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Three-dimensional printing in the fight against novel virus COVID-19: Technology helping society during an infectious disease pandemic

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ABSTRACT

Indeed, the scientific milestones set by the ever-emerging three-dimensional printing (3DP) technologies are tremendous. Till now, the innovative 3DP technologies have benefitted the aerospace, automobile, textile, pharmaceutical, and biomedical sectors by developing pre-requisite designed and customized performance standards of the end-user products. As the scientific world, at this moment, is expediting efforts to fight against the highly damaging novel coronavirus (COVID-19) pandemic, the 3DP technologies are facilitating creative solutions in terms of personal protective equipment (PPE), medical equipment (such as ventilators and other respiratory devices), and other health and welfare tools to aid the personal hygiene as well as safe environment for humans by restricting the communication of risks. Various sources (including journal articles, news articles, white papers of the government and other non-profit organizations, commercial enterprises, as well as academic institutions have been reviewed for the collection of the information relevant to COVID-19 and 3DP. This communication presents the recent applications of the 3DP technologies aiding in developing innovative products designed to save the lives of millions of people around the world. Moreover, the potential of 3DP technologies in developing test swabs and controlled medicines has been highlighted. The literature reviewed in the present study indicated that the fused filament fabrication (FFF) is one of the most preferred technologies and contribute about 62% in the overall production of the protective gears developed through overall class of 3DP.

1. The Alarming safety Concern

The global crisis of novel coronavirus also referred to as COVID-19 or nC0VID-19, has emerged in the Wuhan of mainland China, last year in December [1,2]. Unfortunately, the definitive origin of this virus is still unknown and controversial, and different experts have mentioned their assertions that pinpoint towards animals, especially bats, and snakes [3–5]. Gradually, this localized crisis of the Wuhan has spread rapidly across all continents, including Africa, Asia, Europe, Oceania, North America, and South America [6,7]. According to the World Health Organization (WHO), this crisis has already claimed more than 0.39 million lives, globally, whereas about 6.6 million affected people have suffered with deadly COVID-19 [8]. Fig. 1 shows the demographic representation indicating the COVID-19 global victims [9]. As a virulent infectious disease, the spread of COVID-19 is fast and wide [10,11]. As per the major studies reported by the eminent scientists, it has been found that the COVID-19 virus with 0.1 μm dimension can rest in the air, metallic surface, cardboard, and plastic for many hours that can ease in the transmission of the virus from one to another patient [12–14]. Furthermore, there are many existing controversies about the effect of humidity and temperature on the behaviour of virus [14].

It has been reported that the virus can significantly contaminate the air, surface environment, and protective equipment through droplet transmission. It means that the environment is currently playing a key role in the potential transmission. The COVID-19 attacks the victims, mainly those suffering from pre-medical histories including diabetes, cardio/heart malfunctions, and respiratory issues. As per Worldometer, it has been seen that the mortality rate of the aged population, such as: 80+, 70–79, 60–69, and 50–59 years, is 14.8, 8.0, 3.6, and 1.3%, respectively [15]. Further, the mortality rate of the victims with pre-medical histories of cardiovascular diseases, diabetes, chronic respiratory disorders, hypertension, and cancer is 10.5, 7.3, 6.3, 6, and 5.6%, respectively [15]. Till date, numerous research documents have cited the behaviour of COVID-19 in human body environment [16–21].

Furthermore, efforts are being made on the development of anti-viral vaccines, however, the WHO estimates it can take about 18 months [22].
Epidemiological changes in COVID-19 infection should be monitored by considering potential routes of transmission and subclinical infections. Specially, the adaptation, evolution, and virus spread among humans and possible intermediate animals, and reservoirs must be considered [23]. Presently, most of the COVID-19 treatments are being supported through anti-inflammatory and anti-viral treatments, continuous renal replacement therapy, invasive mechanical ventilation, and extracorporeal membrane oxygenation. Since, various vaccinations, investigated by the different healthcare organizations are still stuck in the clinical trials, the WHO has issued a white paper [24] indicating that the public health and social measures are essential actions to be made by individuals, institutions, communities, local and national governments, and international bodies to contain the transmission of virus. However, the increasing level of asymptomatic carriers and their commutes are the most critical parameters boosting the spread of COVID-19 [25]. To curb the same, the world is currently facing the lockdown, hitting not only the human’s lifestyles but also degrading the world economies [26,27]. Furthermore, it has severely impacted the supply chains of goods and services [28].

