Laboratory Evaluation of the BD MAX MRSA Assay

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A comparison between the BD MAX MRSA and Xpert MRSA assays was performed using 239 nares samples. A 97.9% overall agreement between the two molecular assays was observed. The BD MAX MRSA assay proved to be a reliable alternative for a highly automated system to detect methicillin-resistant *Staphylococcus aureus* (MRSA) in patient nares samples.

Methicillin-resistant *Staphylococcus aureus* (MRSA) is an important cause of community and hospital-acquired infections (1, 2). Screening for MRSA colonization to help identify patients at greater risk for MRSA infection and to allow for initiation of isolation precautions has become standard practice in many institutions (3–7). Molecular amplification methods for MRSA screening of hospitalized patients provides rapid results and have been demonstrated to be more sensitive than culture-based methods (8–15). The BD MAX MRSA assay (BD Diagnostics, Québec, Canada) is a molecular test performed on the BD MAX system (BD Diagnostics, Sparks, MD). The BD MAX is an automated sample-in and answer-out instrument that combines sample extraction, PCR setup, and real-time PCR on a walkaway platform. The objective of this study was to compare the BD MAX MRSA assay to the only other fully automated walkaway MRSA PCR assay, the Xpert MRSA (Cepheid, Sunnyvale, CA), performed on the GeneXpert instrument (Cepheid).

A total of 239 nares samples were collected from August to September 2012 from all patients admitted to any intensive care unit (ICU) at Tampa General Hospital (TGH), using two individually collected traditional swabs (LQ Stuart; BD BBL). One of the swabs was used for the Xpert MRSA assay, and the other was tested by the BD MAX MRSA assay; both assays were performed in parallel on both instruments according to the manufacturer's instructions without the technician having knowledge of the result from either instrument. For the Xpert MRSA assay, samples were placed in the Xpert assay buffer and transferred to the Xpert MRSA cartridge for PCR on the GeneXpert 16 system (Cepheid). For the BD MAX MRSA assay, samples were placed in the BD MAX MRSA sample buffer tube, which was subjected to vortex mixing for 60 s on a multiposition vortex. Sample tubes were placed in the BD MAX system along with the extraction reagent strip and PCR cartridges. The BD MAX MRSA sample buffer supports MRSA viability, which allowed a limited set of samples to be tested by an in-house-validated *mecA* and *femA* PCR, using previously published primers/probes (1), to address discrepant samples.

The limit of detection (LOD) of each assay was assessed using a positive-control strain (MRSA, ATCC 33591). Initially, a 0.5-McFarland-standard suspension of the strain was prepared in saline using fresh colonies from a blood agar plate. The suspension was followed by a series of 10-fold dilutions in saline. Five dilutions (1×10^3 to 1×10^7 CFU/ml) were tested in triplicate by both the Xpert MRSA and the BD MAX MRSA assay. The highest dilution (i.e., lowest concentration) at which all three replicates were positive was considered the LOD of the

TABLE 1 Results from 239 nares swab samples tested by the BD MAX and Xpert MRSA assays

Xpert MRSA assay result	No. of samples with indicated BD MAX MRSA assay result	
	Positive	Negative
Positive	30	0
Negative	5	204

assay. A challenge panel (Microbiologics Inc., MN, USA) comprising 10 lyophilized control strains was evaluated by both assays. The 10-member challenge panel included seven MRSA *mec* right extremity junction (MREJ) genotypes, a methicillin-susceptible *S. aureus* (MSSA) strain, a methicillin-susceptible *S. aureus mecA* dropout strain (MSSA), and a methicillin-susceptible *S. epidermidis* (MSSE) strain. Lyophilized bacterial organisms were reconstituted according to the manufacturer's instructions, and all were tested by both MRSA assays.

