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Letter to the Editor

Rapid detection of SARS-CoV-2 in saliva: can an endodontist take the lead in point-of-care COVID-19 testing?

Dear Editor,

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a highly contagious zoonotic virus that originated from Wuhan, China, in December 2019. The resulting disease known as COVID-19 was declared as a pandemic by WHO on 11 March 2020. As of 25 April 2020, more than 2.72 million cases have been reported across 213 countries and territories, resulting in more than 187 847 deaths (https://www.who.int/emergencies/diseases/novel-coronavirus-2019). The disease spreads through aerosol droplets and has an incubation period of 1–14 days. Research addressing crucial unknowns regarding its clinical severity, the extent of transmission and treatment options is going on all over the world since the inception of the disease. The primary response strategy includes limiting human-to-human transmission. To identify, isolate and care for patients early is the fundamental approach to achieve this goal. Hence, rapid and precise detection is vital in limiting community spread. Nasopharyngeal and oropharyngeal swabs are the advocated specimen modes for diagnostic testing (https://www.who.int/publications-detail/laboratory-testing-for-2019-novel-coronavirus-in-suspected-human-cases-20200117). However, the collection of these specimen types might induce coughing and hence carries the enhanced risk of transmission to the healthcare worker. Furthermore, the specimen collection causes patient discomfort and bleeding in thrombocytopenic patients (Chan *et al.* 2020). Sputum is a noninvasive lower respiratory tract specimen, but only 28% of the infected subjects could produce sputum for diagnostic evaluation (Huang *et al.* 2020). In this context, the role of saliva as a noninvasive specimen for early diagnosis and monitoring of SARS-CoV-2 looks promising. Affinity of SARS-CoV-2 to human angiotensin-converting enzyme-2 receptors present in salivary glands might result in the detection of SARS-CoV-2 in saliva. The virus can enter the saliva from upper and lower respiratory tracts as well as from the gingival crevicular fluid (Sabino-Silva *et al.* 2020). A recent study detected the live virus in the saliva of 91.7% of infected patients (To *et al.* 2020). Saliva from the deep throat is useful for early diagnosis since it is associated with high positive rates. The use of saliva would be advantageous because this would reduce patient discomfort and the transmission to healthcare workers during repeated sampling. The United States Food and Drug Administration gave emergency issued authorization on 13 April 2020 for a saliva-based collection device (https://www.fda.gov/media/136875/download). The device is then transported to the laboratory for the recommended testing, which may be time-consuming.

So far, several articles and letters have been published in leading dental journals regarding the implications of COVID-19 in clinical dental care. All of them focus on patient screening, clinical features, patient management and prevention of cross-contamination. Most of the articles recommend deferring elective dental treatment and concentrate on emergency care for the some time (Ather *et al.* 2020, Meng *et al.* 2020). Yu *et al.* (2020) studied on characteristics of dental emergencies during the COVID-19 epidemic in Wuhan, China. They found that only dental emergency cases were referred to the hospital during online health consultations. The authors also concluded that the majority (50.6%) of the dental emergencies were of endodontic origin in a COVID-19 affected area. These endodontic emergencies include symptomatic irreversible pulpitis, symptomatic apical periodontitis, acute apical abscess and traumatic dental injuries. Endodontists are on the front line to address such a crisis and to prevent distressed patients from attending hospital emergency rooms during this pandemic. They are more at risk than other health workers since most of their work involves aerosol generation. Most cases might be asymptomatic carriers and should be tested beforehand. The current standard approach for screening COVID-19 requires a real-time reverse transcriptase polymerase chain reaction (rRT-PCR) test (https://www.who.int/publications-detail/laboratory-testing-for-2019-novel-coronavirus-in-suspected-human-cases-20200117). This approach relies on expensive facilities, well-trained staff, and is often time-consuming. For these reasons, an alternative, rapid, point-of-care (POC) and sensitive

COVID-19 diagnostic tool is desired that can be routinely used by endodontists utilizing saliva as a specimen before starting an emergency procedure. Several of the diagnostic tools reported in the literature are:

1. *Loop-mediated isothermal amplification (LAMP) tests*: Isothermal amplification techniques are performed at a specific temperature and do not require dedicated laboratory equipment in comparison with PCR. Reverse transcription LAMP (RT-LAMP) tests for SARS-CoV-2 have been proposed and developed by several laboratories (Lamb *et al.* 2020, Yan *et al.* 2020). The analysis can also be utilized on saliva samples. It involves DNA polymerase and four to six primers to bind to the target genome. After the addition of the sample, the amplified DNA is identified by turbidity, colour or fluorescence. The testing occurs in less than an hour. The level of detection can be 75 copies per microlitre. The drawbacks are the difficulty in optimizing primers and reaction conditions (Udugama *et al.* 2020).
2. *Antibody testing*: The presence of SARS-CoV-specific secretory immunoglobulin A in the saliva of immunized rat models has been previously reported (Lu *et al.* 2010). Sabino-Silva *et al.* (2020) proposed a salivary diagnosis of COVID-19 using specific antibodies to the SARS-CoV-2 virus. Limitations of this test include possible cross-reactivity of SARS-CoV-2 antibodies with those produced against other coronaviruses. Furthermore, this test is indicated for surveillance and not for early diagnosis.
3. *Microfluidic RT-PCR devices (Lab-on-a-chip)*: Microfluidic devices consist of a small-sized chip with micrometre-sized channels. The liquid samples are mixed and separated in the chip using an electrokinetic, capillary, vacuum or other forces. The chip has microheater, microchannel and microelectrodes. All the steps, like cell lysis, DNA extraction and PCR amplification, can be integrated on a single microchip (Zhu *et al.* 2020). The advantages of these devices include small specimen volume, fast detection and incorporation of the gold standard test (PCR) for SARS-CoV-2 in a portable miniature form (Udugama *et al.* 2020).

All the methods, as mentioned above, need further research for their sensitivity and validity to be used with a salivary specimen. If approved, it might provide an opportunity to enable salivary virus detection in an endodontic facility without a requirement for complex diagnostic infrastructure. The chair-side test would help in reducing the waiting period and allow immediate intervention. Furthermore, the negative test patients can be treated routinely once the emergency restrictions are over. The use of these tests by an endodontist is proposed as a POC testing method. Though the scope of the profession remains an obstacle, unprecedented shared efforts are required to respond to this global public health crisis named COVID-19. Desperate times breed desperate measures. It is up to us.

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