Original Paper

Proposal of a Novel Diagnostic Device for COVID-19

Saeed Beygzadeh[1], Vahid Beygzadeh[2*] & Zahra Beygzadeh[3]

[1] Ph.D. Student, Dept. of Nano Technology, Nano-Materials Division, Faculty of New Science and Technology, Semnan University, Semnan, Iran

[2] Lecturer, Faculty of Mechanical Engineering, University of Applied Science and Technology, Tehran, Iran

[3] B.Sc, independent researcher, Project Engineering, Miandoab, Iran

[*] Corresponding author: Tel.: +989144098865, E-mail: vbeygzadeh@gmail.com

Abstract

Currently two types of tests are available for COVID-19 (diagnostic tests and antibody blood tests). In this study, we propose a new biosensor based COVID-19 diagnostic device, which can decrease the COVID-19 outbreak in the world. The proposed device offers powerful capabilities to screen for the COVID-19 disease with unprecedented sensitivity that makes detection possible at some of the earliest instances of exposure or infection (before the individual is showing symptoms of the disease) in a patient's exhaled breath, sneeze sample, cough sample, mucus sample and nasal discharge sample. This device consists of bioreceptor, transducer, detector and data processor and it can detect COVID-19 biomarkers from the collected samples in less than one hour. Furthermore, it is a favorable device which has several benefits including fast detection capability, better reproducibility compared to other methods, easier use and high reliability, and it can be designed without negative effect in the clinical analysis.

Keywords

COVID-19, outbreak, diagnostic, disease

1. Introduction

In December 2019, a novel coronavirus was detected in pneumonia patients which was later named COVID-19. Since the first human coronavirus detected in the 1960s, COVID-19 is the seventh coronavirus that is known to infect humans. Among all the human coronaviruses, four of them, including NL-63, HKU1, 229E and OC43, cause mild illness, while the other three, SARS-CoV, MERS-CoV and COVID-19, lead to serious disease (Li, 2020; Habibzadeh, 2021;). The current

potential for global propagation of COVID-19 and the growing number of reported cases, adds immediacy to understanding this outbreak (Yee, 2020). Coronaviruses are minute in size (65–125 nm in diameter) and contain a single stranded RNA as a nucleic material, size ranging from 26 to 32kbs in length (Shereen, 2020). On January 2020, the WHO declared the outbreak of COVID-19 to be a public health emergency of international concern posing a high risk to countries with weak and vulnerable health systems. The emergency committee has stated that the outbreak of COVID-19 may be terminated by early detection, isolation, rapid treatment, and the implementation of a robust system to track contacts (Catrin, 2020). Various organizations including the WHO and US centers for disease control and prevention (CDC) have issued advice on preventing further outbreak of COVID-19. They recommend avoiding travel to highrisk areas, contact with individuals who are symptomatic, and the consumption of meat from regions with known COVID-19 outbreak. Basic hand hygiene measures are also recommended, including frequent hand washing and the use of personal protective equipment such as face masks. Clinical features of COVID-19 include fever, dry cough, vomiting, diarrhoea, and myalgia. Individuals with multiple comorbidities are prone to severe infection and may also present with acute kidney injury. Extensive laboratory tests should be requested for patients with doubtful infection. Patients may present with an elevated C-reactive protein, lactate dehydrogenase, erythrocyte sedimentation rate, creatinine, and a prolonged prothrombin time (World Health Organization and Centers for Disease Control and Prevention, 2020). Rapid and accurate detection of COVID-19 is essential to control the outbreak of COVID-19. Nucleic acid detection is a major method of laboratory diagnosis. Reverse transcription quantitative PCR (RT-qPCR) is a molecular biological diagnosis technology based on nucleic acid sequences. The complete COVID-19 genome sequences are available in GenBank. Thus, the nucleic acid of COVID-19 can be detected by RT-qPCR or by viral gene sequencing of nasopharyngeal and oropharyngeal swabs, sputum, stool or blood samples. However, collection of these specimen types by healthcare personnel requires close contact with cases, which increases a risk of spreading the virus to healthcare personnel. Moreover, collection of oropharyngeal or nasopharyngeal specimens may cause bleeding, especially in patients with thrombocytopenia (Li, 2020). Very few studies on this topic have already been published. For instance, Kudr et al. (2021) presented current state of the art approaches to viral electrochemical biosensors, with a focus on SARS-CoV-2. They provided a brief overview of qRT-PCR and serological tests, and showed their advantages and drawbacks and consider them regarding advances in electrochemical tests. The potential application of electrochemical biosensors in the COVID-19 pandemic was studied by Mahshid et al. (2021), they also reviewed advancements in electrochemical biosensing platforms towards the detection of SARS-CoV-2 through studying similar viruses. Absence of contamination of personal protective equipment by (COVID-19) was studied by Ong et al. (2020). Rao and Vazquez (2020) studied identification of COVID-19 through artificial intelligence framework using a cell phone in the populations when cities are under quarantine. They concluded that, using machine learning algorithms are able to improve possible case identifications of COVID-19, quicker when we use a cell

