Taylor & Francis
Taylor & Francis Group

## ORIGINAL RESEARCH

Check for updates

# Performance comparison of the Cobas® Liat® and Cepheid® GeneXpert® systems on SARS-CoV-2 detection in nasopharyngeal swab and posterior oropharyngeal saliva

Hin Fung Tsang[a,b,*], Wai Ming Stanley Leung[*], Lawrence Wing Chi Chan[b], William Chi Shing Cho [ID][c] and Sze Chuen Cesar Wong[b]

[a]Department of Clinical Laboratory and Pathology, Hong Kong Adventist Hospital, Hong Kong Special Administrative Region; [b]Department of Health Technology and Informatics, Hong Kong Polytechnic University, Hong Kong Special Administrative Region; [c]Department of Clinical Oncology, Queen Elizabeth Hospital, Hong Kong Special Administrative Region

**ABSTRACT**

**Background**: Nucleic acid amplification tests (NAATs) based methods such as real-time reverse transcription polymerase-chain reaction (real-time RT-PCR) are the gold standard for diagnosis of current infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The cobas® Liat® and cepheid® GeneXpert® systems are two rapid real-time RT-PCR platforms offering rapid, specimen-to-answer detection of SARS-CoV-2.

**Research design and methods**: In this study, we compared the performance of these two systems on SARS-CoV-2 detection in 9 nasopharyngeal swab (NPS) and 70 posterior oropharyngeal saliva specimens collected from 79 patients suspected of SARS-CoV-2 infection between August 2020 and March 2021.

**Results**: The Positive Percent Agreement (PPA), Negative Percent Agreement (NPA) and overall Percent Agreement (OPA) between cepheid® Xpress SARS-CoV-2 assay and cobas® Liat® SARS-CoV-2 & Influenza A/B assay were found to be 100%. We demonstrated an excellent overall test concordance of the Liat® SARS-CoV-2 & Influenza A/B assay and Xpress SARS-CoV-2 assay. The small sample size of SARS-CoV-2 positive and weak-positive specimens is the inherent limitation of this study.

**Conclusions**: The performance of the cobas® Liat® SARS-CoV-2 & Influenza A/B assay is equivalent to the cepheid® Xpress SARS-CoV-2 assay for SARS-CoV-2 detection using NPS and posterior oropharyngeal saliva.

## 1. Introduction

The main mode of transmission of Coronavirus Disease-2019 (COVID-19) is by respiratory droplets through close contact among people. Respiratory droplets with viable SARS-CoV-2 can be sneezed and coughed out by infected individuals [1–4]. These droplets can enter the lungs via inhalation or deposited on the mucous membranes of the nose or mouth, and infect people nearby. Environmental contamination is another way to spread the virus indirectly through fomites. Respiratory secretions or droplets with viable SARS-CoV-2 expelled by infected individuals can contaminate surfaces and objects. If a non-infected person touches the contaminated surfaces and then his/her own eyes, mouth and nose, respiratory secretions or droplets with viable SARS-CoV-2 can reach the mouth, nose or eyes of a susceptible person and it may result in infection. This is one of the possible reasons associated with nosocomial spread and super-spreading events [4,5].

The median incubation period of COVID-19 was estimated to be 5.1 days [6] whereas the mean serial interval of COVID-19 was estimated to be 3.96 days [7–13]. The estimated mean serial interval of COVID-19 was found to be shorter than the

mean incubation period, suggesting pre-symptomatic transmission is likely to take place [7,8]. Symptomatic people are the source of COVID-19 whereas those asymptomatic people are the hidden sources in the community [9]. Currently, no effective treatment strategies can act specifically against COVID-19 and the treatment guidelines for COVID-19 vary among countries. Therefore, in addition to public health measures such as maintaining good personal hygiene, wearing mask and maintaining an interpersonal distance of at least 2 meters, early and rapid detection of both symptomatic and asymptomatic infected people, early isolation as well as early treatment are significant to cut off the spread of the virus and the rebound of positive cases in the community.