The demand for medical treatments, personal protective equipment (PPE), essential frontline gadgets, and accessories for the funeral homes, and end-of-life rituals has increased at a drastic rate [29]. The director-general of WHO said, “Without secure supply chains, the risk to healthcare workers around the world is real. Industry and governments must act quickly to boost supply, ease export restrictions and put measures in place to stop speculation and hoarding. We can’t stop COVID-19 without protecting health workers first,” [30]. Admitting that the demand of PPE is huge, many renowned enterprises, such as: SpaceX, Tesla, AirCo, INKSmith, Markforged, Formlabs, Voodoo Manufacturing, and Resonance, 3 M, Johnson Safety Products, Avon Rubber, Alpha ProTech, DuPont, MSA Safety, Honeywell, Ansell, etc., have started converting their regular products into PPE and other protective gears [31,32].

Fig. 1. Demographic representation of COVID-19 victims across the major epicenters and small clusters across (a) Asia and (b) Europe, Middle East and North Africa [9].
In a comparison of the conventional means of producing PPE, the three-dimensional printing (3DP) technologies are offering endless benefits, flexibilities, and customizations. Fox and Mubarak argued that the local users’ needs can be substantially satisfied through the movable factories, while maintaining the peace and prosperity [33]. The commercially available 3DP technologies are most suitable class of movable factories to satisfy the need of PPE of specific societal groups. Further, Corsini et al. explored the impact of digital fabrication tools, such as 3DP technology, in humanitarian and development sectors. It encouraged Do-It-Yourself paradigm by involving the ordinary people in inventing, designing, developing, and supplying the goods [35]. Underlining the various aspects, the users of 3DP technologies can design and produce the protective gears, easily, for satisfying their personal or societal needs.

In this review manuscript, the key applications of the 3DP technologies for fighting against COVID-19 virus have been summarized. Novel applications of the 3DP technologies for designing and developing different types of safety and medical tools have been presented. Particular emphasis has been given to the PPE, testing swabs, and drug delivery devices. Overall, this comprehensive review has been structured to outline the potential of the 3DP technology in developing protective gears to meet the drastically increasing globalized demands.

2. Fighting Pandemic using 3DP

2.1. Personal protective equipment

The 3DP technologies have just begun their career in dealing with the Pandemics. The eminent manufacturers and researchers understood the potential of 3DP technologies and directed them for developing PPE, medical tools, and other gadgets [36,37]. On the same line, the CECIMO Director-General, Filip Geerts said:

“3DP technologies can play an important role in sustaining the effort of hospital workers in the middle of this emergency”

Amid deadly COVID-19, a hospital in Brescia of Italy has set a new example when it got out of the respiratory valves needed to connect the patients to the breathing machines. As a response to the situation, the CEO of Isinnova, Cristian Fracassi, used 3D printing to meet the hospital’s demands and saved the patients’ lives. Similarly, 3D printed hand sanitizer holder, face masks (by Barcelona-based BCN3D and California-based Airwolf3D), medical devices (by SmileDirectClub), quarantine rooms (by Winsun), and respirators (by Zona Franca Consortium) are just a few examples to add-on [38]. Table 1 lists the potential industrial utility perspective of 3DP technologies dealing with COVID-19.

The technological emergence, as stated in Table 1, shows that the 3DP technologies are uniquely positioned to support supply chain and inventory gaps for PPE and other medical equipment. Considering the demands of PPE, the sudden hike in the demand for 3DP technologies has stretched supply chains and the healthcare sector is using it to a breaking point. As an output, these initiatives enabled the producers to efficiently provide the critical components and products as a global response to the COVID-19 pandemic [62]. It is essential to minimize the business disruption to move on-going programs on COVID-19 as well as to contribute to the worldwide community efforts in containing the virus’ spread. However, the response of 3DP technology to this crisis confirmed the on-demand manufacture of essential products.