phone based web survey. Hellewell et al. (2020) studied feasibility of controlling COVID-19 outbreaks by isolation of cases and contacts. They concluded that, in most outbreak scenarios, case isolation and contact tracing alone is insufficient to control outbreaks, and that in some scenarios even near perfect contact tracing will still be insufficient, and further interventions would be required to achieve control. Effective contact tracing and isolation could contribute to reducing the outbreak or bringing it under control over a longer time period. Holland et al. (2020) discussed COVID-19 personal protective equipment for the emergency physician. They concluded that, ancillary personnel, should wear personal protective equipment. After completing patient transport/care duties, and before entering clean areas, personnel should remove and arrange of their personal protective equipment and carry out hand hygiene to avoid contaminating clean areas. Furthermore, EMS clinicians should exercise caution if an aerosol generating procedure, such as oropharyngeal suctioning, bag valve mask ventilation, endotracheal intubation, nebulizer treatment, continuous positive airway pressure, bi-phasic positive airway pressure, or resuscitation involving emergency intubation or cardiopulmonary resuscitation is necessary. Diao et al. (2020) studied diagnosis of severe acute respiratory syndrome COVID-19 infection by detection of nucleocapsid protein. They concluded that, the virus (COVID-19) nucleic acid RT-PCR test has become the standard method for diagnosis of COVID-19 infection due to its high detection rate. However, nucleic acid test results are sometimes unstable and take too long, or can appear false negative and false positive. Moreover, IgG and IgM antibody detection method have been used in diagnosing with a relative higher positive rate. Long et al. (2020) evaluated the diagnostic value of computed tomography and real time reverse transcriptase polymerase chain reaction (rRT-PCR) for COVID-19 pneumonia. They concluded that, rRT-PCR may produce initial false negative results and suggested that patients with typical computed tomography findings but negative rRT-PCR results should be isolated, and rRT-PCR should be repeated to avoid misdiagnosis. Lampariello and Sagratella (2020) proposed a mathematical program to model the problem of establishing how many diagnostic tests the Italian regions must perform in order to maximize the overall COVID-19 disease detection capability. They concluded that, their model is sufficiently flexible to be applied to other federal like health care systems such as, e.g., Germany or USA. Pang et al. (2020) reviewed potential rapid diagnostics, vaccine and therapeutics for COVID-19. They concluded that, rapid diagnostics, vaccines and therapeutics are key pharmaceutical interventions to limit outbreak of severe acute respiratory infectious diseases. However, lessons from MERS-CoV and SARS CoV have shown that the journeys for these developments can still be challenging moving ahead. Yang et al. (2020) proposed RNA-based diagnostic device for COVID-19. They concluded that, the development of a paper-based RNA assay for use in combination with a smart cell phone application can provide new insights into designing COVID-19 diagnostics and ultimately improve the health care system to combat this and similar diseases. According to the literature review, there are two primary methods for diagnosing COVID-19:

•   A lateral flow immunoassay, which is a common point of care diagnostic approach that detects antibodies against COVID-19 in patient samples.

- A molecular based assay. The current standard approach for screening COVID-19 requires a reverse real time assay (rRT-PCR), which can be carried out using a variety of clinical specimens, including bronchoalveolar lavage fluid, fibro bronchoscope brush biopsies, sputum, nasal swabs, pharyngeal swabs, feces, or blood.