Nucleic acid amplification tests (NAATs) based methods such as real-time reverse transcription polymerase chain reaction (real-time RT-PCR) are considered as the gold standard for diagnosis of current infection with SARS-CoV-2 [14]. The cobas® Liat® and cepheid® GeneXpert® systems are two rapid real-time PCR platforms offering rapid, specimen-to-answer detection of SARS-CoV-2 in 20 minutes and 50 minutes respectively. Cepheid® Xpress SARS-CoV-2 assay detects the

---

[*]These authors contributed equally to this work.

presence of SARS-CoV-2 by detecting the N2 region of SARS-CoV-2 specific nucleocapsid (N) gene and pan-sarbecovirus envelope (E) gene. Cobas® Liat® SARS-CoV-2 & Influenza A/B assay detects the presence of SARS-CoV-2 by detecting SARS-CoV-2 specific N gene and open reading frame (ORF) 1 a/b non-structural region of the virus. Upper respiratory specimens such as nasopharyngeal swab (NPS), oropharyngeal and nasopharyngeal wash/aspirate or nasal aspirate are suitable for screening asymptomatic patients whereas lower respiratory specimens such as sputum, lower respiratory tract aspirate and bronchoalveolar lavage are recommended for symptomatic patients or patients with productive cough. In Hong Kong, NPS and posterior oropharyngeal saliva are two widely used specimen types for SARS-CoV-2 detection [14].

The purpose of this study is to compare the performance of the cobas® Liat® and cepheid® GeneXpert® Systems on SARS-CoV-2 detection in the two widely used specimen types in Hong Kong, NPS and posterior oropharyngeal saliva. This is the first study that compares in parallel the performance of the above two systems on SARS-CoV-2 detection in NPS and posterior oropharyngeal saliva.

## 2. Patients and methods

NPS and posterior oropharyngeal saliva were collected from 79 symptomatic and asymptomatic patients suspected of SARS-CoV-2 infection (9 NPS and 70 saliva) between August 2020 and March 2021 at Hong Kong Adventist Hospital in Hong Kong. NPS samples were collected in viral transport medium (VTM) by nurses for the patients who failed to collect posterior oropharyngeal saliva. As for posterior oropharyngeal saliva, patients were instructed to expectorate saliva into a sterile container. No food or drink, mouthwash and brushing teeth within 2 hours before specimen collection. From the specimen collected, 300 uL of saliva was added to 1 mL of VTM. All specimens were tested on the day of collection using both cobas® Liat® SARS-CoV-2 & Influenza A/B assay (Roche Molecular Systems, Inc., Pleasanton, CA) and cepheid® Xpress SARS-CoV-2 assay (Cepheid, Sunnyvale, CA). The mixture of saliva and VTM was added to the test kit, on which the assay was performed according to manufacturer instruction. The cycle threshold (Ct) values of specimens with positive PCR were obtained from the cobas® Liat® and cepheid® GeneXpert® systems. The cepheid® Xpress SARS-CoV-2 assay gives positive results when a signal of N2 gene or signals of both N2 and E genes have a Ct within the valid range (Ct <45) and the endpoint above the minimum setting. A presumptive positive result is given when only a signal of E gene has been detected. The cobas® Liat® SARS-CoV-2 & Influenza A/B assay gives positive results when either or both target genes (ORF1a/b and N gene) of SARS-CoV-2 have been detected.

## 3. Results

From this study, Table 1 shows the comparison of cepheid® Xpress SARS-CoV-2 assay and cobas® Liat® SARS-CoV-2 & Influenza A/B assay. Of the 79 specimens tested (9 NPS and 70 saliva), 34 (43.0%) were SARS-CoV-2 positive (Mean Ct value: 27.1 ± 6.8 obtained by the N2 gene of cepheid®

**Table 1.** Comparison of Cepheid Xpress SARS-CoV-2 assay and Cobas Liat SARS-CoV-2 & influenza A/B assay.

| | | Cepheid Xpress SARS-CoV-2 assay results, n | | |
| --- | --- | --- | --- | --- |
| | | Positive | Negative | Total |
| Cobas Liat SARS-CoV-2 & Influenza A/B assay results, n | Positive (NPS) | 7 | 0 | 7 |
| | Positive (Saliva) | 27 | 0 | 27 |
| | Negative (NPS) | 0 | 2 | 2 |
| | Negative (Saliva) | 0 | 43 | 43 |
| | Overall | 34 | 45 | 79 |
| Positive Percent Agreement (PPA) (95% CI) | | 100% (97.7–100%) | | |
| Negative Percent Agreement (NPA) (95% CI) | | 100% (97.7–100%) | | |
| Overall Percent Agreement (OPA) (95% CI) | | 100% (97.7–100%) | | |

