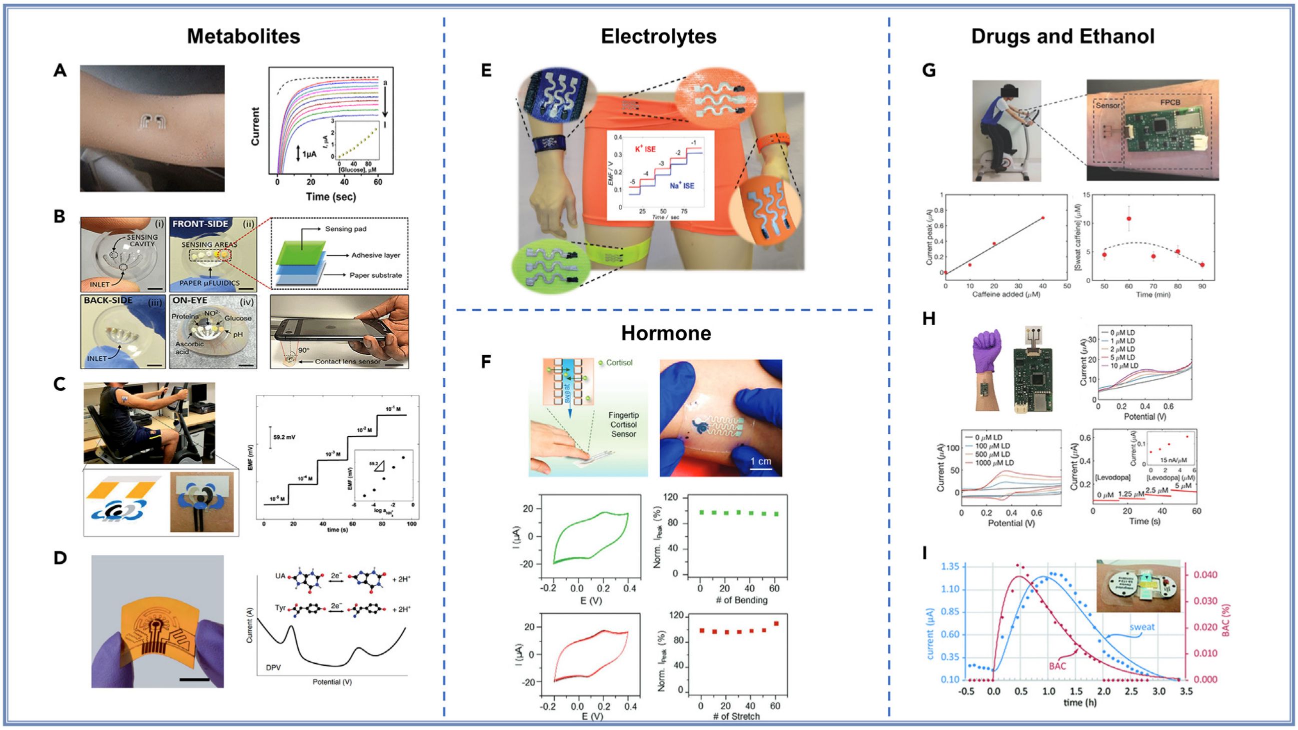

Figure 4. Wearable sensor detection of endocrine and metabolic abnormalities

(A) Photograph of an iontophoretic tattoo-based glucose sensor device applied to a human subject. Chronoamperometric response of the glucose sensor to increasing glucose concentrations from 0 μM to 100 μM in buffer in 10 μM increments. Reproduced with permission, from Bandodkar et al.,[74] Copyright 2014, American Chemical Society.

(B) Contact lens sensor with the laser-inscribed microfluidic system. Image of the frontside, backside, and on-eye view of the contact lens sensor. The schematic structure of the sensing area. Representative photograph of the readout method. Reproduced with permission, from Moreddu et al.,[77] Copyright 2020, Royal Society of Chemistry.

(C) Tattoo-based ammonium sensor placed on the shoulder. Ammonium concentration-dependent potentiometric time trace. Reproduced with permission, from Guinovart et al.,[81] Copyright 2013, Royal Society of Chemistry.

(D) Image of a laser-engraved sensor for the monitoring of tyrosine and uric acid (UA). Differential pulse voltammetry detecting the level of UA and tyrosine by measuring oxidation peak heights. Reproduced with permission, from Yang et al.,[85] Copyright 2020, Nature Publishing Group.

