Title: The Detection of SARS-CoV-2 using the Cepheid Xpert Xpress SARS-CoV-2 and Roche cobas SARS-CoV-2 Assays

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SARS-CoV-2, a novel coronavirus responsible for a December 2019 outbreak in Wuhan, China, causes a syndrome characterized by fever, cough, and dyspnea progressing to acute respiratory distress syndrome (1). SARS-CoV-2 quickly spread to other countries, with the new coronavirus 2019 (COVID-19) disease declared a pandemic in March 2020 (2-4). Rapid testing for SARS-CoV-2 is important for epidemiological tracking and institution of quarantine procedures (5). The clinical description of COVID-19 continues to evolve; with transmission by asymptomatic individuals reported (6-8), widespread testing is necessary.

Multiple RT-PCR assays have received Emergency Use Authorization from the US Food and Drug Administration. The Roche cobas SARS-CoV-2 assay is a qualitative test that detects the SARS-CoV-2-specific ORF1 and part of the E-gene conserved across sarbecoviruses, including SARS-CoV-2 (9). The Cepheid Xpert Xpress SARS-CoV-2 assay also detects the pan-sarbecovirus E-gene but detects the N2 region of the N-gene as its SARS-CoV-2-specific target (10). This report compares results from specimens tested with both assays.

Eight nasal and 95 nasopharyngeal specimens were collected from inpatients and ambulatory patients at the University of Chicago. Samples were tested using the Roche cobas SARS-CoV-2 assay on the cobas 6800 system (Roche Molecular Systems, Branchburg, NJ) and the Cepheid Xpert Xpress SARS-CoV-2 assay on the GeneXpert system (Cepheid, Sunnyvale, CA). Of these 103 specimens, 42 tested positive and 60 tested negative with both systems for agreement of 99%. Testing was repeated on the single specimen with discrepant results. For this specimen, the Roche assay was repeatedly negative for SARS-CoV-2. The initial Cepheid assay result was positive for SARS-CoV-2, though the cycle threshold (Ct) value for detection of the E-gene was

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0.0 (negative) and 42.0 (low positive) for the N-gene. Repeat Cepheid testing was negative for both targets. These results suggest that SARS-CoV-2 was present at a very low concentration, near the detection limit of the Cepheid assay.

For the 42 positive samples, Ct values for the E-gene ranged from 15.05 to 39.75 (mean 26.35, SD 6.69) for the Roche assay and 13.6 to 38.2 (mean 24.8, SD 7.1) for the Cepheid assay. Using Bland-Altman analysis to assess agreement, Ct values were lower on the Cepheid assay in 37 of 42 samples (mean difference -1.57, 95% limits of agreement -5.34, 2.20). This could be due to differences in primer sequences against the E-gene, reagents, or amplification conditions.

Limitations of this study include small sample size of SARS-CoV-2-positive specimens, as testing was limited to patients within our institution. The assays also detect different SARS-CoV-2-specific genes, which could lead to false-negative results if a mutation prevents primer binding. The Cepheid assay is a 45-minute random-access assay, with throughput dependent on number of instrument slots. The Roche platform is batch-based, accommodating 90 samples/run every 90 minutes. As each run requires up to three hours and 45 minutes, throughput is approximately 1 result/minute. Overall, the Cepheid Xpert Xpress SARS-CoV-2 and Roche cobas SARS-CoV-2 assays show excellent agreement (>99%), and their combined usage can be tailored to maximize SARS-CoV-2 testing.

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