

CORONAVIRUS

Continuous on-body sensing for the COVID-19 pandemic: Gaps and opportunities

INTRODUCTION

As of 20 June 2020, the Center for Disease Control's tabulations show more than 2.2 million recorded cases of coronavirus disease 2019 (COVID-19) and nearly 120,000 in deaths in the United States (1). Infected patients present with a wide range of symptoms, from completely asymptomatic to rapidly progressive pneumonia leading to death. Rigorous and widespread testing remains a critical component of strategies for containing this pandemic. The limited availability of molecular diagnostics constrains the use of these technologies to those who present with disease. The current gold standards rely on detection of viral RNA, typically by reverse transcription polymerase chain reaction (RT-PCR), but these approaches, as commonly implemented, have notable disadvantages. First, the nasopharyngeal swab is uncomfortable and may not be tolerated well by all patients, particularly children or the elderly. Second, false-negative test results remain a significant concern, with some RT-PCR tests exhibiting false-negative rates as high as 29% (2). Third, swab samples must be collected by trained staff to avoid false negatives or inconclusive tests (3, 4). Fourth, samples must be transported via viral medium to centralized laboratory facilities, where transport delays from rural or remote areas can reach 48 hours or longer (5). Alternative tests based on antibodies offer some promise, but the appearance of antibodies [immunoglobulin M (IgM) and IgG] can lag weeks to months after the initial exposure (6). Furthermore, positive antibody titers may potentially only reflect prior exposure as opposed to protective immunity. Emerging evidence suggests that re-infection by endemic coronaviruses is not atypical, thereby adding complications to protocols for follow-up molecular testing (6, 7). The net result is a continuing gap between widespread population-level testing and the availability of tests that is likely to persist for the foreseeable future (8–11). These circumstances motivate the development of complementary technologies for diagnosing and monitoring COVID-19 infections (2, 12, 13).

CONSUMER WEARABLES TO THE RESCUE

The demand for systems to diagnose and track COVID-19 infections noninvasively and continuously not only in the hospital but also in-home settings motivates heightened interest in consumer-grade wearables. For instance, re-

cent partnerships between Oura Ring (Oulu, Finland) and the University of California, San Francisco (TemPREDICT Study) and West Virginia University involve digital tracking of physiological parameters in at-risk health care workers. AppleWatch and FitBit have similar relationships with the University of California, San Diego. The underlying premise is that subtle changes in basic vital signs, not readily apparent to the individual, will offer earlier signs of infection compared to those associated with self-reported symptoms. Beyond early diagnosis, the ability to track physiological status after confirmatory molecular diagnosis may also yield insights into the process of recovery or warn of impending deterioration.

While consumer-grade wearables offer the advantage of widespread availability, interoperability with widely available smartphones, and systems for remote data management, they are highly constrained in measurement modalities and accuracy. The early symptoms of COVID-19 infections are well known: fever (98%), cough (65%), and shortness of breath (55%) (14–16). Self-reported symptoms such as the loss of smell and taste also appear to have prognostic value (17). Silent hypoxemia is another sign of infection and evidence impending deterioration (18). The most popular wearables (AppleWatch, FitBit, and Oura Ring) offer continuous heart rate and physical activity measurements. They do not, however, offer pulse oximetry, body temperature, or high-fidelity measurements of respiratory rate. Furthermore, popular FitBit sensors and the Oura Ring are not U.S. Food and Drug Administration (FDA) cleared for remote monitoring. The AppleWatch Series 4 is FDA cleared for episodic electrocardiography and irregular rhythm notification for adults above the age of 22, but with the specification that the watch is not intended to replace gold standard clinical diagnostic tools. These shortcomings may detract from the potential of these technologies to predict, monitor, and track COVID-19.

On-body, skin-integrated sensor systems

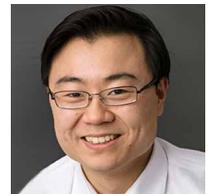
Soft electronic systems that couple intimately to the skin at locations beyond the wrist and the finger offer important advantages in assessing COVID-19 symptoms and recovery. As COVID-19 is predominately a respiratory disease, measurements of respiratory biomarkers such as cough frequency/intensity/sound, respiratory



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rate, and respiratory effort, captured directly from the thorax, are likely to have high information yield. Likewise, measurements of blood oxygenation via pulse oximetry—validated to clinical grade standards—are critically important. VitalConnect (San Jose, CA) has partnered with the U.S. Department of Health and Human Service's Biomedical Advanced Research and Development (BARDA) to deploy their single-use, chest-mounted patch in nursing homes to track vulnerable elderly patients. The focus of these devices is on continuous heart rate monitoring, with basic capabilities in approximate measurements of respiratory rate. A separate, conventional pulse oximeter captures data from the finger, in an episodic mode. Efforts such as these are especially timely, as long-term care facilities (LTCs) present the highest risks of infection and death from COVID-19 (19–21). Furthermore, elderly patients are often less likely to report their symptoms, and care staff in LTCs are often too overburdened to provide reliable tracking.

