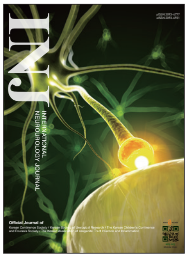

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Recent Patient Health Monitoring Platforms Incorporating Internet of Things-Enabled Smart Devices

Minhee Kang[1,2], Eunkyoung Park[1], Baek Hwan Cho[1,2], Kyu-Sung Lee[1,3]

[1]Smart Healthcare & Device Research Center, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea
[2]Department of Medical Device Management and Research, SAIHST, Sungkyunkwan University, Seoul, Korea
[3]Department of Urology, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea

Synergistic integration of the Internet of Things (IoT), cloud computing, and big data technologies in healthcare have led to the notion of "smart health." Smart health is an emerging concept that refers to the provision of healthcare services for prevention, diagnosis, treatment, and follow-up management at any time or any place by connecting information technologies and healthcare. As a significant breakthrough in smart healthcare development, IoT-enabled smart devices allow medical centers to carry out preventive care, diagnosis, and treatment more competently. This review focuses on recently developed patient health monitoring platforms based on IoT-enabled smart devices that can collect real-time patient data and transfer information for assessment by healthcare providers, including doctors, hospitals, and clinics, or for self-management. We aimed to summarize the available information about recently approved devices and state-of-the-art developments through a comprehensive, systematic literature review. In this review, we also discuss possible future directions for the integration of cloud computing and blockchain, which may offer unprecedented breakthroughs in on-demand medical services. The combination of IoT with real-time, remote patient monitoring empowers patients to assert more control over their care, thereby allowing them to actively monitor their particular health conditions.

Keywords: Healthcare; Self-monitoring; Wearable device

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INTRODUCTION

"Smart health" is an emerging concept that refers to the provision of healthcare services for prevention, diagnosis, treatment, and follow-up management at any time or any place by connecting information technologies and healthcare. Smart health itself incorporates the essence of the digital transformation involved in the fourth industrial revolution, such as hyper-connectivity, superintelligence, and the convergence of science and technology [1,2] in the healthcare industry. Recently, the syner-

Corresponding author: Baek Hwan Cho https://orcid.org/0000-0002-4106-9042
Smart Healthcare & Device Research Center, Samsung Medical Center, 81 Irwon-ro, Gangnam-gu, Seoul 06351, Korea
E-mail: baekhwan.cho@samsung.com / Tel: +82-2-3410-0885 / Fax: +82-2-3410-2968
Co-corresponding author: Kyu-Sung Lee https://orcid.org/0000-0003-0891-2488
Department of Urology, Samsung Medical Center, Sungkyunkwan University School of Medicine, 81 Irwon-ro, Gangnam-gu, Seoul 06351, Korea
E-mail: ksleedr@skku.edu / Tel: +82-2-3410-3554 / Fax: +82-2-3410-3027
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gistic combination of the Internet of Things (IoT) [3], cloud computing [4], and big data technologies [5,6], as well as existing forms of information and communication technology (ICT)-based healthcare (e.g., "mobile health" [m-health] [7,8], "u-health" [9,10], and "tele-health," [11-14]) has led to the notion of smart health. Of particular note, IoT enables physical devices to collect and exchange data in an automated way. IoT-enabled smart devices allow medical centers to provide preventive care, diagnosis, and treatment more competently. They provide solutions to emerging issues in healthcare services, such as real-time patient health monitoring, particularly in patients with acute and chronic diseases (e.g., heart failure, arrhythmias, diabetes, and asthma attacks).

This review focused on recently developed patient health monitoring platforms based on IoT-enabled smart devices, which can collect patient data in real time and transfer their health information for assessment by healthcare providers, including doctors, hospitals, and clinics, or for self-management. We aimed to summarize the available information about recently approved devices and state-of-art developments via a comprehensive, systematic literature review. In this review, we also briefly discuss possible future directions for the integration of cloud computing and blockchain in smart health, which may offer unprecedented breakthroughs in on-demand health services.