(E) Illustration of multi-ion potentiometric sensors on textiles, along with representative time trace plots for potassium and sodium. Reproduced with permission, from Parrilla et al.,[91] Copyright 2016, Wiley-VCH.

(F) Cortisol release from fingertip sweat pores to hydrogel in the natural sweat. Photograph of the wearable sensor patch for on-body cortisol detection. Cyclic voltammetry and the measured peak currents of the cortisol sensor when undergoing repeated bending and stretching. Reproduced with permission, from Tang et al.,[111] Copyright 2021, Wiley-VCH.

(G) Image of a subject performing cycling exercise with a sweatband containing a drug-sensing platform. Calibration curve for the sensor in sweat samples. At 30 min after caffeine intake, sweat caffeine levels were measured during the cycling experiment. Reproduced with permission, from Tai et al.,[113] Copyright 2018, Wiley-VCH.

(H) Wearable sweatband for levodopa sensing. Cyclic voltammetry of levodopa dissolved in phosphate buffered saline (PBS) for different concentration ranges. Typical amperometric response of the levodopa dissolved in PBS. The calibration curve of the current. Reproduced with permission, from Tai et al.,[114] Copyright 2019, American Chemical Society.

(I) Image of an alcohol iontophoretic-sensing tattoo device applied to a human subject. Reproduced with permission, from Kim et al.,[115] Copyright 2016, American Chemical Society.

through a porous adhesive, allowing real-time monitoring of various ionic solutes, including Cl^-, K^+, Mg^{2+}, NH_4^+, and Zn^{2+}.[89]

Potassium ions (K^+) play a vital role in biological systems, maintaining cellular metabolism, resting membrane potential, and regulating the osmotic pressure and acid-base balance.[90] In 2016, Marc Parrilla et al. designed a wearable multi-ion potentiometric sensor based on textiles to monitor the level of sodium and potassium in sweat. This printed textile sensor array, combining stretchable components like polyurethane, Ecoflex, and ink, demonstrated high tensile strength and resistance to cracking (Figure 4E).[91] In addition, Juliane R. Sempionatto et al. have constructed the first fully integrated eyeglasses-based wireless electrolyte and metabolite sensing platform. By integrating a potentiometric K^+-selective electrode and an amperometric lactate biosensor on two nose pads of the glasses and connecting them to a wireless electronic backbone on glasses' arms, the sensor enabled real-time monitoring of sweat lactate and potassium levels.[92]

The level of calcium (Ca^{2+}) can serve as a monitoring index for diseases including hyperparathyroidism,[93] chronic kidney failure,[94] and vitamin D deficiency.[95] A wearable electrochemical device has been reported for continuous monitoring of Ca^{2+} and pH in body fluids including sweat, urine, and tears for diagnosis of diseases like primary hyperparathyroidism and kidney stones.[96]

pH values offer insights into electrolyte variations in sweat, enabling the monitoring of metabolic alkalosis or metabolic acidosis. In 2013, a tattoo-based potentiometric ion-selective sensor was developed for monitoring a wide range of pH changes of skin without carry-over effects.[97] In general, the performance and applications of the wearable pH sensors largely depend on the properties of the pH-sensitive materials, including polyaniline, hydrogen ionophores, and metal oxides. Each material type possesses distinct characteristics in terms of sensitivity, response speed, and biocompatibility.[98–102]

Hormones

Cortisol is a vital steroid hormone that regulates metabolism, immune system, and stress response.[103] Abnormal cortisol levels can occur in various diseases, including Cushing's syndrome (excessive cortisol secretion),[104] Addison's disease (inadequate cortisol secretion),[105] and in response to stress, depression, and anxiety. For continuous monitoring of cortisol in sweat, the changes of time, pH, and temperature of sweat can affect the conformation of aptamer and its binding ability, making it difficult for stable detection.[106,107] To address this challenge, Prasad and his colleagues developed an antibody-functionalized sensor in 2017. They used nanoporous substrates to fabricate a sensing array and immobilized the capture probe in room temperature ionic liquids, which enabled stable detection of interleukin-6 and cortisol in human sweat.[108] Additionally, in 2018, Onur Parlak et al. achieved stable and selective molecular recognition of cortisol in sweat by integrating an organic electrochemical transistor and a synthetic and biomimetic polymeric membrane based on molecular imprinting polymers (MIPs).[109] In 2020, a wireless cortisol sensor combining laser-induced graphene and immunosensing was reported. This sensor exhibited high sensitivity, selectivity, and efficiency due to the large surface area and rapid electron transfer characteristics of laser-induced graphene.[110] Later in 2021, Tang et al. described a touch-based noninvasive MIP electrochemical sensor for rapid, simple, and reliable detection of cortisol in fingertip sweat (Figure 4F).[111]

