



Emerging COVID-19 diagnostics in context—what about testing saliva?

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Nucleic acid tests (NATs), specifically polymerase chain reaction (PCR)-based detection of viral pathogens had significantly contributed to the diagnosis, monitoring and management of patients in the past viral outbreaks, for example, the SARS epidemic and H1N1 2009 pandemic more a decade ago. Molecular diagnosis of the SARS-CoV-2 has also heavily relied on reverse-transcription PCR (RT-PCR) assays since its outbreak in early 2020. In between the past SARS-CoV and the current SARS-CoV-2 outbreaks, significant improvements in viral diagnostics such as automated sample-to-result platforms with enhanced throughput and point-of-care molecular devices have been achieved. Although these advancements contribute to the ease of laboratory operations and rapid turn-around time, the current laboratory testing of SARS-CoV-2 is still largely subject to the bottleneck of acquisition of respiratory samples during this unprecedented global crisis.

In the clinical setting, nasopharyngeal (NP) swab is the current gold-standard specimen type for SARS-CoV-2 detection. This apparently “invasive” sampling method is associated with a few downsides which hinder it from being scaled up for asymptomatic carrier screening (1). There have been several promising studies (1-4) utilizing saliva as diagnostic or screening specimens. Evidence suggests saliva as a reliable specimen type in which SARS-CoV-2 is detectable in symptomatic patients (1,2) and asymptomatic carriers (3). Saliva testing is recommended to overcome the obstacles to COVID-19 mass testing (5) of which the

importance and urgency are apparent in the midst of this ongoing pandemic. Self-collection of saliva removes the need for healthcare workers to swab the patients hence also eliminates their risk of exposure to the virus and reduces usage of personal protective equipment. It also offers an advantage in comparison to NP swab that it is non-invasive. Saliva was recently demonstrated to possess high sensitivity and specificity comparable to those of NP swab for mass screening in both contact tracing and airport quarantine cohorts (4). Pooling of saliva could scale up the testing capacity (1). Saliva was also shown to be comparable to NP swab for inpatients (6). With the time and cost associated with the collection of saliva only half of those of NP swab (7), saliva appears to offer a more economical testing mode for respiratory viruses. There are currently more than a dozen of different saliva COVID-19 RT-PCR kits with emergency use authorization by Food and Drug Administration (8), and some of them are designed for home collection. With the new waves of SARS-CoV-2 infections in many countries, there is an urgent need to adopt innovative tools and strategies in order to curb the pandemic. Emerging diagnostic innovations validated saliva in parallel with paired NP swab (9) again illustrating that saliva could potentially be a game-changer in SARS-CoV-2 diagnosis. Although some studies showed promising results, it must also be underscored that not all studies had proven that saliva is comparable to NP swabs. Chong *et al.* concluded saliva is not a useful specimen for diagnosing COVID-19 in children due to poor sensitivity compared to paired NP swab (10).

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NAT performances may vary for deep throat and oral saliva, and this highlights the importance of a consistent collection procedure. Therefore, molecular diagnostic laboratories have to consider the patient population they serve and the intended sensitivity level, and balance these factors against the ease of obtaining the saliva samples. In view of these, laboratories must carefully evaluate the NAT performance on saliva for clinical use.

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