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(Review Article)

A comprehensive look at the current and future technologies suitable for at home detection and management of viruses and virus causing diseases, Part I: point of care detection technologies

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Abstract

Home-based point-of-care diagnostic systems have proved to be transformative in the containment of COVID-19 pandemic. They are likely to a critical role in similar pandemics of the future. Some of the systems developed in recent years were used to control the pandemic and many more such systems are at various stages of development and evaluation. Appropriate use of some of the technologies has been shown to yield desired results through early detection and control of the virus. These technologies also assisted attempts to confine people within restricted quarters. This paper takes an outside look at many attempts made around the globe to mold and adopt these technologies to help mitigate the impact of COVID-19 and other similar outbreaks of the future. In addition to some of the implemented technologies, this paper also looks at potential untapped technologies that have prospective applications in controlling pandemic situations. Among the detection technologies reviewed are electrochemical sensors, microfluidic sensors, droplet collection and detection systems, transmucosal-extraction and detection systems, bi-dimensional graphene sensors, bi-conjugate quantum dot sensors, silicon nanowire sensors, nano-bio hybrid material sensors, and nano-sized cantilever sensors.

Keywords: Electrochemical Sensors; Microfluidic Devices; On-Body-Sensing; Cantilever Sensors; Remote Monitoring; Nano-wire Sensors

1. Introduction

The scarcity of resources to endure the COVID-19 outbreak combined with the fear of overburdened healthcare systems has forced a majority of countries around the world into a state of partial or complete lockdown. The number of laboratory-confirmed coronavirus cases which dropped significantly after a global shutdown again showed an increasing trend in certain parts of the world in response to the relaxation of the shutdown restrictions. Elderly people with comorbidities were shown to be more prone to serious clinical outcomes that are often linked to acute respiratory distress syndrome (ARDS). Currently, treatment is essentially supportive, and the role of many antiviral agents is yet to be fully established. Multiple vaccines that are capable of reducing infections and the spread of the disease have become available around the globe in recent months. While the rate of infection has slowed down with increasing vaccination, reducing the spread to negligible levels is also becoming a reality.

The clinical spectrum of COVID-19 has been shown to range from mild to critically ill cases. While remote monitoring was recommended for mild cases, early detection and continuous monitoring within a clinical environment were

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recommended for critical cases. The fear of contamination in clinical environments has led to reduction in on-site referrals for routine care, at least in some parts of the world. There has also been a perceived need to continuously monitor non-severe COVID-19 patients, either from their quarantine site at home, or at dedicated quarantine locations. Thus, the pandemic has forced the healthcare sector to innovate and enhance or create new routes for providing healthcare services at distance. In particular, this has created a dramatic impetus to find innovative ways to monitor patient health status remotely and effectively.

2. Facts gathered from select group of research papers

In a recently published review article [1] entitled 'Electrochemical Detection of Viruses and Antibodies,' the authors observed that near patient detection of viral infection represents a powerful approach for the control of emerging threats to global health. According to the authors, the ability to identify individuals who have contracted the disease is central for a return to normal daily activities. The review covered the latest advances in electrochemical sensors applicable for virus detection and concluded the report with the following highlights:

- Given the speed, portability, sensitivity, and selectivity achieved using electrochemical detection, these sensor systems hold the promise of transformative change in clinical practice.
- Highly sensitive electrochemical sensors for viral DNA enable early detection of disease.
- Antibody testing allows the assessment of the extent of disease regression and the immunity status of recovered individuals.
- Sample-to-answer devices open up opportunities for testing people in their own homes and communities.
- Integration of sensors and wireless technologies may enable autonomous, point-of-care applications.
- Challenges remain in terms of selectivity, shelf-life, manufacturability, and use of sustainable materials.

In another study [2] involving electrochemical sensing, the authors observed that correct detection and routing of the signal from epidermally retrieved biofluid to a readout unit are critical to render high-fidelity wearable biomarker data. The study thus demonstrated the feasibility for high-fidelity biomarker data acquisition through wearable sensors and sensor integration with consumer electronics.

A third study that focused on electrochemical biosensors [3], covered transduction elements, biorecognition elements, electrochemical techniques, and biosensor performance. Transduction elements were discussed in terms of the electrode material used and the form factor. Biorecognition elements for pathogen detection, including antibodies, aptamers, and imprinted polymers, were discussed in terms of their availability, production, and the immobilization approach. Emerging advances of electrochemical biosensor design were reviewed, including electrode modification and transducer integration. Measurement formats for pathogen detection were classified in terms of sample preparation and secondary binding steps. Future directions and challenges associated with electrochemical biosensors for pathogen detection were highlighted.