Cavallo et al. mitigated the shortage of respiratory devices during the COVID-19 epidemic and investigated the efficacy of 3DP process for developing Charlotte and Dave connectors of breathing devices; refer

Table 1

| Type of 3DP | Application(s) | Manufacturer(s) | Status | Material | Ref. |
|------------|----------------|-----------------|--------|---------|------|
| Fused filament fabrication (FFF) | Critical face-shields, masks, mask adjusters, respirator parts, hands-free door openers, and nasal swabs | Hewlett-Packard Company | Released | Plastic | 39 |
| Selective laser sintering (SLS) | Ventilator parts, face masks, and face shields | 3D Systems | Medical grade | nylon | 40 |
| – | Disposable face shields | Stratasys Inc. | – | Plastic | 41 |
| – | Medical devices and protective clothing | EOS | – | Plastic | 42 |
| – | Medical equipment | Volkswagen | – | Plastic | 43 |
| – | Printed fixtures for diagnostic equipment development | Protolabs and Lumines Corporation | – | Metallic | 44 |
| FFF | Face masks | Monterey Peninsula College | Released | Plastic | 45 |
| – | Open Source Venturer | In-progress | Poly-lactic-acid (PLA) | 46 |
| – | Medical supplies | SMILEDIRECCLUB | Released | Plastic | 47 |
| FFF | Face masks, purifying ventilators, and face shielding | Ford Motor Company, 3 M and GE Healthcare | Released | Plastic | 48 |
| – | Face masks | Carbon3D | – | Plastic | 49 |
| – | Face shields | Somerset Community College, USA | In-progress | Plastic | 50 |
| – | Face shields | Polytechnic University, Hong Kong | – | Plastic | 51 |
| – | Quarantine booths | Welsh Building Technique Co Ltd | Released | Plastic | 52 |
| FFF | Medical gears | Ultimaker/Prusa | – | Plastic | 53 |
| – | Ventilators | SpaceX and Tesla | – | Plastic | 54 |
| – | Ventilators | General Motor | – | PLA | 55 |
| – | Hospital visors | Airbus | – | Plastic | 56 |
| – | Medical visors | Balkan Tech | Released | Plastic | 57 |
| – | Design for medical gadgets | Siemens Inc. | – | PLA | 58 |
| – | Headbands for face masks | Tennessee Tech University, USA | – | Plastic | 59 |
| – | Door openers | University of Sunderland, England | Released | Plastic | 60 |
| – | Headbands for face masks | Western Carolina University, USA | – | Plastic | 61 |
| – | Open source ventilator | Gui Calavanti, Ireland | In-progress | Plastic | 62 |
| – | Respirator | Jet Propulsion Laboratory, NASA, USA | Released | Plastic | 63 |

The list of notable 3DP technologies against COVID-19.
Indeed, the servicing standards of PPE devices prepared through 3DP technologies should be tightly regulated, for instance, the inbuilt porosity of the 3D printed device can pose adverse effect on the resulting face masks and face shielding as viral droplets of COVID-19 can enter and persist through the porous channels [64]. Conversely, the 3D printed face shield is arguably easier to build and assemble the parts because it does not need to seal tightly against the skin. Moreover, there exist many examples of completely printed stand-alone components [65]. For instance, manual ventilators (given in Fig. 2(b)) [66] have been repaired with 3D printed replacement parts and respiratory parts of ventilators (refer Fig. 2(c)) [67].

Elkington et al. developed pressurized air purified respiratory unit through FFF technology [68]. In their work, a headband has been printed by FFF using acrylonitrile-styrene-acrylate material, while the breather tube clips and duct components were manufactured with carbon fiber-filled nylon and acrylonitrile-butadiene-styrene, respectively. The developed device is undergoing testing to BS-EN 1294116 or any other required standard set by the Health and Safety Executive (HSE, UK). However, it is important to minimize the number and complexity of manufacturing steps [68]. In another work reported by Pereira et al. researchers fabricated a customized PEEP valve through FFF with polylactic acid to execute 6 independent flow exhausts to minimize the turbulence in water during the expiration period [69]. The new open-source FFF printers have been used to fabricate face shields for local hospitals [70]. The versatile materials can easily be translated into complex microfluidic functionalities through 3DP [71]. Nicholson et al. presented the pictorial view; refer Fig. 3, of snorkel mask with adaptor and filter made with FFF technology using black polylactic acid feedstock. The developed mask was further tested the fitness, include normal breathing, deep breathing, turning the head side to side, moving the head up and down, talking, grimace, bending over, and normal breathing [72]. Cote et al. found this technology cost-effective and flexible owing to the availability of a wide range of thermoplastic materials [73]. It has been mentioned by the research team that customized protective gears could be easily manufactured by adopted the digitized data from conventional 3D scanners, ultrasound scans, computerized tomography, or magnetic resonance imaging.