The above mentioned approaches rely on expensive equipment, well trained personnel, and are often time consuming, leaving a rapidly rising number of potential cases untested and opening a gaping hole in COVID-19 prevention and outbreak efforts. Moreover, going to a clinical setting for testing increases the risk of spreading the COVID-19 and adds strain to a vulnerable healthcare system. For these reasons, an alternative, rapid, inexpensive, easy to use, and sensitive COVID-19 diagnostic device must be developed for the early diagnosis and detection of patients with COVID-19.

For COVID-19, the incubation lasts in a reported range of 2 to 14 days from infection to symptoms surfacing. Even worse, COVID-19 can spread from human to human even before any actual clinical manifestations, leading to very challenging conditions for detecting and isolating potential patients, which makes it more difficult to control the pandemic. COVID-19 is thought to be transmitted through close contact, aerosol and droplets, and patients in the incubation period can transmit the COVID-19 virus to other persons. In order to speed up the COVID-19 virus detection in individuals and households, and rapid isolation of the patients, in this study, we propose a new biosensor based COVID-19 virus diagnostic device.

2. Method

Early detection of COVID-19 is crucial in decreasing its outbreak and gives exposed individuals more treatment options. The proposed device offers powerful capabilities to screen for COVID-19 disease with unprecedented sensitivity that makes detection possible at some of the earliest instances of exposure or infection (before the individual is showing symptoms of the disease) in a patient's exhaled breath sample, sneeze sample, cough sample, mucus sample and nasal discharge sample. Each exhaled breath sample, sneeze sample, cough sample, mucus sample and nasal discharge sample contain analytes that can be produced by bodily fluid or emitted by COVID-19. The proposed device detects biomarkers (Diseases will produce a specific analytes, which act as biomarkers that alert medical professionals to the presence of the diseases. Biomarkers are the signature of a disease and discovering them can give medical professionals the ability to make an early diagnosis and begin potentially lifesaving treatment.), which act as chemical signatures for COVID-19, and it has potential to be a powerful tool in stopping the spread of COVID-19 disease in the world. The proposed COVID-19 diagnostic device is illustrated schematically in Figure 1.
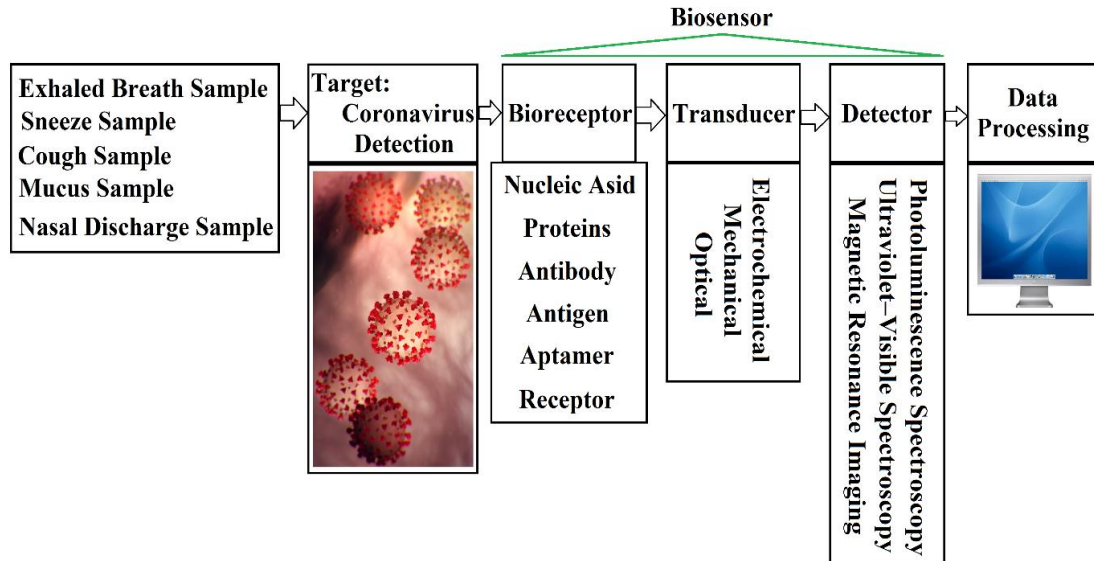
Figure 1. The Proposed Coronavirus Diagnostic Device

