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LETTER TO THE EDITOR

Test Agreement between Roche Cobas 6800 and Cepheid GeneXpert Xpress SARS-CoV-2 Assays at High Cycle Threshold Ranges

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The SARS-CoV-2 pandemic has changed the face of the globe and upended the daily lives of billions. In an effort to bring mass testing to as many as possible, multiple diagnostic tests, including molecular, antigen detection, and serological assays, have been rapidly developed. Under U.S. Food and Drug Administration (FDA) Emergency Use Authorization (EUA), several reverse transcription-PCR (RT-PCR) assays have reached U.S. laboratories, each with its own testing capacity and proprietary methods (1, 2). Multiple logistical challenges have required laboratories to validate and implement multiple platforms for testing, but data on positive percent agreement across platforms are limited. Our institution utilizes the Roche Cobas 6800 SARS-CoV-2 assay, the Cepheid GeneXpert Xpress SARS-CoV-2 assay, and a laboratory-developed test (LDT) based on a modified CDC protocol, but there is no gold standard for the diagnostic accuracy of these assays. Thus, our objective was to determine the degree of agreement between two tests by running the same samples across both platforms and comparing the cycle threshold (C_T) values (E target to E target) among samples with high (>30) C_T values, corresponding to lower viral loads. We collected 35 positive (positivity determined per assay instructions) nasopharyngeal samples with an E target C_T value of ≥30 on the Roche Cobas 6800 assay; those samples then underwent secondary testing on the Cepheid GeneXpert assay within 3 days of initial testing. Discrepancies were resolved using the LDT. All specimens were tested using each manufacturer's protocol. E target C_T values were compared by Bland-Altman analysis. Of 35 samples, 34 tested positive on both instruments. One sample tested positive on the Cobas 6800 assay ($C_T = 37.9$) and negative by the GeneXpert assay and was confirmed to be negative on the LDT. Among the positive samples, C_T values were similar between the two assays ($P = 0.06$). The values ranged from 30.1 to 37.9 (mean, 36.7 ± 1.88) on the Roche Cobas 6800 assay and 24.6 to 42.4 (mean, 32.8 ± 4.07) on the GeneXpert assay. Bland-Altman analysis revealed a bias of 0.33 ± 3.21 (mean difference of −1.59, 95% limits of agreement of −5.97 and 6.63), signifying close agreement between the 2 instruments with a high standard deviation (Fig. 1). Our findings corroborate recently published results which show close agreement between the Cobas 6800 and GeneXpert instruments, in particular, among samples with lower viral loads (3). Our in-house laboratory test determined that the limit of detection (LoD) of the Cobas 6800 assay is 100 copies/ml, and the LoD specified in the GeneXpert package insert is 250 copies/ml. This difference in LoD becomes significant at higher C_T values, where the negative bias becomes more pronounced (4, 5). Previous studies have shown that substantial viral loads can be detected around day 5 of infection and drop at

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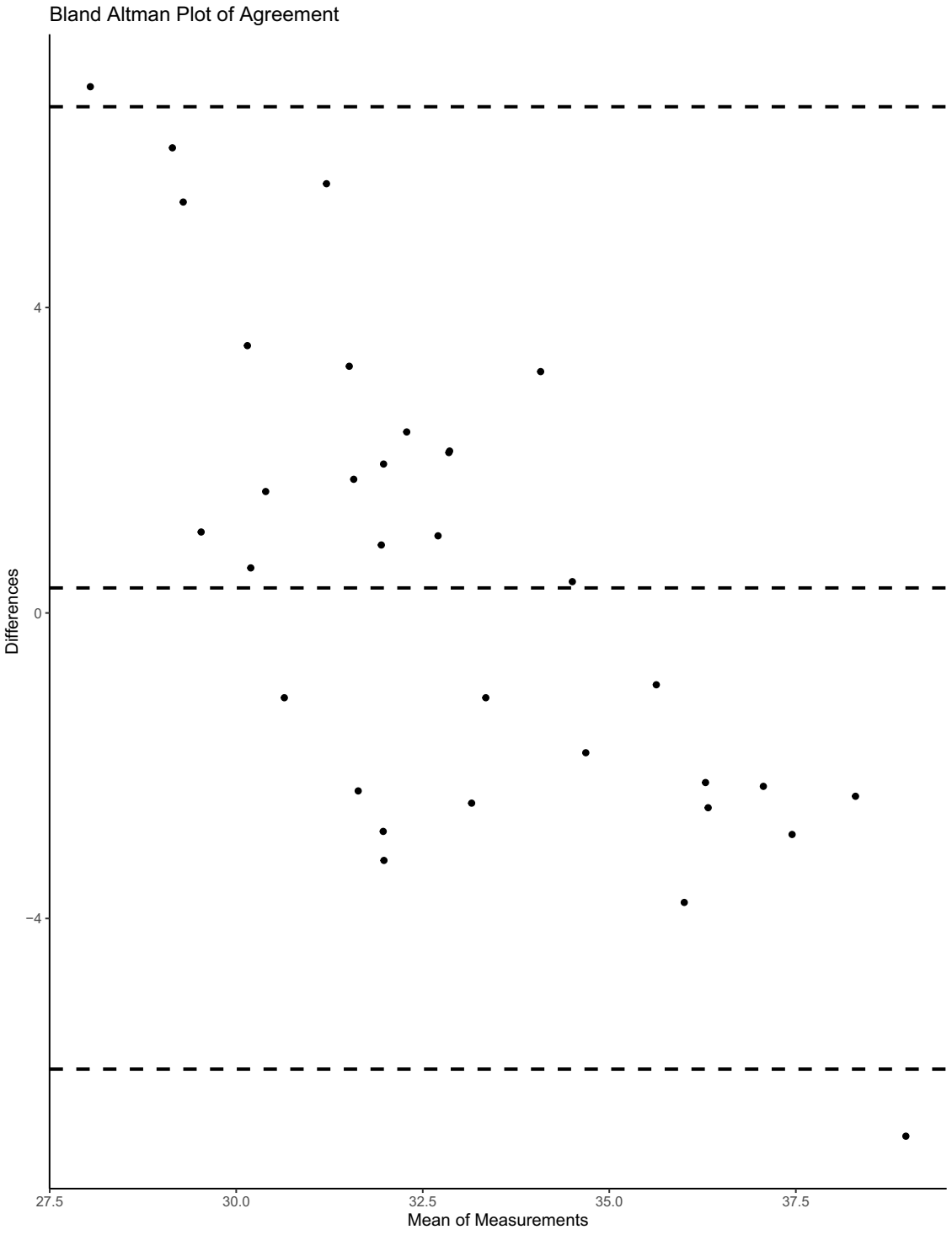

FIG 1 Bland Altman plot of agreement. The Bland Altman plot shows C_T values with bias of 0.33 ± 3.21 (95% limits of agreement, −5.97 and 6.63).

differing rates over the course of the illness (6). At our institution, the GeneXpert is utilized as a rapid test (turnaround time, 45 min) to triage patients for admission among other criteria; therefore, it is imperative that our testing modality can capture patients who present at either end of their illness course and who may have lower viral counts/higher C_T values. Overall, the Cepheid GeneXpert Xpress SARS-CoV-2 assay and the Roche Cobas 6800 SARS-CoV-2 assay showed a high level of agreement among

patients with high C_T values. This allows the laboratories to utilize both assays concurrently as fits with local testing algorithms. Further studies are required to confirm percent agreement across different platforms and specimen types to expand on our findings.

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