THE IoT-ENABLED PATIENT HEALTH MONITORING SYSTEM

IoT technology now allows doctors to monitor patient health data in real time. Recently, some pioneering studies have investigated patient health monitoring using advanced bioengineering technologies combined with an IoT-embedded device. Noninvasive biosensors that allow for real-time patient monitoring promise to improve patient satisfaction, to increase the timeliness of care, to boost treatment adherence, and to drive improved health outcomes [15]. For example, sensors based on stretchable material enable noninvasive and comfortable physiological measurements by replacing the conventional methods that use penetrating needles, rigid circuit boards, terminal connections, and power supplies [16]. Currently, the need for noninvasive health monitoring has led researchers to utilize alternative analytes, such as tears, urine, sweat, and saliva.

Among various emerging breakthrough technologies, smartphone-based colorimetric analysis appears to be a promising platform for noninvasive patient health monitoring due to its accessibility. Using smartphones, colorimetric data can be rapidly converted to digital images. Jalal et al. [17] reported a disposable hybrid microfluidic device for smartphone-based colorimetric analysis of common urine analytes such as glucose, pH, and red blood cells. Wang et al. [18] reported a self-referenced portable plasmonic sensing platform integrated with an internal reference sample, along with an image processing method to reduce errors in smartphone-based colorimetric analysis. Similarly, Ra et al. [19] proposed doughnut-shaped reference swatches surrounding each detection pad on a colorimetric strip and an algorithm for a smartphone-based application.

Meanwhile, recent advanced achievements in micro-/nanofabrication, flexible and stretchable functional materials, and wireless communications offer attractive and versatile capabilities in wearable electrochemical sensors. Biomarkers in saliva, tears, sweat, and even exhaled breath provide new opportunities for noninvasive, real-time patient monitoring (Fig. 1). For example, Park et al. [20] recently reported smart contact lenses integrated with glucose sensors, wireless power transfer circuits, and LED pixels to monitor the glucose level in tears (Fig. 1A). Although debate continues regarding the correlation of glucose levels in tears with blood glucose levels, many attempts have been made to develop glucose sensors for tears due to the potential tremendous advantages of being noninvasive and continuous, making them an appealing potential alternative to blood tests [15,20]. For example, the use of a real-time glucose monitoring system led to meaningful improvements in glycated hemoglobin levels and a reduction of hypoglycemic events [21], thereby improving patients' quality of life by reducing their fear of hypoglycemia [22]. In the meantime, several recently reported wearable platforms have incorporated perspiration sensors for continuous, noninvasive monitoring of biomarkers in sweat [23,24]. Sweat sensors can provide real-time measurements of patients' metabolites (e.g., lactate for muscle fatigue and glucose) [25,26] and electrolytes (e.g., sodium, potassium, and other trace minerals [27,28]). Emaminejad et al. [29] demonstrated an autonomous sweat extraction and sensing platform based on an electrochemically enhanced iontophoresis interface (Fig. 1B). The iontophoresis and sensor electrodes with a wireless flexible printed circuit board were patterned on a mechanically flexible polyethylene terephthalate substrate to form a stable and conformal contact interface. Gao et al. [28,30] also reported an IoT-embedded sweat monitoring system that used a mechanically flexible sensor array for multiplexed *in situ* perspiration analysis of parameters such as sweat metabolites, electro-

