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Comparison of the Clinical Performance of the Point-of-care STANDARD M10 SARS-CoV-2 and Xpert Xpress SARS-CoV-2 Assays

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Dear Editor,

Point-of-care (POC) molecular assays are vital in diagnosing severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in acute care settings [1]. As various POC molecular assays with widely varying performance are used worldwide, performance validation is important [2, 3].

The STANDARD M10 SARS-CoV-2 assay (M10; SD Biosensor, Suwon, Korea) is a new, compact, fully automated PCR-based POC assay recently approved by the Korean Ministry of Food and Drug Safety (KMFDS). We evaluated its clinical performance as a confirmatory assay for the diagnosis of coronavirus disease (COVID-19) in comparison with the Xpert Xpress SARS-CoV-2 assay (Cepheid, Sunnyvale, CA, USA)—a POC molecular assay widely used in Korea. This study was approved by the Institutional Review Board of Yonsei University Health System, Seoul, Korea (approval number: 4-2021-1624).

Nasopharyngeal swabs submitted for SARS-CoV-2 PCR testing in a tertiary medical center in Korea were collected between October 11, 2021 and January 10, 2022. All samples were collected in universal transport medium (Noble Bio, Hwasung, Korea). After SARS-CoV-2 PCR testing, the residual samples were refrigerated.

In total, 342 SARS-CoV-2-positive samples yielding amplification of all three genes targeted (E, RdRp/S, and N) and confirmed using the real-time PCR-based Allplex SARS-CoV-2 Assay (Seegene, Seoul, Korea) were selected for this study. As the KMFDS approved the M10 assay as a confirmatory SARS-CoV-2 test, it needs to accurately detect SARS-CoV-2 in samples with low viral loads. Therefore, 60% of the samples selected for this study had high cycle threshold (Ct) values (E gene Ct ≥30). The 342 positive samples were tested using the M10 and Xpert assays in a head-to-head manner, using aliquots of the same clinical sample for both assays. One hundred residual samples confirmed as being SARS-CoV-2-negative using the Allplex assay were also tested. All assays were performed according to the manufacturers' instructions. The results produced by each automated assay (positive, inconclusive, or negative) were used for test interpretation. Statistical analysis was performed using MedCalc (version 20.027; MedCalc, Ostend, Belgium).

The clinical sensitivities of the M10 and Xpert assays were 68.1% (95% confidence interval [CI]: 62.9%–73.0%) and 99.4% (95% CI: 97.9%–99.9%), respectively (Table 1). In samples with

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Table 1. Comparison of the STANDARD M10 SARS-CoV-2 and Xpert Xpress SARS-CoV-2 assays for detecting SARS-CoV-2 according to the Ct value of the sample

Allplex *E* gene	STANDARD M10			Xpert Xpress			Total
	Positive	Inconclusive	Negative	Positive	Inconclusive	Negative	
Ct < 20	43	0	0	43	0	0	43
20 ≤ Ct < 25	23	0	1	24	0	0	24
25 ≤ Ct < 30	59	0	0	59	0	0	59
30 ≤ Ct < 35	89	35	15	139	0	0	139
Ct ≥ 35	19	27	31	75	0	2	77
	233	62	47	340	0	2	342