According to Perez-Marmol et al (4) frailty is one of the first insights of decline in elderly people and its progression can be slowed down if it is detected at an early stage. The authors observe that at present most health professionals measure and characterize frailty through questionnaires and through tests of strength or gait focused on the physical dimension. According to the authors, the use of sensors to measure and monitor different e-health indicators while the user is performing basic activities of daily life (BADL), can improve the current status of frailty measurement. In this context, they discussed a new system developed on the basis of microservices architecture, which collects sensory data while older adults perform instrumental activities of daily life (IADLs) in combination with BADLs. IADLs involved not only physical dimension, but also cognitive and social dimensions. They applied machine learning models on both (BADL and IADL) sets of data to assess the frailty status and they reported that the new system outperformed the previous system which used only BADL data. They concluded that their new model was accurate, ecological, non-intrusive, flexible and can help health professionals to automatically detect frailty.

According to Zhaung and his co-authors (5), microfluidic chips, known as "lab-on-a-chip" are one of the most promising tools for the detection of viruses. They reviewed the development of microfluidic chips which can be used for viral detection, specifically viruses of recent origin such as COVID-19. The advantages and disadvantages of microfluidic systems were discussed and analyzed. Ideas were proposed for future development of microfluidic chips to be used for the control of viral outbreaks.

Malik's patent (6) which bears the title, " Biological Sample Extraction and Detection System", describes an oral transmucosal-extraction device that can be inserted or imbedded in an animal or human oral cavity for blood or interstitial fluid extraction, viral detection, and analysis. The device incorporated a receptacle for transmucosal extraction, and it has been configured to interface with multiple customizable applications. The applications include auxiliary body wearables, medical devices, blood and biological fluid analyzers, and diagnostic and therapeutic tools. A part of the device or the entire device can also be inserted into a "reader" which is external to the oral cavity. The reader can be any smart device or a smart phone that contains one or more sensors for the detection of viruses and other elements of interest.

A patented invention described by Kanzer (7) relates to droplet collection devices and methods that can be used to detect and control airborne communicable diseases in humans and/or animals utilizing RFID (Radio Frequency Identification) technology. The new arrangement described by Kanzer can serve as an expiratory droplet collection device and can be incorporated into face masks. They can detect and control outbreaks of airborne communicable diseases through the identification, tracking and quarantine of potentially infectious humans and/or animals, utilizing RFID.

According to Hamid and his co-workers (8), the current rapid testing procedures involving nasopharyngeal and oropharyngeal swabs, bronchoalveolar lavage, sputum, urine, and blood are not only invasive procedures but also cause embarrassment to people. They recommend the use of saliva for quick and easy detection of the virus with minimal inconvenience to people.

Palmieri and Papi (9) report that functionalized graphene demonstrates a good viral capture capacity and that combined with heat or light-mediated inactivation, graphene could be used as a disinfectant. According to them, bidimensional graphene material has already captured much attention due to its promising antimicrobial properties and antiviral efficacy. They believe that antibody-conjugated graphene sheets can rapidly detect targeted virus proteins and can be useful for large population screening; they can also serve as inexpensive environmental sensors and filters, given their low cost. Graphene sensor arrays can also be implemented on standard utility textiles to serve screening, detection, and elimination functions.

A recent journal article bearing the title, "Continuous On-Body Sensing for the COVID-19 Pandemic: Gaps and Opportunities" (10), concludes that rigorous and widespread testing continues to be critical for containing the COVID-19 pandemic. It observes that the molecular diagnostics technology used for detection relies on detection of viral RNA, typically by RT-PCR and that the approach has significant disadvantages. The article stated that alternative tests based on antibodies may be more reliable, but the appearance of antibodies (IgM and IgG) can take weeks or even months after the initial exposure. Furthermore, positive antibody titers may only reflect prior exposure as opposed to protective immunity. Based on a review of emerging evidence, the article observes that re-infection by endemic coronaviruses is not atypical and that re-infection could complicate the protocols for follow-up molecular testing. After taking a comprehensive look at the overall situation, the article concludes that a continuing gap between widespread population level testing and the availability of tests is likely to persist for the foreseeable future.

After identifying abnormal breathing as one important characteristic feature of COVID-19 infected patients, Jiang and his co-authors (11) proposed a portable non-contact method to screen the health condition of people wearing masks through the analysis of their respiratory characteristics using RGB-infrared sensors. They developed a respiratory data capture system for people wearing masks using face recognition tools. Then they applied a bidirectional GRU neural network system to the respiratory data to determine health status from respiratory data. Validation experiments showed that their model can identify the health status from respiratory data with 83.7% accuracy, 90.2% sensitivity. The work demonstrated that RGB-infrared sensors on portable devices can be used as pre-scan tools for respiratory infections.