Detection of drugs, ethanol, and heavy metals

Drug monitoring plays a crucial role in doping control and precision medicine, as it helps doctors understand the intricate pharmacokinetics of drugs and adjust medication dosages for optimal effects.[112] In 2018, Li-Chia Tai et al. reported a wearable platform equipped with an electrochemical DPV sensing module for real-time monitoring of the methylxanthine drug caffeine in sweat (Figure 4G).[113] Levodopa, a standard medication for patients with PD, requires careful monitoring and dosage optimization to alleviate adverse physical and emotional fluctuations. Based on the correlation between the concentration of levodopa in sweat and plasma, in 2019, Li-Chia Tai et al. designed a wearable sweatband on a nanodendritic platform that quantitatively monitored the kinetics of levodopa metabolism in the body, showing promising prospect for the routine PD management (Figure 4H).[114] In addition, the concentration of sweat ethanol is also highly correlated with that in blood. In 2016, Kim et al. developed a skin-worn alcohol monitoring platform based on an iontophoretic-biosensing tattoo system. By applying the alcohol oxidase enzyme and the Prussian Blue electrode sensing, the sensor enabled amperometric detection of ethanol in pilocarpine-induced sweat (Figure 4I).[115]

Sweating is also an important way for the detoxification of heavy metals, including arsenic, cadmium, lead, and mercury.[116] In 2015, a wearable electrochemical sensor was developed by Joseph Wang and his colleagues for the detection of trace metals. A bismuth/Nafion film electrode and stripping voltammetry were utilized to enable real-time monitoring of zinc levels in human sweat, which achieved outstanding performance.[117] In 2016, Gao et al. fabricated a flexible and wearable microsensor array through the electrochemical square wave anodic stripping voltammetry (SWASV) method. They also developed a calibration and compensation method for the oxidation peaks of the detected metals by using a skin temperature sensor, enabling simultaneous detection of copper, zinc, lead, cadmium, and mercury ions in human sweat.[118] In 2022, a microfluidic nanosensor was developed for detecting copper in sweat. The sensor was easily applied to the skin and actively induced sweating for detection and quantification of copper secretion in sweat.[119]

CHALLENGES AND PERSPECTIVES

Wearable sensors that meet the clinical requirements are gaining popularity among the public. This review focuses on their applications in various medical scenarios (Table 1). Compared to traditional medical devices, wearable sensors possess several advantages that can aid in early diagnosis, health monitoring, and treatment adjustments for patients. Furthermore, the widespread adoption of 5G technology and IoT enables higher device density and faster data transmission rates, which benefits the application of wearable sensors. However, the use of wearable sensors in medical practice and daily life still presents challenges. Future wearable sensors need to consider further optimization in the following aspects (Figure 5).

Comfort and safety of materials: Many wearable sensors are designed to adhere closely to the skin or tissue surface for long periods to collect biological information. The softness and breathability of sensor materials are crucial for the experience of patients in diseased states. Some sensors may contain adhesive materials or sensor components that have sensitizing chemical constituents, which can cause allergic contact dermatitis. For example, acrylate derivatives have been identified as the primary allergen in many cases of allergic contact dermatitis induced by continuous glucose monitoring.[120] Therefore, the use of acrylate derivatives in sensor devices should be limited to ensure comfort and safety during sensor usage.

