Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Mini-evaluation of the Lyra SARS-CoV-2 assay to detect Omicron BA.1 and BA.2 in nasopharyngeal swabs

As of this writing, there are more than 400 million COVID-19 cases and nearly 6 million deaths (https://coronavirus.jhu.edu/map.html), making this infectious disease a significant challenge we face at the present time. Early and accurate diagnosis of COVID-19 is important to improve patient care outcomes and reduce spread of SARS-CoV-2. After two years into the COVID-19 pandemic, we have had more testing options to detect SARS-CoV-2 such as nucleic acid, antigen or antibody-based tests; however, their clinical performance characteristics vary [1,2]. Among many NAAT tests, RT-PCR is still the gold standard for testing SARS-CoV-2 with the high sensitivity and specificity [3]. While diagnostic RT-PCR testing is an important tool, there have been challenges in scaling up testing due to increasing supply shortages and limitations in personnel [4]. This situation is getting worse due to the significant surge of SARS-CoV-2 Omicron variant worldwide. Of note, Omicron is spreading quickly in many regions, even where there have high COVID-19 vaccination rates or high levels of immunity in the population [5,6]. To address limitations in our laboratory capacity for SARS-CoV-2 testing, we evaluated the Lyra SARS-CoV-2 assay to detect SARS-CoV-2 including Omicron BA.1 and BA.2 in upper respiratory tract infections.

The Lyra SARS-CoV-2 assay (Quidel, San Diego, CA, USA) is a real-time RT-PCR assay intended for the in vitro qualitative detection of SARS-CoV-2 from extracted viral RNA. The Lyra SARS-CoV-2 assay targets the non-structural polyprotein of SARS-CoV-2. The Lyra SARS-CoV-2 assay received FDA emergency use authorization for nasal and nasopharyngeal swabs collected in viral transport medium (https://www.quidel.com/molecular-diagnostics/lyra-sars-cov-2-assay). According to the American Society for Microbiology Clinical and Public Health Microbiology Committee, the primary materials required to conduct a verification procedure for commercial EUA tests include, at a minimum, 10 positive and 10 negative specimens, which can be commercially available reference material or residual patient specimens [7]. Therefore, a total of 20 nasal and nasopharyngeal swab specimens (10 residual clinical SARS-CoV-2 negatives and 10 residual clinical SARS-CoV-2 positives) were used for this evaluation study. These specimens were collected from patients with suspected COVID-19. All 10 positives were previously SARS-CoV-2 tested by the Cepheid Xpert Xpress SARS-CoV-2/Flu/RSV test (Cepheid, Sunnyvale, CA, USA) and all 10 negatives by the Hologic Aptima SARS-CoV-2 test (Hologic, Bedford, MA, USA). The Ct values of the positives as determined by Cepheid Xpress testing ranged from 12.2 to 36.4 (Table 1). The specimens were extracted using the EasyMag (bioMérieux, Marcy-l'Etoile, France). The specimen input and elution output volumes were 180 μl and 50 μl, respectively. The Lyra SARS-CoV-2 kit provided a convenient, ready-to-use master mix formulation. The total RT-PCR reaction volume was 20 μl. The Lyra SARS-CoV-2 assay was run on the Applied Biosystems 7500 Fast Dx Real-Time PCR System (ThermoFisher, Waltham, MA, USA) with the thermal cycling condition according to the manufacturer's instructions. The results from the Lyra SARS-CoV-2 assay were compared to the original results from the Cepheid Xpert Xpress SARS-CoV-2/Flu/RSV test or the Hologic Aptima SARS-CoV-2 test, which served as the reference methods. We did not see any discordant results among them. In addition, there were no false positives or false negatives. Therefore, the sensitivity of the Lyra SARS-CoV-2 assay was 100% (10/10) and the specificity of the Lyra SARS-CoV-2 assay was 100% (10/10). An overall agreement between the Lyra SARS-CoV-2 assay and the reference methods was 100% (20/20). Precision analysis was also performed by testing 4 clinical specimens (2 negatives and 2 positives), which were selected from the above mentioned 20 clinical specimens, by three different technologists on three different days, and they had the same results as expected.

