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LETTER TO THE EDITOR

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Clinical evaluation of the Cue's COVID-19 diagnostic test to detect SARS-CoV-2 in the upper respiratory tract

1.1 | The study

Point-of-care testing (POCT) known as near-patient testing has a relatively lower cost and short turnaround time. It is obvious that a short turnaround time can potentially improve patient care and outcomes by providing quick access to test results, expediting medical diagnosis, and facilitating earlier and more rapid decisions on treatment.[1,2] Another benefit of POCT is that it can be performed by clinical staff without laboratory training. POCT can be done at a healthcare provider's office, outpatient clinic, emergency room, and healthcare nursing home.[3,4] More than 2 years into the COVID-19 pandemic, the pandemic phase of COVID-19 looks to be ending in many regions; however, several parts of the world are still experiencing health crisis due to a new variant emergence. Timely and widespread diagnostic testing for SARS-CoV-2 remains critical for patient care, and it is an essential part of a comprehensive COVID-19 control and preparedness strategy.[5,6] POCT has been in high demand for COVID-19, and one significant reason is that it helps to address the SARS-CoV-2 testing backlog in clinical laboratories.[7,8]

In the United States, the Cue's COVID-19 test (Cue Health Inc.) is a POCT under Emergency Use Authorized (EUA) by Food and Drug Administration. It is an isothermal nucleic acid amplification assay intended for the qualitative detection of nucleic acid from SARS-CoV-2 in direct anterior nasal swabs or in previously collected anterior nasal swabs in viral transport media. The test is run using the Cue health monitoring system known as the Cue cartridge reader, the Cue COVID-19 test cartridge, the Cue specimen wand, and the Cue health app, which is available at www.Cuehealth.com. The Cue COVID-19 test's primers amplify the nucleocapsid gene enabling the detection of SARS-CoV-2. When the user inserts the Cue nasal specimen wand into the cartridge, the test automatically begins. All the processing steps such as heating, mixing, amplification, and detection take place within the cartridge. Results are displayed directly on a connected mobile smart device in about 20 min via the Cue health app (https://www.cuehealth.com/products/how-cue-detects-covid-19/). Since the Cue's COVID-19 test is a fully integrated specimen-to-answer assay and its supply is currently available and accessible, we performed the clinical evaluation of the Cue's COVID-19 test to detect SARS-CoV-2 in the upper respiratory tract.

To assess clinical performance characteristics of the Cue's COVID-19 test, a total of 84 nasopharyngeal and nasal swabs in viral transport medium (67 residual clinical nasal negatives and 17 residual clinical nasopharyngeal positives) were tested using the Cue's COVID-19 test. These clinical specimens were previously SARS-CoV-2 tested by the Cepheid Xpert Xpress SARS-CoV-2/Flu/RSV test or the Hologic Aptima SARS-CoV-2 test. These two tests were considered as the standard tests available in our clinical laboratory, and which have been reported to have excellent analytical performance.[9,10] The invalid rate on the first attempt for the Cue's COVID-19 test was calculated to be 10.7% (9 of 84). While five specimens gave a valid result (one positive and four negatives) after retesting, four specimens remained double or triple invalid. These four specimens having the double or triple invalid result were excluded from all subsequent analyses and specimen counts. To verify the lower sensitivity of the Cue's COVID-19 test related to the cycle threshold (Ct) obtained by the Cepheid Xpress testing, we tested a series of the previously positive specimens with increasing Ct values ranging from 12.2 to 36.4 as shown in Table 1. It was found that 13 (76.5%) of 17 positives were correctly detected by the Cue's COVID-19 test. All the four false negatives had the high Ct values (>30.0), suggesting that the Cue's COVID-19 test has acceptable performance for strong and moderate positive specimens, but lacks sensitivity with low viral load specimens. Of note, we did not observe any false-positive results, and the Cue's COVID-19 test had a high negative agreement of 100% (63/63, excluding four invalid specimens). In comparison with the reference methods, the Cue's COVID-19 test demonstrated an overall concordance of 95.0% (76 of 80, excluding four invalid specimens).