Portability and good battery life of the device: There is a high demand for portability in sensors used for bedside monitoring, continuous monitoring, and motion disorder tracking. In hospitals, critically ill or postoperative patients often face restricted mobility. The use of large-scale stationary diagnostic equipment is unable to meet their immediate testing requirements, while portable sensors facilitate bedside testing for these patients. For individuals with chronic diseases like diabetes, bulky sensors can hinder patient compliance and result in incomplete monitoring data. Additionally, continuous monitoring places higher demands on the battery life of the device, necessitating further optimization of battery structure and performance. When sensors are used for motion monitoring in patients with abnormal posture or gait, excessively heavy instruments can cause posture changes, affecting the accuracy of disease diagnosis. Therefore, the portability and battery life are crucial in clinical applications.

Accuracy and stability of detection: Physical examinations and laboratory tests serve as important foundations for clinical disease diagnosis and monitoring. The accuracy of these results is vital for making treatment decisions and achieving favorable disease outcomes. However, biochemical sensors based on biomarkers may experience inaccuracies due to biomarker contamination or degradation. For instance, saliva can be contaminated by food residue, the evaporation of sweat can alter substance concentrations, and the current protocols for collecting tear samples can cause eye irritation and reflex tears, affecting sensor test results.[121] Therefore, the development of robust sensing platforms is essential to ensure sensor device functionality in harsh environments. Additionally, when monitoring physiological and motion signals, sensors should closely adhere to the human body, especially at joint and other sites, to guarantee stable detection signals. Sensors should also consider the interference caused by motion artifacts and improve the signal-to-noise ratio of the device.[122,123]

Identification and analytical performance of data: In the era of IoT and 5G networks, intelligent sensor devices capable of acquiring vast amounts of patient health data are becoming increasingly popular. Data processing technologies, such as cloud computing, machine learning, and artificial intelligence, offer immense potential for transforming raw data into clinical-grade information and identifying abnormal data patterns. However, current signal processing and machine learning methods still require further optimization. Additionally, the identification and analysis of data also require the involvement of healthcare professionals in order to establish unified standards for disease diagnosis.

Security of patient health data: Inadequate system security of wearable sensors can expose them to data interception and manipulation by hackers, leading to patient data breaches and privacy exposure. To ensure comprehensive information security, data transmission channels and data storage in wearable sensor systems must be encrypted. Furthermore, access to health data generated by patients should be strictly limited through reliable authentication and encryption technologies.

Table 1. Summary of recently developed wearable systems for medical applications

Diseases and Abnormalities	Location	Sensing type	Target analytes	Sensor architectures	Features	Medical applications	References/Figures
Skin diseases and injuries	Dorsal hand	Acousto-mechanic	Acousto-mechanic signatures of scratching	BLE, electronics, a rechargeable battery, and a millimeter-scale, three-axis accelerometer	Small, soft, stretchable, and wireless	Objective quantification of pruritus	Chun et al.[17]/Figure 1A
	Skin surface	Thermal	Skin hydration	Silicone shell, f-PCB, SiO_2, fabric, and silicone gel	Soft, thin, wireless, and battery-free	Monitoring and diagnosis of inflammatory skin diseases	Madhvapathy et al.[19]/ Figure 1B
	Skin surface	Thermal	Skin hydration	Silicone encapsulation, Li-polymer battery, f-PCB, fabric-reinforced silicone bottom layer, and adhesive layer	Wireless, soft and measuring more sensitively and accurately	Monitoring and diagnosis of inflammatory skin diseases	Shin et al.[20]/Figure 1B
	Skin surface	Electrochemical	Tyrosinase	A bandage electrochemical sensor, a catechol-containing agarose gel, and the three-electrode system	Compact, wireless, easy-to-use, low cost, and noninvasive	Melanoma screening	Ciui et al.[25]/Figure 1C
	Within skin moles	Electrochemical	Tyrosinase	Polymeric hollow microneedles packed with catechol-coated carbon-paste, and the portable electronic board	Minimally invasive	Melanoma screening	Ciui et al.[25]/Figure 1C
	Skin surface	bio-FETs	Tyrosinase	Self-assembling nanostructured tetrapeptide WVFY on n-type metal oxide transistors	Robust flexible and biocompatible	Melanoma screening	Ren et al.[26]/Figure 1D

(Continued on next page)