The continued development in such direction is likely to result in low-cost integrated microfluidic devices during the time of the epidemic. During the current time when the manufacturing sectors are badly hit by the epidemic, the emerging applications of 3DP technologies are helping industries in transforming their regular products to specialized protective gears [74].

### 2.2. Test swabs

There is a worldwide lack of supplies of nasopharyngeal swabs, required to conduct COVID-19 testing, owing to the current and forthcoming increase in their demands. Owing to this various commercial manufacturers and public/private research organizations are developing test swabs, through 3DP technologies, by using the different types of polymeric feedstock materials. It has been found that some of the efficient 3DP technologies are capable of printing can print up to 1500 swabs in 8hrs [75]. The design of the nasal swab has already been patented by the Northwell Swab and granted the University of South Florida, USA to print proprietary designs of the swabs for non-commercial purposes [76]. Williams et al. incorporated iterative design of the swab prototype on the basis of regular feedbacks received from clinical and engineering investigators. In their study, the laboratory evaluations comprised of in-vitro studies have been carried out on
Furthermore, Cox and Koepsell developed swabs by using FFF technology owing to readily availability and comparative cost-effectiveness [79]. Fig. 3 shows the snorkel mask developed with FFF [72].

It has been found that the designed matured in their study is suitable for performing required tests with high level of accuracy [77]. As per Ishack and Lipner the 3D printed test swabs can be sourced from calcium alginate hydrogels using 3D tissue engineering to increase the COVID-19 testing capacity. Apart from this, the nasopharyngeal and oropharyngeal swabs can be made from a flexible polymer consisting of polystyrene shaft [78]. Callahan et al. carried out multi-step preclinical evaluation on 160 swab, 35 designs, and 48 materials from 24 companies, laboratories, and individuals. It has been concluded that the 3DP technologies can assist in developing matured designs with customized settings [79]. Furthermore, Cox and Koepsell developed swabs by using FFF technology owing to readily availability and comparative cost-effectiveness (<$800 USD), when compared to stereolithography [80]. Fig. 4 shows the as printed test swab.

Further, Callahan et al. reported that the test swab prototypes developed through the 3DP technology exhibited a single false positive and 1–2 false negative results owing to various reasons [81]. According to the on-going research trends, the 3DP technology is addressing the critical shortages of test swabs brought about by the COVID-19 pandemic. However, for the long term effectiveness, it is required to assess the strengths and shortcomings of printed test swabs under controlled centric studies to lower the apparent rate of false results [82].

2.3. Drug delivery

At the new vaccinations are currently undergoing various development activities, the medical experts are treating their patients with the existing medical drugs. Therefore, to use the available drugs in the best way, it has been asserted by the various professionals to adopt the novel 3DP technologies in delivering controlled healing chemical compounds. Apart from this, the 3DP of new drugs during development stages reduces the economic costs and risks of upscale that are essential to considered [83]. In 2015, the very first 3DP drug Spritam was approved by the US Food and Drug Administration (FDA) [84]. Currently, 3DP systems are being investigated for the fabrication of tablets and injectable systems with immediate-release or sustained-release properties [85]. The macro/micro-sized structures for drug delivery produced using 3DP technologies are believed to be highly effective in curing patients suffering from pandemic. These systems will allow simultaneous use of multiple drug ingredients and other spatial patterns of drug deposition within the hydrogel or polymer matrix capable of solving a long-standing clinical problem. Goyanes et al. revealed that 3DP technologies can personalize anti-ace drug-loaded masks/patches with FFF based medicated filament [82]. The loading of the drug can be customized according to the need of the hour. Fig. 5 shows the therapeutic applications of 3DP technologies [87].