The Cue's COVID-19 test is one of NAAT POCTs under EUA to detect SARS-CoV-2. To date, the Cue's COVID-19 test's performance data is very limited, and our keyword (Cue health and SARS-CoV-2 or COVID-19) search in PubMed identified only one paper.[11] Compared to the reference methods, Donato and colleagues reported a good overall concordance of 97.8%,[11] which was similar to our data (95.0%). In addition, their invalid rate seemed lower than ours (8.6% vs. 10.7%), and their false positive rate seemed higher than ours (1.7% vs. 0%), however, these discrepancies are minor. While this study group showed a good positive agreement (95.7%, 22 of 23) of the Cue's COVID-19 test,[11] our result was much lower (76.5%, 13 of 17). The false-negative result occurred in one specimen with a high Ct value (35.0), which was also seen in our evaluation. The substantial difference in the reported positive agreement between two studies could be explained by the different collection designs.

TABLE 1 SARS-CoV-2 results for nasal and nasopharyngeal swab specimens by Cue health.

Specimen	Reference (Ct value)	Cue health	Invalid
Nasopharyngeal swab	Positive (12.2)	Positive	
Nasopharyngeal swab	Positive (14.3)	Positive	
Nasopharyngeal swab	Positive (18.3)	Positive	
Nasopharyngeal swab	Positive (21.4)	Positive	
Nasopharyngeal swab	Positive (21.8)	Positive	
Nasopharyngeal swab	Positive (24.5)	Positive	
Nasopharyngeal swab	Positive (31.4)	Positive	
Nasopharyngeal swab	Positive (31.5)	Positive	
Nasopharyngeal swab	Positive (32.0)	Positive	
Nasopharyngeal swab	Positive (32.6)	Positive	
Nasopharyngeal swab	Positive (33.5)	Positive	One
Nasopharyngeal swab	Positive (34.6)	Positive	
Nasopharyngeal swab	Positive (36.4)	Positive	
Nasopharyngeal swab	Positive (30.5)	Negative	
Nasopharyngeal swab	Positive (33.7)	Negative	
Nasopharyngeal swab	Positive (34.5)	Negative	
Nasopharyngeal swab	Positive (35.3)	Negative	
59 Nasal swabs	Negative	Negative	
4 Nasal swabs	Negative	Negative	One
3 Nasal swabs	Negative	Invalid	Two
1 Nasal swab	Negative	Invalid	Three

Donato and colleagues performed the prospective study in the outpatient setting, and the Ct value or viral load of the positive specimens was random.[11] Our positive specimens were carefully selected to verify the lower sensitivity, and a majority of them (61.1%, 11 of 18) had high Ct values (>30.0). In our evaluation, the clinical performance of the Cue's COVID-19 test started to decline as the Ct values increased reflecting decreasing viral loads. This phenomenon was also observed in other rapid NAAT POCTs such as the ID NOW COVID-19 test which has the lower performance for specimens displaying the Ct value higher than 30.0.[12] Given the persistence of the SARS-CoV-2 testing backlog, low availability of testing supply, and shortage of licensed personnel in clinical laboratories, we need to migrate more testing capacity to the outpatient setting and the Cue's COVID-19 test is a good option.

AUTHOR CONTRIBUTIONS

Tung Phan and Alan Wells designed the study and wrote the manuscript. Zachary Cravener, Melissa McCullough, Ashley Mays, and Jamie Gribschaw managed the testing.

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CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

Data sharing not applicable to this article as no datasets were generated or analyzed during the current study. All relevant data are presented in the article.

ETHICS STATEMENT

All testing was performed as apart of routine clinical care and performed according to CLIA '88 regulations by the 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.

Tung Phan[1]
Zachary Cravener[2]
Melissa McCullough[2]
Ashley Mays[2]
Jamie Gribschaw[2]
Alan Wells[1]

[1]*Department of Pathology, University of Pittsburgh, Pittsburgh, Pennsylvania, USA*
[2]*Clinical Microbiology Laboratory, UPMC Hospital System, Pittsburgh, Pennsylvania, USA*

Correspondence
Tung Phan, Department of Pathology, University of Pittsburgh, Pittsburgh, PA 15213, USA.
Email: phantg@upmc.edu

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