The device consists of three stages. In the first stage, the collected samples (exhaled breath sample, sneeze sample, cough sample, mucus sample and nasal discharge sample) are used for the COVID-19 detection test. In the second stage, the device uses a biosensor for sample processing and COVID-19 biomarker detection, a biosensor is an analytical device that convert a biological response into a quantifiable and processable signal. The biosensor comprised of three components:

• Bioreceptor: It is the first component of the biosensor and is used to detect the target analytes (nucleic asid, proteins, antibody, antigen, aptamer and receptor) from the samples.

• Transducer: It is the second component of the biosensor, which plays an important role in terms of converting the biorecognition event into an optical signal, mechanical signal and electrochemical signal.

• Detector: It is the third component of the biosensor and is used for detecting the presence of an optical signal, mechanical signal and electrochemical signal by using photoluminescence spectroscopy or ultraviolet visible spectroscopy or magnetic resonance imaging.

In the final third stage, the inputted data to the computer is processed for interpretation (the conversion of data into usable and desired form).

3. Results and Discussion

In medical diagnosis, testing for COVID-19 biomarker is carried out in laboratories using automated analyzers (a lateral flow immunoassay and a molecular based assay). They usually allow detection of several analytes but require hardworking trained personnel and long time. The rapid development of nanotechnology and nanobiotechnology has improved the design of new devices for diagnosis in medical applications. The proposed biosensor based COVID-19 diagnostic device is a favorable device which has several benefits including fast detection capability, better reproducibility compared to other

methods, easier use and high reliability, and it can be designed without negative effect in the clinical analysis. The aim of this study is firstly to present a new applied device for the earlier detection of COVID-19. Secondly it is to put biosensor based diagnosis in practical use and raise the level of medical practice. The device is independent of any specific method and will be a useful diagnostic tool in the future. Furthermore, ease of use of the proposed device make it an essential device for facilities anywhere in the world where COVID-19 could spread, including clinics, airports, border crossings and other relevant sites.

4. Conclusions

A new diagnostic device to decrease the COVID-19 outbreak has been proposed. Our device shows the possibility of detecting COVID-19 in the patient's exhaled breath sample, sneeze sample, cough sample, mucus sample and nasal discharge sample within less than one hour using a nanoscale biosensor based device. Our device is not restricted only for COVID-19 detection but could also detect other viruses. Additionally, it gives doctors the ability to make an early diagnosis and begin potentially lifesaving treatment. Other concluding remarks follow:

• This device to be far more effective at detecting COVID-19 than other current technologies.

• This device to be widely affordable than current technologies.

• This device can detect the COVID-19 biomarker, in the sample in only a few minutes.

• This device will allow for rapid early screening and diagnosis of COVID-19 disease, by checking a patient's exhaled breath sample, sneeze sample, cough sample, mucus sample and nasal discharge sample for biomarkers.

• This device will generate very early stage screening and diagnosis via a noninvasive test.

• This proposed device will be available in every medical clinic, hospital and etc., in order to provide rapid screening and diagnosis for COVID-19 disease, leading to effective, treatments that will save lives, improve quality of life and decrease the costs of medical care.

• By seeking out chemicals produced by such disease, this device will be more sensitive and accurate to those currently in use.

As perspective for future works it could be mentioned:

• Using smart nano materials to improve the COVID-19 virus detection in individuals and households.

• The use of nano tissue paper as a sustainable, simple and reliable COVID-19 diagnostic device which can be acquired and maintained easily by persons who are not medical specialists.

References

Diao, B., Wen, K., Chen, J., Liu, Y., Yuan, Z., Han, C., & Wu, Y. (2020). Diagnosis of acute respiratory syndrome coronavirus 2 infection by detection of nucleocapsid protein. *MedRxiv*.