Table 1. ***Continued***

Diseases and Abnormalities	Location	Sensing type	Target analytes	Sensor architectures	Features	Medical applications	References/Figures
	Near the wounds	Thermal	Temperature and thermal conductivity	Metal traces with fractal geometries in an interconnected collection of ultrathin FS traces in an open mesh configuration	Stretchable, conformal, biocompatible, easily disinfected, and reusable	Quantitative, clinical monitoring of cutaneous wound healing	Hattori et al.[29]/Figure 1E
	Wounds	Electrochemical	pH	Two-terminal pH sensor made of a semiconducting polymer and iridium oxide particles, and an absorbent layer	Real-time	Wound healing monitoring	Mariani et al.[31]/Figure 1F
	Wounds	Electrochemical	pH	An FLEX-AI wearable sensor interacting with a smart wound dressing-integrated bandage via radio frequency identification technology	Contactless	Contactless chronic skin monitoring and predicting tissue regeneration using AI	Kalasin et al.[32]/Figure 1G
Cardiovascular diseases	Inner wrists and left dorsal hand	Bioelectric	ECG	WPU, PEDOT:PSS, and D-sorbitol	Highly conductive, self-adhesive, mechanically flexible /stretchable, and biocompatible	Detecting cardiac arrhythmias	Zhang et al.[35]/Figure 2A
	Chest	Textile electronic	ECG	CNTT and stretchable textiles	Washable, sewable, all-carbon	Continuous ECG monitoring	Taylor et al.[36]/Figure 2B
	Wrist	Textile triboelectric	Pulse wave	Outer textile layer, CNTs, FEP, Al, and PDMS	Machine-learning-assisted, low-cost, lightweight, and mechanically durable	Ambulatory blood pressure monitoring	Fang et al.[41]/Figure 2D
	Fingertip, wrist, ear, and ankle	Mechanoelectric	Pulse wave	PET, ITO, PTFE, and PDMS	Flexible weaving constructed, self-powered	Continuous measurement of cuffless blood pressure	Meng et al.[42]/Figure 2E
	Neck, arm, wrist, and foot	Ultrasonic	Blood-pressure waveforms	Polyimide, Cu Electrode, Cu/Zn electrode, piezo pillar, filling epoxy	Ultrathin, stretchable, and non-invasive	Monitoring of the central blood pressure	Wang et al.[44]/Figure 2F

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Table 1. *Continued*

Diseases and Abnormalities	Location	Sensing type	Target analytes	Sensor architectures	Features	Medical applications	References/Figures
	Wrist	Optoelectronic	PPG	Ultra-thin optoelectronics, watch-chain interconnects, and biocompatible package	Skin-like, ultra-thin, and flexible	Cuff-less continuous blood pressure monitoring	Li et al.[45]/Figure 2G
	Chest and limb	Optoelectronic	PPG	A-20 and OO-30 polyorganosiloxane elastomers, OOO-35 polyorganosiloxane gel, and AMPS/AA hydrogel	Wireless, continuous, and noninvasive	Blood pressure monitoring for pediatric critical care	Liu et al.[46]/Figure 2H
	Fingertip	Optoelectronic	PPG	PLEDs and OPDs	Ultrathin, ultraflexible, skin-like	Measurement of pulse oximetry	Yokota et al.[48]/Figure 2i
	Hand and foot	Optoelectronic/ Mechanoelectric	PPG/Pressure signals	3D printing of PDMS elastomer and f-PCB	Patient-specific	Measurement of pulse oximetry	Abdollahi et al.[49]/Figure 2J
	Finger	Optoelectronic	PPG	OPDs and spectral filters	Powered by ambient light	Measurement of pulse oximetry	Han et al.[50]/Figure 2K
	Finger, wrist, neck, and nose	Optoelectronic	PPG	Flexible OLEDs and OPDs	Ultralow-power and reflective patch-type	Continuous pulse oximetry monitoring	Lee et al.[51]/Figure 2L
Abnormal human motion	Neck	Triboelectric	Neck movement	Four flexible and stretchable silicon rubber based triboelectric sensors integrated on a neck collar	Highly accurate	Neck monitoring, rehabilitation, and control	An et al.[54]/Figure 3A
	Shoulder	Physical	Shoulder motion	A flexible resistive sensor network embedding in fabrics	Accurate, lightweight and affordable	Shoulder motion tracking	Samper-Escudero et al.[59]/ Figure 3B
	Wrist	Mechanical	Minute deformation of the wrist	A skin-like sensor with laser-controlled cracking and serpentine patterning	Ultrasensitive, stable regardless of its position on the wrist	Five fingers' motion detection	Kim et al.[60]/Figure 3C
	Scapula and the thoracic spine region	Physical	Compensatory movement of the trunk and shoulder complex	Sensors integrating an accelerometer, gyroscope and a magnetometer and embedding in an elastic Velcro strip	Aesthetic and well-fitting	Posture monitoring, upper extremity rehabilitation training of stroke patients	Wang et al.[67]/Figure 3D