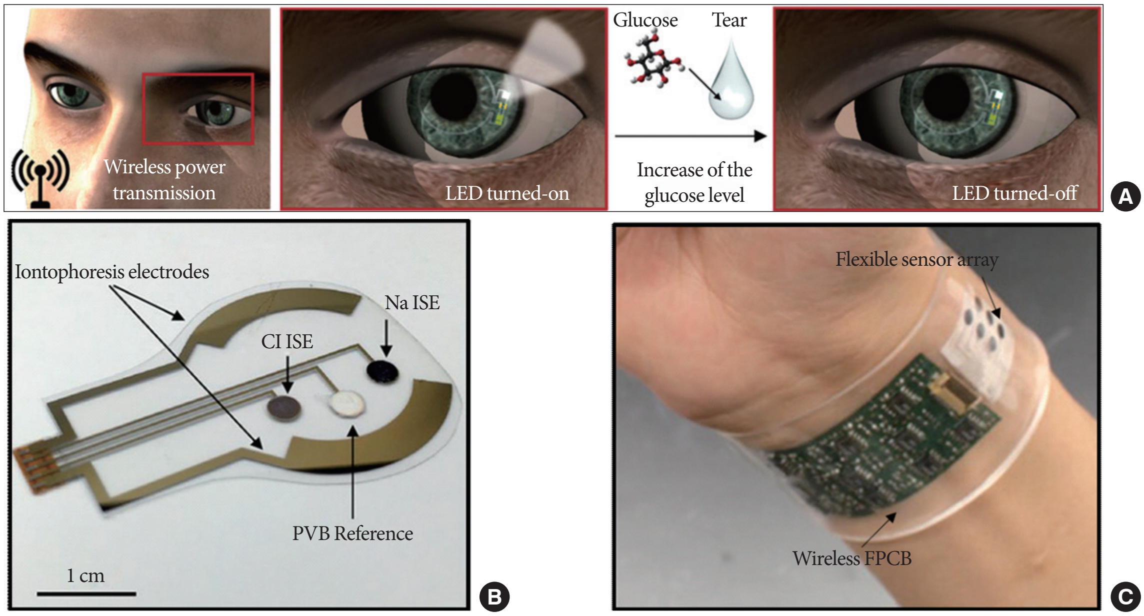

Fig. 1. IoT-enabled smart devices for the non-invasive monitoring of biomarkers. (A) Stretchable, transparent smart contact lens to detect the glucose level in tears. Electric power, which activates the LED pixel and the glucose sensor is wirelessly transmitted to the lens through the antenna. In the device, this pixel turns off after detecting a glucose level in the tear fluid above the threshold. Reprinted from Park et al. Sci Adv 2018;4:eaap9841 [16] under open access license CC BY-NC. (B) The iontophoresis and sensor electrodes with a wireless flexible printed circuit board patterned on a mechanically flexible polyethylene terephthalate substrate. Reprinted from Emaminejad et al. Proc Natl Acad Sci U S A 2017;114:4625-30 [29] under open access license CC BY-NC. (C) Electrochemical sensors for analyzing the concentration of glucose, lactate, potassium, and sodium in sweat. Wrist-mounted platform that combines an array of sensors with battery-powered electronics for digital signal acquisition and Bluetooth wireless data transmission. Reprinted from Choi et al. Sci Adv 2018;4: aar3921 [30] under open access license CC BY-NC. IoT, Internet of Things; Cl ISE, chloride ion-selective electrodes; Na ISE, sodium ion-selective electrodes; PVB, polyvinyl butyral; FPCB, flexible printed circuit board.

lytes, and skin temperature (Fig. 1C).

All these platforms are capable of sending information in real time either to a smartphone or directly to the cloud. Until now, sweat analysis was not a standard test. However, continued miniaturization, the development of flexible electronics, and improvements in biosensor technology have made it a possible option.

Research involving smart health devices is already moving the industry forward, and many smart health devices have already received U.S. Food and Drug Administration (FDA) approval (Table 1) [31-34]. Medtronic received FDA clearance for its Mobile Patient Management System, which is intended to continuously measure, record, store, and periodically transfer physiological data for patients who require monitoring for the detection of nonlethal cardiac arrhythmias. The system uses a wearable sensor and patient-held transceiver that sends information to a secure server. The FDA has also approved Abbott's Confirm Rx Insertable Cardiac Monitor (Abbott, Lake Bluff, IL, USA), an implantable cardiovascular monitoring device that continuously tracks patients' heart rhythms and sends the data to a smartphone app via Bluetooth. The device is placed just under the skin of the chest in a minimally invasive outpatient procedure. Encoded data from the device is coordinated by the mobile app, then sent from the patient's phone to a physician at predetermined intervals. Additionally, Sensimed announced that it received de novo FDA clearance for its connected contact lens, Triggerfish (Sensimed, Lausanne, Switzerland), which helps doctors track the progression of glaucoma in patients. A soft disposable silicone contact lens embedded with a microsensor continuously records spontaneous ocular dimensional changes for a day. The data are sent from the lens wirelessly to a recorder that users wear around their neck. After the recording period has ended, the data are transmitted from the recorder to a doctor's computer via Bluetooth. Andon Labs, the parent company of iHealth Labs, received FDA clearance for its iHealth Track Blood Pressure Monitor (iHealth Labs Inc., Mountain View, CA, USA), a new smartphone-connected blood pressure

Table 1. Commercially available and recently approved[a] IoT-enabled smart devices