Xing et al. highlighted that the two-photon polymerization microfabrication can be used for micro/nano-photonics, micro-electromechanical systems, microfluidics, biomedical implants, and micro-devices [88]. It has been found that the 3DP technologies are suitable for dispensing low volumes of drugs with extremely high accuracy and precise spatial control [89]. Further innovation can be led by the combination of 3DP technologies and smart hydrogels for producing customized organs/tissues to replace the infected ones. Focusing COVID-19, the 3DP merits align well with the current demands of the pharmaceutical sector. Prof. Soh of the National University of Singapore has developed a low cost 3DP based pill, solidified in a silicon based mould, until the whole tablet is cured [90]. He quoted, “every single person is different, based on many factors such as genetics, age, and body mass and so on. Therefore, the different activity levels and consumption habits can be met through 3DP based controlled drug delivery”. Solanki et al. studied the pharmaceutically acceptable polymers for the formulation of 3D printed tablets by FFF to provide rapid drug release [91].

Currently, the 3DP technologies can avail the unique opportunities for the preparation of personalized doses to address individual needs of the infected patients. At the moment, very few studies are concentrated on the treatment of the COVID-19 patients as the current regulations are highly stringent due to the risk level. Therefore, the preliminary studies investigating the effectiveness of the drug delivery during in-vitro animal trials can be initiated. The research activities should also aim to categorize the 3DP technologies based on their superiorities in the fabrication of drug delivery systems as well as the formulation.

3. End Note

Apparently, the on-going infectious agent is capable of destabilizing the populations, economies, and governments [92]. The socio-economic impact of the biological COVID-19 pandemic is quite difficult to forecast. One of the major on-going crises is the shortage of PPE and medical devices for the protection the frontline worker and general population. Indeed, the timely breakthroughs of 3DP technologies in containing the spread of infectious disease virus as described in the present work. The
emergence of 3DP technology at this time of pandemic has brought high hopes by producing the required PPE and medical tools. It has been determined that the on-going demands of the protective gears, such as face shields and masks, is about 62% and 20%, respectively, refer Fig. 6(a). Furthermore, the FFF technology has been identified as one of the most useful 3DP technologies to meet with the increasing market demands of protective gears, refer Fig. 6(b).

In particular, the FFF technology has overwhelmed the total supply of the protective gears. The widespread utility of FFF technology during the pandemic time is mainly due to:

- Most of the PPE as well as in-demand medical tools are made of medical-grade plastics and FFF is one of the most cost-effective technologies.
- The processing time of the FFF is lower that SLS and SLA, therefore yields more.
- Finally, the capital cost, operational cost, and cost of the feedstock of FFF technology is low.

The benefits of digital 3DP tools have been widely reported in the context of high-resource settings [34]. It has been found that due to inbuilt porosity, the facial shields and masks prepared through 3DP technologies are being criticized. However, low-cost post-processing techniques could be adopted to deliberately eliminate such limitations. Since these technologies are of great industrial repute, hence, for building the forever trust following four-point eligibility checks must be considered:

- Safety and reusability: The PPE and medical tools should be approved by the regulatory bodies.
- Experience: The protective gears must be made of materials less suitable for the survival of the virus. Furthermore, these products could be sanitized before the next use, without any contamination.
- Communication: The frontline health workers using the 3DP face mask or shield must be able to communicate without impedance to hearing.
- Comfort and endurance: The PPE should be comfortable and not claustrophobic.

Apart from this, there should be specialized protection equipment for the workers at funeral homes. The WHO, through a white paper, suggested that personnel interacting with the body must apply standard precautions, including frequent sanitization and use of the appropriate PPE, for instance gown, gloves, face shield, and medical mask [94,95]. Therefore, the use of 3DP technologies in designing and fabrication of specialized PPE should not be neglected. During the current and potential future pandemics, there is a need to limit liability on the part of the designers, makers, and users of open-source medical hardware. Moreover, the impact of existing regulatory issues, challenges, and possible disruptions on implications of 3DP technologies on healthcare should be discussed, extensively.

**Fig. 5.** Therapeutic applications of 3DP technologies to support the speedy control of infectious diseases [87].

**Fig. 6.** Market demands of the various protective gears (a) and the usefulness of the various 3DP technologies (b) [93].
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