**Table 2.** Cycle threshold (Ct) values of positive specimens obtained by Cepheid® Xpress SARS-CoV-2 assay and Cobas® Liat® SARS-CoV-2 & influenza A/B assay.

| Specimen | Specimen type | Cepheid® Xpress SARS-CoV-2 assay | | Cobas® Liat® SARS-CoV-2 & Influenza A/B assay |
| --- | --- | --- | --- | --- |
| | | E gene | N2 gene | |
| 1 | Saliva | 25.0 | 28.3 | 23.5 |
| 2 | NPS | 16.9 | 19.2 | 15.4 |
| 3 | Saliva | 27.7 | 29.9 | 23.2 |
| 4 | NPS | 17.2 | 18.8 | 13.4 |
| 5 | Saliva | 20.3 | 21.8 | 16.0 |
| 6 | Saliva | 29.4 | 32.2 | 30.2 |
| 7 | Saliva | 18.2 | 20.6 | 16.4 |
| 8 | Saliva | 26.4 | 28.6 | 24.2 |
| 9 | Saliva | 17.4 | 19.9 | 15.9 |
| 10 | Saliva | 20.3 | 22.6 | 21.0 |
| 11 | Saliva | 0.0 | 40.6 | 33.5 |
| 12 | NPS | 35.9 | 39.2 | 29.4 |
| 13 | NPS | 33.4 | 38.2 | 34.6 |
| 14 | Saliva | 16.1 | 18.6 | 12.1 |
| 15 | Saliva | 20.1 | 21.8 | 17.8 |
| 16 | NPS | 20.3 | 22.7 | 19.7 |
| 17 | NPS | 23.7 | 25.9 | 20.1 |
| 18 | Saliva | 26.0 | 28.1 | 21.5 |
| 19 | Saliva | 27.4 | 30.2 | 32.9 |
| 20 | Saliva | 32.3 | 36.1 | 28.1 |
| 21 | Saliva | 28.3 | 30.5 | 36.6 |
| 22 | Saliva | 25.3 | 27.7 | 24.5 |
| 23 | Saliva | 24.6 | 27.7 | 24.4 |
| 24 | NPS | 20.2 | 22.3 | 17.8 |
| 25 | Saliva | 23.9 | 25.9 | 21.3 |
| 26 | Saliva | 24.9 | 27.2 | 22.8 |
| 27 | Saliva | 18.1 | 20.8 | 11.3 |
| 28 | Saliva | 26.2 | 28.5 | 22.8 |
| 29 | Saliva | 0.0 | 40.9 | 32.9 |
| 30 | Saliva | 18.3 | 20.5 | 18.5 |
| 31 | Saliva | 27.9 | 30.6 | 25.5 |
| 32 | Saliva | 29.4 | 32.3 | 27.1 |
| 33 | Saliva | 20.8 | 22.9 | 15.8 |
| 34 | Saliva | 22.6 | 25.2 | 18.9 |

NPS: nasopharyngeal swab.

Xpress SARS-CoV-2 assay) and 45 (57.0%) were SARS-CoV-2 negative. Table 2 shows the Ct values of the positive specimens obtained by cepheid® Xpress SARS-CoV-2 assay and cobas® Liat® SARS-CoV-2 & Influenza A/B assay. Positive specimens were sent to Public Health Laboratory Services Branch, Center for Health Protection, Department of Health, Hong Kong for confirmation by RT-PCR. The Positive Percent

Table 3. The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy of Cepheid Xpress SARS-CoV-2 assay and Cobas Liat SARS-CoV-2 & Influenza A/B assay on SARS-CoV-2 detection.

| | | Positive specimens | Negative specimens | Sensitivity | Specificity | PPV | NPV | Accuracy |
|---|---|---|---|---|---|---|---|---|
| Cobas Liat SARS-CoV-2 & Influenza A/B assay results | Test positive | 34[a] | 0[b] | 100% | 100% | 100% | 100% | 100% |
| | Test negative | 0[c] | 45[d] | | | | | |
| Cepheid Xpress SARS-CoV-2 assay results | Test positive | 34[a] | 0[b] | 100% | 100% | 100% | 100% | 100% |
| | Test negative | 0[c] | 45[d] | | | | | |

Sensitivity = [a/(a + c)] x 100%; Specificity = [d/(b + d)] x 100%; PPV = [a/(a + b)] x 100%; NPV; NPV = [d/(c + d)] x 100%; accuracy = [(a + d)/(a + b + c + d)] x 100%.