SARS-CoV-2 NAATs have been developed based on genomic information of SARS-CoV-2. As SARS-CoV-2 circulated globally, the viral genome continued to acquire new mutations. Due to a possible misdiagnosis due to mutations, these NAATs often target at least one conserved region, which is less susceptible to the effects of genetic variation [8]. The first case of the new SARS-CoV-2 Omicron Variant of Concern was discovered in South Africa in mid-November 2021 [9]. Later, the Omicron subvariants (known as BA.2 and BA.3) have emerged, and BA.2 is reported to have increased transmissibility compared to BA.1 [10]. In United States, Omicron is responsible for an unprecedented surge of patients in the fifth COVID-19 wave. According to the Lyra SARS-CoV-2 assay's package insert, the primers and fluorescent-labeled probes target a conserved region of the non-structural polyprotein of SARS-CoV-2. Therefore, the Lyra SARS-CoV-2 assay's performance is not affected by Omicron since this variant shows a large number of mutations widely distributed on the spike gene of SARS-CoV-2. However, it is important to make sure that the Lyra SARS-CoV-2 assay can detect Omicron in clinical specimens collected from patients with suspected COVID-19. Another set of 22 SARS-CoV-2 positive specimens, which included 21 Omicron BA.1 and 1 Omicron BA.2 determined by the RT-PCR Omicron BA.1 assay and next-generation sequencing in the previous studies [11,12], were tested by the Lyra SARS-CoV-2 assay; all of them were reported as detected.

The Lyra SARS-CoV-2 assay can be used to detect SARS-CoV-2 infection by the Omicron variants. We had 100% concordance of detection with Cepheid Xpress or Hologics Panther detections. We did not address the analytical sensitivity of the Lyra assay since its limit of detection was already determined as 800 copies/ml per the package insert and concordant with our other assays as determined during our in-house validation (data not shown), and we have no reason to believe that this analytical sensitivity is any different for the Omicron variants. To the best of our knowledge, this is the first study independently evaluating the performance the Lyra SARS-CoV-2 assay against the Omicron variant.

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Table 1
SARS-CoV-2 results for nasal and nasopharyngeal swab specimens by Lyra SARS-CoV-2 assay (Quidel, San Diego, CA, USA).

Specimen	Reference method	Result (CT value)	Lyra SARS-CoV-2
Nasopharyngeal swab	Cepheid SARS-CoV-2/Flu/RSV	Positive (12.2)	Positive
Nasopharyngeal swab	Cepheid SARS-CoV-2/Flu/RSV	Positive (14.3)	Positive
Nasopharyngeal swab	Cepheid SARS-CoV-2/Flu/RSV	Positive (18.3)	Positive
Nasopharyngeal swab	Cepheid SARS-CoV-2/Flu/RSV	Positive (21.4)	Positive
Nasopharyngeal swab	Cepheid SARS-CoV-2/Flu/RSV	Positive (21.8)	Positive
Nasopharyngeal swab	Cepheid SARS-CoV-2/Flu/RSV	Positive (24.5)	Positive
Nasopharyngeal swab	Cepheid SARS-CoV-2/Flu/RSV	Positive (31.4)	Positive
Nasopharyngeal swab	Cepheid SARS-CoV-2/Flu/RSV	Positive (31.5)	Positive
Nasopharyngeal swab	Cepheid SARS-CoV-2/Flu/RSV	Positive (32.6)	Positive
Nasopharyngeal swab	Cepheid SARS-CoV-2/Flu/RSV	Positive (34.6)	Positive
4 Nasal swabs	Hologic Aptima SARS-CoV-2	Negative	Negative
6 Nasopharyngeal swabs	Hologic Aptima SARS-CoV-2	Negative	Negative

from any commercial sources. The funders did not have input into study design, analysis, nor generation of this communication.

Ethical approval

All testing was performed as apart of routine clinical care and performed according to CLIA '88 regulations by appropriate personnel. The entire study was deemed to be a Quality Improvement initiative by the UPMC IRB and approved by the UPMC QI Review Board.

Declaration of Interest

The authors declare no competing financial interests.

CRediT authorship contribution statement

Tung Phan: Visualization, Writing – review & editing. **Stephanie Boes:** Methodology. **Melissa McCullough:** Methodology. **Jamie Gribschaw:** Methodology. **Alan Wells:** Visualization, Writing – review & editing.

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