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Table 1. *Continued*

Diseases and Abnormalities	Location	Sensing type	Target analytes	Sensor architectures	Features	Medical applications	References/Figures
	Hip and Knee	Triboelectric	Lower-limb motion	A sliding block-rail piezoelectric generator and a ratchet-based triboelectric nanogenerator	Economic and energy-efficient	Lower limb rehabilitation and sports training	Gao et al.[69]/Figure 3E
Endocrine and metabolic abnormalities	Skin surface	Electrochemistry	Interstitial glucose	An Ag/AgCl electrode as a counter/reference electrode, a printable Prussian-Blue transducer, an additional Ag/AgCl reverse iontophoretic electrode, and chitosan immobilizing the enzyme on the transducer surface	Accurate and specific	Diabetes management	Bandodkar et al.[74]/Figure 4A
	Cornea	Electrochemistry	Hydrogen ions, proteins, glucose, nitrites and l-ascorbic acid	Colorimetric sensors are deposited on paper, and then embedded as a paper microfluidic sensor within a laser-inscribed acrylate contact lens	Potential of medical diagnosis or disease screening	Ocular infections, uveitis, diabetes, keratopathy monitoring, and oxidative stress assessment	Moreddu et al.[77]/Figure 4B
	Skin surface	Electrochemistry	Sweat ammonium levels	A screen-printed tattoo paper with an ammonium-selective polymeric membrane and solid-state reference electrode	Stable when stretching or bending	Sport performance monitoring and metabolic disorders detection	Guinovart et al.[81]/Figure 4C
	Skin surface	Electrochemistry	Uric acid and tyrosine in sweat	A highly sensitive laser-engraved graphene-based chemical sensor and a laser-engraved multi-inlet microfluidic module	Scalable and flexible for the wearer's comfort	Gout and metabolic disorders detection	Yang et al.[85]/Figure 4D
	Skin surface	Electrochemistry	Sodium and potassium in sweat	PU, Ecoflex and stretch-enduring inks, along with a serpentine design	Textile-based, stretchable, real-time, and non-invasive	Simultaneous multi-ion sweat analysis	Parrilla et al.[91]/Figure 4E
	Fingertip	Electrochemistry	Sweat cortisol levels	A touch-based non-invasive molecularly imprinted polymer electrochemical sensor, a highly permeable sweat-wicking porous hydrogel	Rapid, simple, reliable, and accessible	Quantitative stress management	Tang et al.[111]/Figure 4F

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Table 1. ***Continued***

Diseases and Abnormalities	Location	Sensing type	Target analytes	Sensor architectures	Features	Medical applications	References/Figures
Others	Skin surface	Electrochemistry	Sweat caffeine levels	An electrochemical differential pulse voltammetry sensing module	Noninvasive and continuous-monitoring	Point-of-care drug monitoring and management	Tai et al.[113]/Figure 4G
	Skin surface	Electrochemistry	Sweat levodopa levels	A functionalized levodopa sensing electrode as working electrode, an Ag/AgCl top layer as reference electrode, and an Au top layer as counter electrode	Real-time	Administering of levodopa and management of Parkinson's disease	Tai et al.[114]/Figure 4H
	Skin surface	Electrochemistry	Alcohol in induced sweat	A skin-worn alcohol sensor, a flexible electronics board controlling the iontophoresis/ amperometry operation to induce sweat	Noninvasive, highly selective and sensitive	Alcohol monitoring	Im et al.[115]/Figure 4I

ECG, electrocardiograms; PPG, photoplethysmography; BLE, Bluetooth Low Energy; f-PCB, flexible printed circuit board; bio-FETs, field-effect transistor-based biosensors; WVFY, tryptophan–valine–phenylalanine–tyrosine; FS, filamentary serpentine; FLEX-AI, flexible artificial intelligence-guiding; WPU, waterborne polyurethane; PEDOT:PSS, poly(ethylenedioxythiophene):poly(styrenesulfonate); CNTT, neat carbon nanotube threads; CNTs, carbon nanotubes; FEP, fluorinated ethylene propylene; PDMS, poly(dimethylsiloxane); PET, polyethylene terephthalate; ITO, indium–tin oxide; PTFE, polytetrafluoroethylene; AMPS/AA, 2-acrylamido-2-methylpropane sulfonic acid/acrylic acid; PLEDs, polymer light-emitting diodes; OPDs, organic photodetectors; PU, polyurethane.