Agreement (PPA), Negative Percent Agreement (NPA) and overall Percent Agreement (OPA) between cepheid® Xpress SARS-CoV-2 assay and cobas® Liat® SARS-CoV-2 & Influenza A/B assay were found to be 100%. Both assays demonstrated sensitivities of 100% in this study. The positive predictive value (PPV), negative predictive value (NPV) and accuracy of both assays were found to be 100% (Table 3). Assay specificity was examined using another cohort of 27 specimens. Neither assays demonstrated cross-reactivity from other coronaviruses (229E, HKU1, NL63 and OC43) and respiratory pathogens (influenza A virus, rhinovirus/enterovirus, bocavirus and *Staphylococcus aureus*).

## 4. Discussion

The purpose of this study is to compare the performance of the cobas® Liat® and cepheid® GeneXpert® Systems on SARS-CoV-2 detection in NPS and posterior oropharyngeal saliva. This is the first study that compares in parallel the performance of the above two systems on SARS-CoV-2 detection in NPS and posterior oropharyngeal saliva, which are the two widely used specimen types in Hong Kong for SARS-CoV-2 screening. From this study, we demonstrated an excellent overall test concordance of the cobas® Liat® SARS-CoV-2 & Influenza A/B assay and cepheid® Xpress SARS-CoV-2 assay. The performance of the cobas® Liat® SARS-CoV-2 & Influenza A/B assay is equivalent to the cepheid® Xpress SARS-CoV-2 assay for SARS-CoV-2 detection using NPS and posterior oropharyngeal saliva. The PPA, NPA and OPA between the two assays were all found to be 100%. However, this study has its inherent limitations because of the small sample size of SARS-CoV-2 positive and weak-positive specimens. From the data provided by the manufacturers, the limit of detection (LoD) of SARS-CoV-2 by cobas® Liat® SARS-CoV-2 & Influenza A/B assay was 12 copies/mL, whereas the LoD of SARS-CoV-2 by cepheid® Xpress SARS-CoV-2 assay was 250 copies/mL. Compared to cepheid® Xpress SARS-CoV-2 assay, cobas® Liat® SARS-CoV-2 & Influenza A/B assay offers an even shorter turnaround time (20 minutes) of rapid diagnosis and differentiation of SARS-CoV-2 and influenza infections. It is particularly suitable for small- to medium-sized diagnostic laboratories or international airport to perform rapid and early SARS-CoV-2 detection to contain the spread of infection both within and outside the healthcare setting in this challenging time.

From this study, we also demonstrated the protocol and the use of posterior oropharyngeal saliva as an alternative specimen type for the detection of SARS-CoV-2 by cobas® Liat® SARS-CoV-2 & Influenza A/B assay and cepheid® Xpress SARS-CoV-2 assay. NPS and posterior oropharyngeal saliva are two widely used specimen types for SARS-CoV-2 detection in Hong Kong. Collecting posterior oropharyngeal saliva over NPS for SARS-CoV-2 detection has several advantages. First, posterior oropharyngeal saliva can be collected by the patients after receiving simple instruction whereas NPS can only be collected by a trained healthcare personnel. Collecting saliva can reduce the workload of healthcare personnel and reduce the delay in specimen collection [15]. Second, collecting saliva rather than NPS can avoid patient discomfort. It is particularly suitable for patients for whom collecting NPS is not recommended, such as those with severe bleeding tendency [15]. Third, the procedure for collecting NPS may generate aerosol that would pose significant risk to the healthcare workers and other people nearby. Appropriate infection control precautions including the use of N95 respirator or equivalent, gloves, face shield, eye protection and gown are required. The procedure for processing the specimens should also be performed in a negative pressure isolation room. However, collection of saliva does not require special infection control precautions and the procedure can be performed in any clinical setting with standard precautions [15]. One of the technical challenges when testing oropharyngeal saliva is the presence of mucus and its high viscosity. Homogenization with VTM is required and non-viscous part of the specimens should be used for testing.