A workflow analysis was performed by four time and motion studies, focusing on the collection of the following metrics: total cycle time (amount of time required to perform testing across the batch of specimens; includes all manual and automated activities), total processing steps (number of steps required to perform testing across the batch of specimens), hands-on time (amount of time that lab personnel must devote to physically performing testing), and walkaway time (amount of time that testing was being performed but during which the operator was not actively engaged in hands-on testing activities). Four separate batches of specimens (2 batches of 16 specimens and 2 batches of 24 specimens) were analyzed with the two methods (BD MAX and GeneXpert), and a regression analysis was performed to ensure consistency in the measurements and processes. Time and process measurements were collected and analyzed from the time the specimens were acquired from the bins on the processing counter to the time that actionable results were generated. Times collected were then compared to

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TABLE 2 Challenge panel results for 10 strains tested by the Xpert MRSA and BD MAX MRSA assays

Sample identification	Description	MREJ type ^a	Xpert MRSA assay result	BD MAX MRSA assay result
1	MRSA	MRSA i	Positive	Positive
2800	MRSA	MRSA ii	Positive	Positive
9	MRSA	MRSA iii	Positive	Positive
11	MRSA	MRSA iv	Positive	Positive
16	MRSA	MRSA v	Positive	Positive
19	MRSA	MRSA vii	Positive	Positive
ATCC 2312	MRSA (<i>mecC</i>)	MRSA xxi	Negative	Negative
3097	MSSA (empty cassette)	NA	Positive	Positive
ATCC 29213	MSSA	NA	Negative	Negative
ATCC 14990	MSSE	NA	Negative	Negative

^a NA, not applicable.

the manufacturer's package insert to ensure that processing adhered to manufacturer guidelines.

Identical results were obtained for 234 of the 239 paired samples tested by both tests (Table 1). A total of 30 (12.5%) samples sets were positive and 204 samples sets were negative by both assays. Five sample sets were positive only by the BD MAX assay. BD MAX residual samples from these five sets were tested using the in-house-validated PCR test, and all of them were positive for both *mecA* and *femA*, suggesting that MRSA was present in these samples. Both assays demonstrated equivalent LODs by detecting up to a 1×10^5 dilution of the original suspension.

Strains from the challenge panel representing six out of seven MREJ types were correctly identified by both the Xpert and the BD MAX MRSA assay. Negative results were reported for MSSE, and one was reported for MSSA. The MSSA *mecA* dropout strain and the MRSA MREJ type xxi (*mecC*) were incorrectly identified by both tests (Table 2). The current BD MAX MRSA XT and StaphSR assays, however, can correctly identify both *mecA* dropout and *mecC* strains (16, 17). Workflow analysis results of hands-on times and walkaway times for the 16-sample and 24-sample batch studies, respectively, are summarized in Fig. 1 and 2. The total times to a result were as follow: (i) with 16 samples, 90 min for the GeneXpert and 125 min for the BD MAX assay, and (ii) with 24 samples, 169 min for the GeneXpert and 146 min for the BD MAX assay.

Rapid detection of MRSA in nares samples using molecular amplification methods has been recognized as an effective method to address the problem of MRSA infection and the

nosocomial transmission of MRSA (3, 9–12, 14, 15, 18–26). This study compared the two automated, sample-in, answer-out, walkaway PCR assays for MRSA, the Xpert MRSA assay and the BD MAX MRSA assay. Overall, there was 97.9% (234/239 samples) agreement between the two assays. In spite of exhibiting a small number of discrepant results, the two methods displayed an excellent concordance of results. Moreover, the two methods had identical LODs and were able to identify 8 out of 10 strains comprising the challenge panel. Both assays, however, produced a false-positive MRSA result with the *mecA* dropouts in the MSSA strain.

Workflow analysis showed that the Xpert MRSA assay provided a faster time to a result than did the BD MAX assay when 16 samples were tested. With 24 samples, the time to a result was faster with the BD MAX assay. The Xpert assay required slightly more total hands-on time than the BD MAX assay to process 16 and 24 samples.

There are several limitations to this study. The study was limited to a single site, with the primary service area being central Florida. We identified only 30 positives in the study, which is consistent with our historical positivity rate of just over 10%. A final but important limitation is the fact that two separate swabs were collected, leading to the possibility of errors due to unequal collection quality. In summary, both assays tested presented consistent and comparable results provided with a fast turn-around time. The BD MAX MRSA assay represents a reliable alternative for a highly automated system to detect MRSA in patient nares samples.

FIG 1 Comparison of hands-on times and walkaway times for the Xpert and BD MAX MRSA assays for 16 samples, displayed as hours:minutes:seconds.

FIG 2 Comparison of hands-on times and walkaway times for the Xpert and BD MAX MRSA assays for 24 samples, displayed as hours:minutes:seconds.

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