In a novel approach to detect influenza virus, Yeo and co-workers (12) developed a rapid and simultaneous detection toolkit for influenza A H5 subtype viruses in humans, using a bioconjugate quantum dot (QDs) assembly and a smartphone-based rapid dual fluorescent diagnostic system (SRDFDS). Two types of QDs were assembled on a latex bead to enhance the detection sensitivity and specificity of influenza A infection (QD580) and the H5 subtype (QD650). The dual signals of influenza A and H5 subtype of H5N1-infected patients were detected simultaneously and quantified separately. Results showed a high sensitivity of 92.86% and 78.57% for influenza A and H5 subtype detection with corresponding specificities of 100% and 97.37%. It was concluded that tool kits based on multiplex QD bioconjugates and SRDFDs can provide accurate and meaningful diagnosis information with improved detection accuracies and sensitivities for H5N1 patients.

In another study (13) the authors discussed the use of double etched porous silicon (DEPSi) nanowire arrays for impedance sensing of influenza viruses such as H1N1. The proposed double-etched porous silicon structure provided efficient penetration of virions into sensitive layers and also effectively trapped them in the pores. Adsorption of the viruses led to a significant shift in the resonant frequency of DEPSi which was measured by an impedance spectrometer. The study concluded that double etched porous silicon nanowire arrays can facilitate rapid, label-free and low-cost detection of influenza.

According to Alshammari and Mikler (14), the extensive use of digital devices and internet access by the participants of large gatherings is a boon when it comes to collecting and analyzing massive amounts of site-specific data. The availability of large- scale site specific data coupled with the need to establish real-time disease outbreak surveillance at global mass gatherings, drives the need for the development of advanced computational methods. Once collected and processed, the new data along with other health-related information can facilitate the establishment of disease surveillance systems at global mass gatherings. In this paper, the authors reviewed the existing approaches for monitoring outbreak of infectious diseases in large gatherings and highlighted the opportunities for big data in this application.

According to Taek Lee and co-authors (15), there are a few traditional techniques available to detect avian influenza virus (AIV) in chickens, ducks, humans, and other living organisms. However, the authors also see the need to develop a new technique that allows for more rapid diagnosis of AIV. To achieve this goal, the authors explored the use of nano-bio hybrid materials as AIV biosensors. These materials, according to the authors can enhance the sensitivity and selectivity of the technique while also reducing the detection time and high-throughput process time.

In their work, Davies and Williams (16) demonstrated the feasibility of measuring capillary oxygen saturation (SpO2) from the ear canal which they believe is a more convenient site for long term monitoring of patients compared to the right index finger. It was concluded that SpO2 measurement from the ear canal may be both convenient and superior to conventional finger measurement for continuous non-intrusive long- term monitoring in clinical and everyday-life settings.

In a review (17) of micro and nano sized cantilever sensors, the authors introduced the basic principles of operation of cantilever biosensors in static and dynamic modes. They summarized a range of approaches to cantilever design, fabrication, and instrumentation according to individual applications. More specifically, they described cantilever-based detection of proteins, DNA molecules, bacteria, and viruses and discussed current challenges that are thrown by the biophysical characteristics of the detection targets.

3. Summary and Conclusion

Many new and potentially useful technologies have surfaced not only to quickly detect the problem at the source but also to manage and stop the spread of communicable diseases. A new understanding that contact tracing of individuals is as important as virus detection itself has given new impetus for the development and evaluation of rapid contact tracing technologies that can operate in tandem with disease detection, monitoring and treatment tools. This understanding and the impetus it provided to quickly trace individuals who unknowingly get exposed to asymptomatic or delayed symptomatic diseases is likely to be of great benefit in the future.

Among the promising sensing technologies that are likely to dominate the source detection of viruses and bacteria are:

- Electrochemical sensors which can be easily integrated with a range of electronic wearables to serve as sample-to-answer devices.
- Microfluidic chips which are also known as “lab-on-a-chip” devices.
- Functionalized graphene materials which can serve not only as efficient viral capture materials but also as effective disinfectants with heat or light-mediated inactivation.
- Droplet collection devices that can incorporate a multitude of sensors of different types.
- Non-contact type of sensors that can detect abnormal breathing patterns and sounds.
- Nano-bio hybrid sensing materials capable of rapid detection and instant identification of viruses
- Conjugate quantum dot (QD) assemblies capable of exhibiting fluorescence through viral impact.
- Etched porous silicon nanowire arrays capable of sensing virus induced impedance changes.
- Micro and nano sized cantilever sensors

Compliance with ethical standards

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Disclosure of conflict of interest

All three authors declare that the information presented in this article is free of any type of conflict of interest.

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