Product (company)	Features
AVIVO Mobile Patient Management System (Medtronic, Minneapolis, MN, USA)	Wearable, wireless physiological detection system applies to arrhythmia monitor
Confirm Rx Insertable Cardiac Monitor (Abbott, Lake Bluff, IL, USA)	Continuously tracks patients' heart rhythms and sends the data to a smartphone app via Bluetooth.
ADAMM Intelligent Asthma Monitoring (Healthcare Originals, Rochester, NY, USA)	Wearable IoT device Attaches to the upper torso using skin-safe adhesive Tracks precursor symptoms of asthmatic attacks, including cough rate, respiration patterns, heartbeat, and body temperature
Triggerfish (Sensimed, Lausanne, Switzerland)	A soft disposable silicone contact lens embedding a microsensor that captures spontaneous circumferential changes at the corneoscleral area
iHealth Track Blood Pressure Monitor (iHealth Labs Inc., Mountain View, CA, USA)	Smartphone-connected blood pressure cuff
BioStamp nPoint system (MC10, Lexington, MA, USA)	Wireless, biometric data collection Flexible, body-conforming rechargeable sensor patches Measures, records, and displays general activity, postural classifications, vital signs, and sleep metrics
Elemark (BBB Inc., Seoul, Korea)	Smartphone-based blood tester Shares data with health providers automatically
iBGStar (Sanofi Inc., Paris, France)	Blood glucose monitoring dongle for smartphone Sync with app

IoT, Internet of Things; FDA, U.S. Food and Drug Administration.
[a]Reference from FDA Medical Device 510 (k) Premarket Notification [33] and FDA Medical Device Classification under Section 513 (f) (2) (de novo) 510 (k) [34].

cuff. Recently, the US healthcare company MC10 received FDA 510(k) clearance for the BioStamp nPoint system (MC10, Lexington, MA, USA), which is a wireless, biometric data collection platform intended for use by healthcare professionals and researchers for the continuous collection of direct and derived data such as posture classification [35]. In addition, a wearable IoT device to predict asthma attacks and chronic obstructive pulmonary disease exacerbation, ADAMM Intelligent Asthma Monitoring (Healthcare Originals, Rochester, NY, USA), is expected to receive FDA clearance soon. It is a soft, flexible, waterproof, wearable IoT device that communicates with a smartphone app and web portal using Bluetooth, WiFi, and cellular connections. It attaches to the upper torso using skin-safe adhesive and tracks precursor symptoms of asthmatic attacks, including cough rate, respiration patterns, heartbeat, and body temperature. All these systems wirelessly sync with smartphones over Bluetooth, providing diagnostics and trends for patients and providers.

In addition to these recently developed devices, some IoT-enabled smart devices, such as iBGStar (Sanofi Inc., Paris, France), PixoTest (iXensor, Taipei City, Taiwan), and Elemark (BBB Inc., Seoul, Korea), are already commercially available. These products feature a patient health-monitoring dongle for a smartphone or their own mobile device. The data measured using the devices are automatically transferred to a cloud server, so that trends can be instantly tracked, and results can be shared with doctors who can easily check the medical records of the patients and consistently give them feedback. Consequently, patients can receive a customized and highly personal care experience, and clinics and hospitals are able to address problems proactively and reduce readmissions. Simultaneously, shared health records allow hospitals to customize their own patient database to fit seamlessly into the standard hospital workflow.

CLOUD-BASED SMART HEALTH MONITORING

The current developments of patient health monitoring devices are readily incorporated into the cloud. Cloud connectivity provides substantial healthcare computing features, enables data storage and analysis, and allows medical authorities to be notified as appropriate [36]. Adoption of the cloud in healthcare will continue to evolve and accelerate due to the increasing usage of IoT-enabled smart devices. For example, IBM announced a new business unit, Watson Health, that will offer cloud-based access to its analytical power for interpreting healthcare data [37]. The Watson Health Cloud will be an open-source but secure platform on which care providers and researchers can share and translate health data for better insight into trends, which will help them make more-informed decisions, thereby improving overall patient outcomes. Recently, Google introduced the Cloud Healthcare Application Programming Interface (API), which aimed to make it easier for health organizations to collect, store, and access health data. The industry-grade API platform allows users to run advanced analytics and machine learning-based predictive models on electronic health records. In addition, Google signed a key cloud computing deal with Flex, a traded electronics manufacturer, which provides components for a huge number of medical devices around the world.