Abbreviations: Ct, cycle threshold; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.
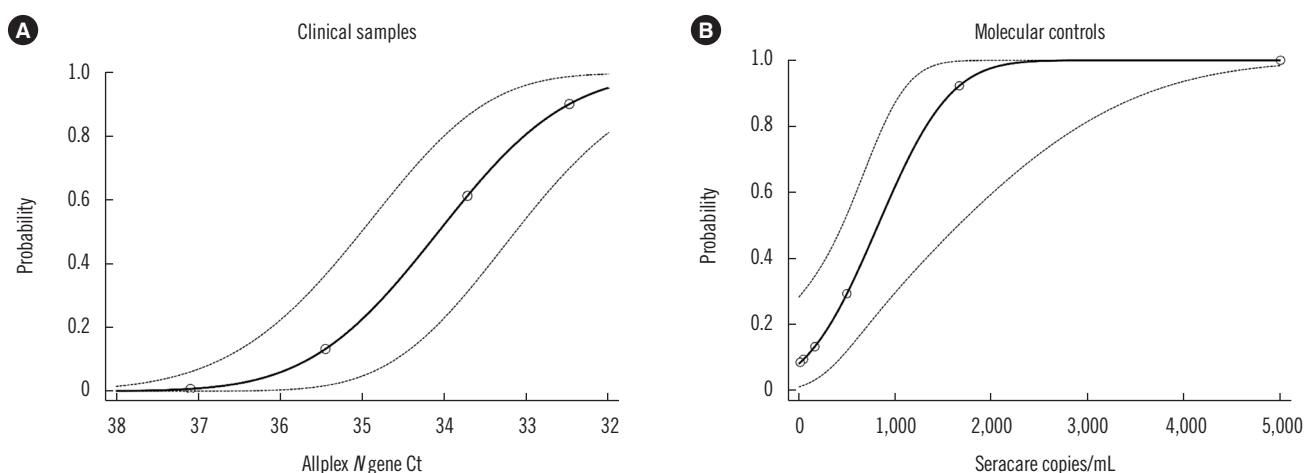
Fig. 1. Probit analysis of the LoD of the STANDARD M10 SARS-CoV-2 assay using (A) clinical samples and (B) the AccuPlex SARS-CoV-2 Molecular Controls Kit - Full Genome (SeraCare, Milford, MA, USA).
Abbreviations: Ct, cycle threshold; LoD, limit of detection; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

Ct values ≥ 30, the clinical sensitivities of the M10 and Xpert assays were 50.5% (95% CI: 43.6%–57.3%) and 99.1% (95% CI: 96.7%–99.9%), respectively.

Because samples with high Ct values were overrepresented, the results did not reflect the clinical sensitivity in clinical settings. Therefore, we calculated the corrected clinical sensitivity of the M10 and Xpert assays in the general Korean population using previously published data on the Ct distribution in this population [4]. The results were weighted as follows: Ct < 20, 27.5%; 20 ≤ Ct < 25, 21.6%; 25 ≤ Ct < 30, 23.2%; 30 ≤ Ct < 35, 24.9%; and Ct > 35, 2.8%. The corrected clinical sensitivity of the M10 assay was 87.7%, which is lower than the KMFDS clinical sensitivity threshold of 95% required for *in vitro* diagnostics use authorization. The corrected clinical sensitivity of the Xpert assay was 99.5%.

As two samples that tested negative using the Xpert assay also tested negative using the M10 assay, we suspected RNA degra-

dation. However, they had been refrigerated for short periods (35 and 46 days, respectively) before testing using the M10 and Xpert assays. Because the residual sample volumes were insufficient, we could not retest the discrepant samples using the Allplex assay. Therefore, all four results were recorded as negative.

The clinical specificity of the M10 assay was 100%. This included three invalid results due to cartridge errors that were confirmed to be negative when retested using new cartridges. The specificity of the Xpert assay was not evaluated because of a shortage of kits.

We evaluated the limit of detection (LoD) of the M10 assay through probit analysis using SARS-CoV-2-positive clinical samples and the AccuPlex SARS-CoV-2 Molecular Controls Kit - Full Genome (SeraCare, Milford, MA, USA). Clinical samples and molecular controls with different concentrations were tested five times. The estimated LoD for the clinical samples was an *N* gene Ct value of 32.05 (95% CI: 30.96–33.54). The LoD for the mo-

lecular controls was 1,797 copies/mL (95% CI: 1,207–4,188) (Fig. 1).

In conclusion, the STANDARD M10 SARS-CoV-2 assay shows suboptimal performance for detecting SARS-CoV-2 in samples with low viral loads. The users should be cautious when using M10 for diagnosing COVID-19 in the early and late stages. Moreover, the STANDARD M10 SARS-CoV-2 assay might be unsuitable for use in pooled testing because of the possibility of decreased sensitivity because of dilution [5].

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AUTHOR CONTRIBUTIONS

Hong KH and Lee H designed the study and wrote the manuscript. Hong KH and Oh Y performed the experiments. Lee J and Kim SY contributed to the statistical analysis and performed the limit of detection study. Cho HW contributed to the selection and management of clinical specimens. All authors reviewed and approved the final version of the manuscript.

CONFLICTS OF INTEREST

None declared.

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