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Saliva as an Alternate Specimen Source for Detection of SARS-CoV-2 in Symptomatic Patients Using Cepheid Xpert Xpress SARS-CoV-2

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Running Title: Saliva as a source for Xpert Xpress SARS-CoV-2

Among the many facets of the SARS-CoV-2 pandemic is the unprecedented pressure it has placed on different points of the supply chain for hospital systems worldwide such as collection devices for the diagnosis of COVID-19. The emergency use authorization of most of the commonly used platforms for SARS-CoV-2 testing is approved for nasopharyngeal swab (NPS) specimens. However, with the increasing need for alternative sources due to the NPS shortage, our institution sought to validate saliva specimens for diagnosis of COVID-19 using the Cepheid Xpert Xpress SARS-CoV-2 (Sunnyvale, CA) PCR test. The Xpert SARS-CoV-2 assay is a sample to answer real-time RT-PCR test with a run time of approximately 30-51 minutes[1]. There are two targets, E and N2, where detection of both targets or N2 alone is considered positive and detection of E alone is considered presumptive positive.

We compared NPS using 3 mL universal transport media (UTM) (Becton, Dickinson and Company, Franklin Lakes, NJ) with unpreserved saliva samples collected in the ED (Emergency Department) and from in-patients in a COVID positive hospital unit. The specimens were collected prospectively in the ED, when a patient with suspected COVID-19 was being investigated following institutional and national guidelines for testing[2] or randomly in the hospital COVID unit from patients not requiring mechanical ventilation. Education to the ED nursing staff and the nurses on the COVID unit was disseminated to encourage saliva, not sputum collection. Also, it was highly recommended that patients not have any food, drink, tobacco or gum for 30 minutes prior to collection. Saliva was collected in sterile urine cups or sterile 50 mL conical tubes. Five mL of saliva was requested; however, specimens were considered acceptable if approximately 1 mL saliva was submitted. Once specimens were

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collected, they were labeled with a demographic label, double-bagged and submitted to the laboratory through the pneumatic tube system. The liquid, non-viscous components of each specimen were drawn into the disposable pipettes (300 µl) issued with Xpert SARS-CoV-2 cartridges and directly inoculated and run according to the manufacturer's instructions[1]. The NPS were collected in the standard fashion and, similarly, testing was performed according to the manufacturer's instructions. All NPS samples were tested on demand. The saliva samples were held at 2-8^{o}C for up to 12 hours prior to testing (validation of saliva was performed on first shift only).

A total of 156 paired NPS and saliva specimens were tested. The overall positivity was 50/156 (32.1%); the average age was 47.8 years old with a M/F ratio of 90/66. The community rate of positivity during the week of collection was 11.1%[3]. 153/156 (98% [94.48-99.60%, 95% Confidence Interval (CI)]) samples were in overall agreement. 47/49 samples were positive in saliva when compared to the NPS resulting in a positive percent agreement of 96% (86.02-99.5%, 95% CI). 105/106 samples had a negative saliva and NPS. A single sample demonstrated detectable levels of SARS-CoV-2 nucleic acid in the saliva, but the NPS was negative (1/106) resulting in a negative percent agreement of 99% (94.86-99.98%, 95% CI). The average cycle threshold values are summarized and compared in Table 1.

We conclude that saliva is an acceptable alternative source for detecting SARS-CoV-2 nucleic acid. Another advantage to saliva versus NPS is that the process to collect saliva is non-invasive and a patient, with education and coaching, could self-collect the specimen. These differences could reduce the risk to healthcare workers, decrease personal protective equipment usage, and provide less discomfort to patients

during collection. Furthermore, an important pre-analytical variable for SARS-CoV-2 testing is proper nasopharyngeal collection which may have been a contributing factor for the discrepant saliva positive/nasopharyngeal swab negative sample. Because saliva has excellent agreement as compared to NPS in UTM, saliva could potentially be used for diagnosis of COVID-19 in symptomatic patients using the Cepheid Xpert Xpress SARS-CoV-2 PCR test.

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References:

1) Cepheid Xpert Xpress SARS-CoV-2 Instructions for Use. 302-3562, Rev C, April 2020.
2) Centers for Disease Control Clinical Criteria for COVID testing: https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-criteria.html
3) Dallas County Health and Human Services 2019 Novel Coronavirus (COVID-19) Summary. https://www.dallascounty.org/Assets/uploads/docs/hhs/2019-nCoV/COVID-19%20DCHHS%20Summary_050520.pdf

Table 1: Average cycle threshold values for targets E and N2 in nasopharyngeal and saliva specimens (n = 50) from Xpert Xpress SARS-CoV-2 PCR assay.

	E	Ct Range	N2	Ct Range
Nasopharyngeal	23.83 ± 7.78	0-37.5	26.70 ± 7.61	0-42.2
Saliva	26.10 ± 11.20	0-41.1	30.40 ± 9.67	0-41.4
P value	0.21		0.73	

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