Our research group has also partnered with BARDA and a commercial entity, Sonica Health, to deploy advanced wearable technologies configured to directly address needs in COVID-19 monitoring, tailored specifically to the key symptoms. Here, a thin, soft sensor with a high-bandwidth accelerometer and a precision temperature

sensor mounts in direct mechanical communication with the skin overlying the suprasternal notch (Fig. 1) (22). This small area of the body at the base of the neck provides an excellent interface to the intrathoracic cavity for high-fidelity recordings of respiratory activity from cough frequency, intensity, and duration, to respiratory rate and effort, to high frequency respiratory features associated with wheezing and sneezing. The same data streams include information on heart rate, heart sounds, and cardiac amplitude. A thermally insulating pocket around the temperature sensor enables measurements of skin temperature, with robust correlations to core body values largely independent of ambient conditions. The compliant mechanics of these sensors support comfortable interfaces that are compatible with the full range of natural motions of the neck. Figure 1 shows the device and some representative data collected from a patient with COVID-19. These systems, as well as a related platform developed by Sibel Health for wireless ICU-grade monitoring of complete vital signs, including pulse oximetry, are currently deployed at scale on patients, physicians, nurses, and respiratory rehabilitation specialists at the Shirley Ryan AbilityLab and Northwestern Memorial Hospital in Chicago (23). Initially, on-going pilot studies on ~50 subjects over the past 2 months reveal many interesting features of the disease