Habibzadeh, P., Mofatteh, M., Silawi, M., Ghavami, S., & Faghihi, M. A. (2021). Molecular diagnostic assays for COVID-19: An overview. *Critical Reviews in Clinical Laboratory Sciences*, 1-20.

Hellewell, J., Abbott, S., Gimma, A., Bosse, N. I., Jarvis, C. I., Russell, T. W., & Eggo, R. M. (2020). Feasibility of controlling COVID-19 outbreaks by isolation of cases and contacts. *The Lancet Global Health*, *8*(4), e488-e496.

Holland, M., Zaloga, D. J., & Friderici, C. S. (2020). COVID-19 Personal Protective Equipment (PPE) for the emergency physician. *Visual journal of emergency medicine*, *19*, 100740.

http://www.cdc.gov

http://www.who.int

Kudr, J., Michalek, P., Ilieva, L., Adam, V., & Zitka, O. (2021). COVID-19: a challenge for electrochemical biosensors. *TrAC Trends in Analytical Chemistry*, 116192.

Lampariello, L., & Sagratella, S. (2021). Effectively managing diagnostic tests to monitor the COVID-19 outbreak in Italy. *Operations Research for Health Care*, *28*, 100287.

Li, H., Liu, S. M., Yu, X. H., Tang, S. L., & Tang, C. K. (2020). Coronavirus disease 2019 (COVID-19): current status and future perspectives. *International journal of antimicrobial agents*, *55*(5), 105951.

Li, J. Y., You, Z., Wang, Q., Zhou, Z. J., Qiu, Y., Luo, R., & Ge, X. Y. (2020). The epidemic of 2019-novel-coronavirus (2019-nCoV) pneumonia and insights for emerging infectious diseases in the future. *Microbes and infection*, *22*(2), 80-85.

Long, C., Xu, H., Shen, Q., Zhang, X., Fan, B., Wang, C., & Li, H. (2020). Diagnosis of the Coronavirus disease (COVID-19): rRT-PCR or CT? *European journal of radiology*, *126*, 108961.

Mahshid, S. S., Flynn, S. E., & Mahshid, S. (2021). The potential application of electrochemical biosensors in the COVID-19 pandemic: A perspective on the rapid diagnostics of SARS-CoV-2. *Biosensors and Bioelectronics*, *176*, 112905.

Ong, S. W. X., Tan, Y. K., Sutjipto, S., Chia, P. Y., Young, B. E., Gum, M., & Ng, O. T. (2020). Absence of contamination of personal protective equipment (PPE) by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). *Infection Control & Hospital Epidemiology*, *41*(5), 614-616.

Pang, J., Wang, M. X., Ang, I. Y. H., Tan, S. H. X., Lewis, R. F., Chen, J. I. P., ... Hsu, L. Y. (2020). Potential rapid diagnostics, vaccine and therapeutics for 2019 novel coronavirus (2019-nCoV): A systematic review. *Journal of clinical medicine*, *9*(3), 623.

Rao, A. S. S., & Vazquez, J. A. (2020). Identification of COVID-19 can be quicker through artificial intelligence framework using a mobile phone-based survey when cities and towns are under quarantine. *Infection Control & Hospital Epidemiology*, *41*(7), 826-830.

Shereen, M. A., Khan, S., Kazmi, A., Bashir, N., & Siddique, R. (2020). COVID-19 infection: Origin, transmission, and characteristics of human coronaviruses. *Journal of advanced research*, *24*, 91-98.

Sohrabi, C., Alsafi, Z., O'Neill, N., Khan, M., Kerwan, A., Al-Jabir, A., & Agha, R. (2020). World Health Organization declares global emergency: A review of the 2019 novel coronavirus (COVID-19). *International journal of surgery*, *76*, 71-76.

Yang, T., Wang, Y. C., Shen, C. F., & Cheng, C. M. (2020). Point-of-care RNA-based diagnostic device for COVID-19.

Yee, J., Unger, L., Zadravecz, F., Cariello, P., Seibert, A., Johnson, M. A., & Fuller, M. J. (2020). Novel coronavirus 2019 (COVID-19): Emergence and implications for emergency care. *Journal of the American College of Emergency Physicians Open*, *1*(2), 63-69.