At the same time, advances in artificial intelligence (AI) have led to improved possibilities for processing and leveraging health data. Most of all, the application of AI in healthcare can be expected to have overwhelming impacts on patient monitoring due to its predictive capabilities [38-40]. For example, IBM Watson focuses on decision-making support, while Google's AI has a self-decision-making function. Numerous smart device and wearable applications that use AI algorithms to monitor an individual's health are already available. The combination of AI with real-time, remote patient monitoring empowers patients to assert more control over their care, thereby allowing them to actively monitor their particular health conditions.

However, healthcare companies still suffer from a centralized and decentralized data problem, which is a source of confusion and poses security and privacy challenges. A promising and functional solution to these challenges is the use of blockchain, which provides a secure, decentralized framework for controlled sharing of patient information. Blockchain enables storing and exchanging information without the need for third-party services. Every record stored on the blockchain is encrypted and replicated across thousands of computers. None of those computers can access the content of that record because the decryption key is in the hands of its true owner. In 2017, IBM Watson Health announced a research initiative with the FDA aimed at applying emerging blockchain technology applications towards the advancement of public health. The blockchain technology enables a highly secure, efficient, scalable exchange of health data from a variety of sources, including clinical trials, genomic databases, and electronic health records, as well as miscellaneous IoT data from wearables, apps, and connected devices.

TOWARD ON-DEMAND SMART HEALTH SERVICES

Undoubtedly, IoT technology has dramatically changed the healthcare industry by transforming the way devices, apps, and users connect and interact with each other for delivering healthcare services. A tangible benefit of the IoT is real-time, remote monitoring of patient health. As previously discussed, patient health monitoring via smart devices provides solutions for emerging problems in healthcare services, such as the increasing number of acute and chronic diseases (e.g., heart failure, diabetes, and asthma attacks) [41]. Sensors have been integrated into a variety of platforms, including watches [42,43], soft lenses [15,20], skin patches [44-46], wristbands, shoes [47], belts, and smartphones, which aim to collect and transfer health data (e.g., heartbeat, blood pressure, glucose levels, and body movements). These data are stored in the cloud and can be shared with authorized person such as physicians, insurance companies, participating health firms, or external consultants, and allow them to look at the collected data regardless of their location, time, or device.

Currently, telemedicine continues to move from the periphery of healthcare into the mainstream. Telemedicine refers to the use of digital ICT to access healthcare services remotely and to manage patient health care. Some of the key players operating in the global telemedicine market are Phillips Healthcare, GE Healthcare Ltd., Cerner Corporation, IBM, Mckesson Corporation, AMD Global Telemedicine, Inc., and Honeywell Life Care Solutions. Due to the growing demand for remote patient monitoring, major companies in the telemedicine market are focusing on expanding their services and intensifying their partnerships.

CONCLUSIONS

Smart health is a major up-and-coming research topic that is based on emerging ICT and has attracted cross-disciplinary researchers. The use of IoT technology helps automate the entire patient care workflow. In other words, IoT-enabled smart devices have started to facilitate care and accurate treatment services and strategies by healthcare providers, including doctors, hospitals, and clinics. Patients can use these devices anywhere and immediately transmit their health conditions and test results using IoT-enabled devices and integrated apps, making it easier to fit testing into daily life. For doctors, real-time, remote patient monitoring makes it easier to stay up-to-date and in contact with patients without in-person visits.

In this review, we discussed the current state-of-the-art patient health monitoring devices and possible directions for the integration of cloud computing and blockchain, which may offer unprecedented breakthroughs in on-demand health services. IoT-enabled smart devices with cloud computing and blockchain enable a highly secure, efficient, scalable exchange of health data from a variety of sources. Furthermore, the combination of AI with real-time, remote patient monitoring empowers patients to assert more control over their care, thereby allowing them to actively monitor their particular health conditions.

AUTHOR CONTRIBUTION STATEMENT

· Full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis: *KSL, BHC*
· Study concept and design: *KSL, BHC, MK*
· Acquisition of data: *KSL, MK, EP*
· Analysis and interpretation of data: *KSL, MK*
· Drafting of the manuscript: *MK*
· Critical revision of the manuscript for important intellectual content: *KSL, EP*
· Statistical analysis: *BHC, MK, EP*
· Obtained funding: *KSL, MK*
· Administrative, technical, or material support: *KSL, BHC, MK, EP*
· Study supervision: *KSL, BHC*

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