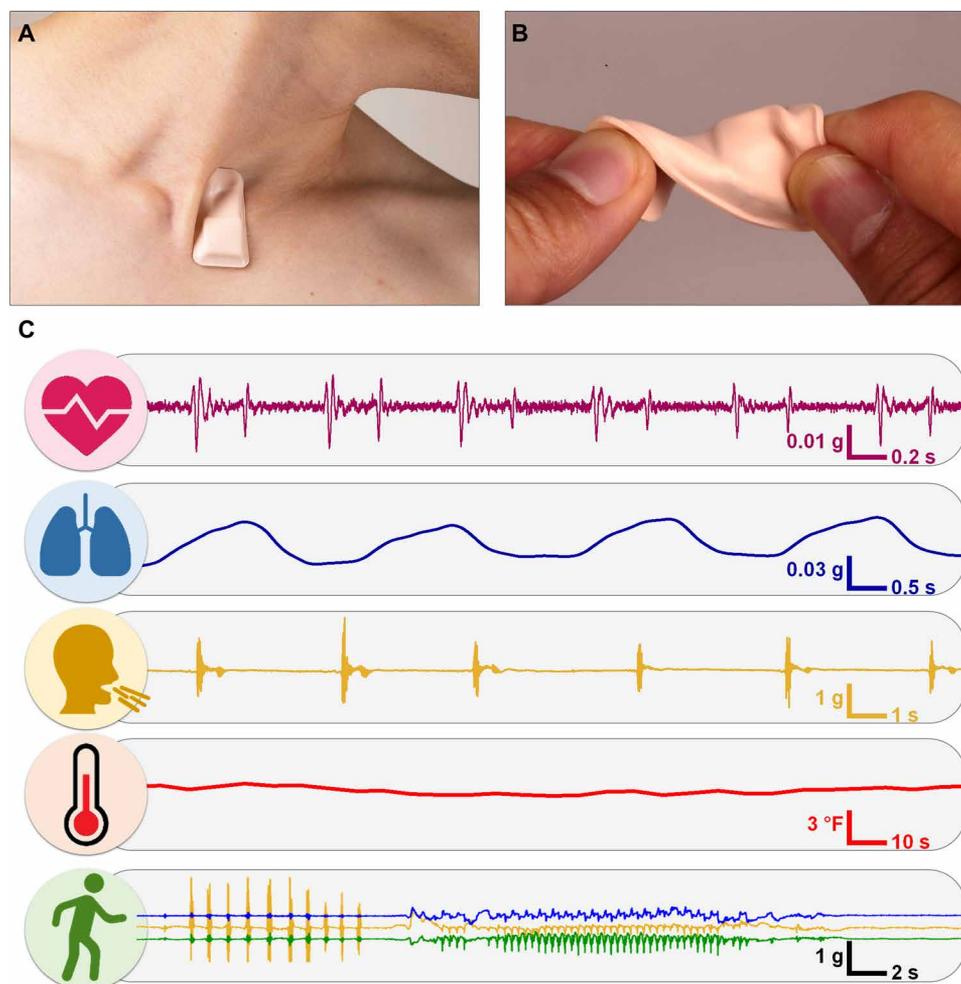


Fig. 1. Wireless, soft, skin-interfaced sensor platform designed for mounting on the suprasternal notch. (A) Image to highlight the ability of the device to conform to natural movements of the neck, without mechanical constraint, as the basis for a comfortable interface for measurements of respiratory activity and core vital signs. (B) Image of the device under severe twisting deformation. (C) Continuous wearable monitoring: cardiac- and respiratory-related signals, coughing, body temperature, and patterns of activity collected from a COVID-19 patient. Photo credit: (A and B) KunHyuk Lee, Northwestern University. Photo credit: (A and B) KunHyuk Lee, Northwestern University.

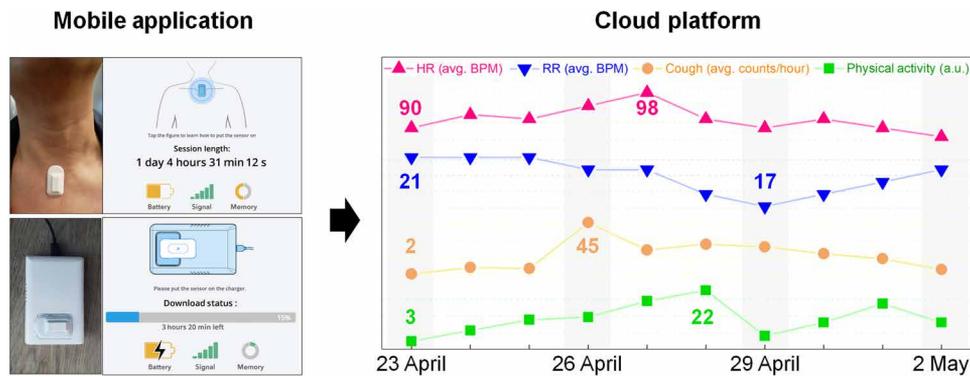


Fig. 2. Automated data management system for individual data acquisition, secure data upload, and machine learning algorithms for assessing COVID-19 symptoms and recovery. Representative data collected from a COVID-19 patient. HR, heart rate (beats per minute); RR, respiratory rate (breaths per minute); a.u., arbitrary units. Photo credit: Yoonseok Park, Northwestern University.

and its progression, extracted from several terabytes of raw data, including those collected on patients released to the home. The overall flow of data from these devices to data analytics tools, cloud servers, and physician dashboards appears in Fig. 2. Given the expected second surge of COVID-19 infections in the fall of 2020, the results of these studies, to be published in the near future, have the potential to catalyze expansion for wide-scale deployment.

Data management, machine learning, and the hope for predictive algorithms

Continuous monitoring using these technologies presents not only opportunities but also challenges in data analytics and in data management, given the exceptionally high volumes and wide diversity of health information generated by each device. Thus, these sensor systems must include scalable data backends that securely transfer, store, process, and make available patient information in a HIPAA compliant manner (Fig. 2). Furthermore, the need for linking these data to other disparate sources such as electronic health records to enhance the information content motivates the development of designs for interoperability. The challenge is that digital health data involve proprietary formats and incompatible systems, leading to fragmented silos (24). Data sharing protocols must extend across both consumer wearables and medical grade systems to combine these disparate data streams. The National Institutes of Health recently launched the National COVID Cohort Collaborative to build a centralized national data resource. While the initial focus is on increasing the wide availability of clinical data to accelerate the development of therapeutics, this framework can be leveraged as a data repository for continuous sensors and physiological outputs (25). Linking this physiological data with clinical outcomes, the effect of experimental therapeutics, and results of molecular testing will create a valuable global resource for the development of machine learning techniques to detect COVID-19 infections in the asymptomatic, to establish digital biomes of expected recovery specific to a patient's health status, and to provide guidelines for workers to return to their jobs safely.

CONCLUSION

Continuous physiological monitoring has well-established clinical benefits across a wide range of medical applications when deployed in noncritical care settings (26). For COVID-19, the extension of

continuous monitoring from the hospital to the home offers hope. Ongoing clinical studies will demonstrate the extent of this benefit with technologies that measure parameters directly relevant to the infection with clinical-grade accuracy. A focus on data interoperability and sharing will accelerate the development of predictive algorithms that are generalizable across different populations. In parallel with global efforts to develop effective vaccines and drugs to prevent and treat COVID-19, continuous skin-integrated sensors, positioned at optimal locations of the anatomy, will address the ongoing and critical need for objective, continuous, and sensitive tools to detect COVID-19 symptoms early in the general population, to direct limited molecular testing, to recognize the need for an escalation of care, and to track recovery curves.

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