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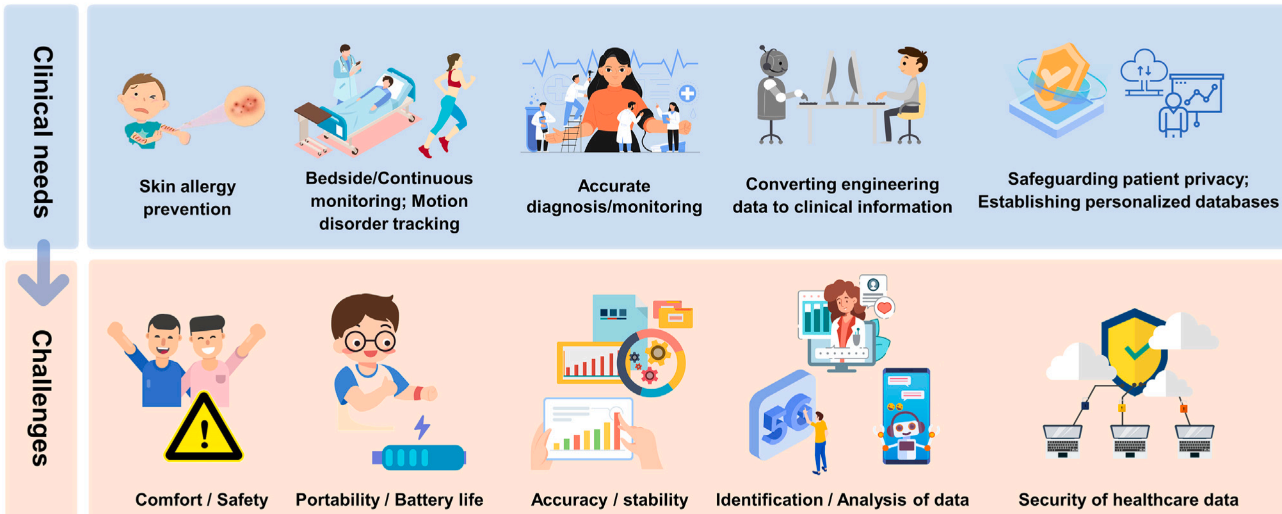

Figure 5. Clinical needs and challenges faced by wearable sensors in medical applications
(Some image materials are from OfficePLUS.).

Conclusion

In recent years, the application of wearable sensors in various diseases has been continuously expanding. Firstly, from the perspective of patient care, the widespread use of wearable sensors will facilitate the realization of remote healthcare and personalized medicine. In the context of uneven allocation of medical resources, the popularization of wearable sensors will benefit the diagnosis and continuous monitoring of patients in remote areas, promoting the implementation of healthcare measurements. Furthermore, current healthcare mainly relies on medical solutions based on population averages, sometimes neglecting individual patient differences. In the future, it is anticipated that individuals will be able to obtain customized databases of personal health records through various wearable sensors, which can provide more reliable diagnoses, convenient continuous monitoring, and timely prevention of diseases. Besides, from the perspective of medical advancement, wearable sensors can collect user information that may become an integral part of medical big data, facilitating real-world medical research and providing valuable information for disease diagnosis and treatment. In the future, with advancements in material technology, signal processing, machine learning, IoT, 5G networks, and continuous collaboration among engineering, medical, and data professionals, wearable sensors hold vast prospects for application in the field of healthcare. The reliance on wearable sensors for remote healthcare and personalized medicine is expected to become a reality.

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AUTHORS CONTRIBUTIONS

Q.T., S.L., and J.Z. drafted the manuscript under the supervision of H.C. and G.T., and all authors have commented on and approved the final manuscript.

DECLARATION OF INTERESTS

The authors declare no competing interest.

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