## 5. Conclusions

From this study, we demonstrated an excellent overall test concordance of the cobas® Liat® SARS-CoV-2 & Influenza A/B assay and cepheid® Xpress SARS-CoV-2 assay. The performance of the cobas® Liat® SARS-CoV-2 & Influenza A/B assay is equivalent to the cepheid® Xpress SARS-CoV-2 assay for SARS-CoV-2 detection using NPS and posterior oropharyngeal saliva.

## Declaration of interest

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes

employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

## Reviewer disclosures

Peer reviewers on this manuscript have no relevant financial or other relationships to disclose.

## ORCID

William Chi Shing Cho   http://orcid.org/0000-0003-4174-4586

## References

Papers of special note have been highlighted as either of interest (•) or of considerable interest (••) to readers.

1. Tsang HF, Chan LWC, Cho WCS, et al. An update on COVID-19 pandemic: the epidemiology, pathogenesis, prevention and treatment strategies. Expert Rev Anti Infect Ther. 2020;1–12. DOI:10.1080/14787210.2021.1863146.
   •• **This review summarizes the epidemiology, pathogenesis, prevention and treatment strategies of COVID-19.**
2. Zhang JJ, Dong X, Cao YY, et al. Clinical characteristics of 140 patients infected by SARS-CoV-2 in Wuhan, China. Allergy. 2020;75:1730–1741.
3. Spinato G, Fabbris C, Poiesel J, et al. Alterations in smell or taste in mildly symptomatic outpatients with SARS-CoV-2 infection. JAMA. 2020;323:2089–2091.
4. Van Doremalen N, Bushmaker T, Morris DH, et al. Aerosol and surface stability of SARS-CoV-2 as Compared with SARS-CoV-1. N Engl J Med. 2020;382:1564–1567.
5. Centers for Disease Control and Prevention. Coronavirus Disease 2019. Laboratories; [cited 2020 Apr 25]. Available from: https://www.cdc.gov/coronavirus/2019-nCoV/lab/index.html
6. Lauer SA, Grantz KH, Bi Q, et al. The incubation period of coronavirus disease 2019 (COVID-19) from publicly reported confirmed cases: estimation and application. Ann Intern Med. 2020;172:577–582.
7. Du Z, Xu X, Wang Y, et al. Serial interval of COVID-19 among publicly reported confirmed cases. Emerg Infect Dis. 2020;26(6):1341–1343.
8. Nishiura H, Linton NM, Akhmetzhanov AR. Serial interval of novel coronavirus (COVID-19) infections. Int J Infect Dis. 2020;93:284–286.
9. Rothe C, Schunk M, Sothmann P, et al. Transmission of 2019-nCoV infection from an asymptomatic contact in Germany. N Engl J Med. 2020;382:970–971.
10. Li H, Liu SM, Yu XH, et al. Coronavirus disease 2019 (COVID-19): current status and future perspectives. Int J Antimicrob Agents. 2020;55:105951.
11. Liu Y, Gayle AA, Wilder-Smith A, et al. The reproductive number of COVID-19 is higher compared to SARS coronavirus. J Travel Med. 2020;27(2):taaa021.
12. Zhai P, Ding Y, Wu X, et al. The epidemiology, diagnosis and treatment of COVID-19. Int J Antimicrob Agents. 2020;105955. DOI:10.1016/j.ijantimicag.2020.105955
13. Zhang S, Diao MY, Yu W, et al. Estimation of the reproductive number of novel coronavirus (COVID-19) and the probable outbreak size on the Diamond Princess cruise ship: a data-driven analysis. Int J Infect Dis. 2020;93:201–204.
14. Wu SYW, Yau HS, Yu MY, et al. The diagnostic methods in the COVID-19 pandemic, today and in the future. Expert Rev Mol Diagn. 2020;20(9):985–993.
   •• **This review summarizes the current and future diagnostic methods of COVID-19.**
15. To KKW, Lu L, Yip CCY, et al. Additional molecular testing of saliva specimens improves the detection of respiratory viruses. Emerg Microbes Infect. 2017;6:1–7.
   • **This article describes the application of saliva as an alternative sample to the detection of respiratory viruses.**