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# MULTI-CENTER EVALUATION OF THE PORTRAIT STAPH ID/R BLOOD CULTURE PANEL

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## REVISED ABSTRACT

**Background:** Blood stream infections (BSI) are a leading cause of morbidity and mortality in the United States. For hospitalized patients, MRSA BSI are associated with increased healthcare cost. The Portrait Staph ID/R Blood Culture Panel (BCP) from Great Basin Scientific (Salt Lake City, UT) is a rapid, automated, DNA multiplex PCR assay performed on the Portrait Dx Analyzer for simultaneous identification (ID) of *Staphylococcus aureus*, *S. lugdunensis* and *Staphylococcus* species to the genus level and the detection of *mecA* gene directly from positive blood culture bottle. We evaluated the performance of the Portrait Staph ID/R BCP compared to standard reference methods.

**Methods:** A total of 762 positive blood culture bottles (BD BACTEC™) yielding Gram positive cocci (GPCC) in clusters were analyzed at 3 clinical sites using the Portrait Dx System. Aliquots of positive blood cultures were sent to a reference site for analysis. Reference ID methods included catalase and coagulase tests, BD Phoenix instrument, and MALDI-TOF MS. Detection of methicillin resistance was tested by cefoxitin disk diffusion according to CLSI. Discordant resolution of *Staphylococcus* ID and *mecA* detection was performed on colonies by *rpoB* gene sequencing and *mecA* gene sequencing, respectively.

**Results:** Of the 762 positive blood culture bottles with GPCC, 658 had *Staphylococcus* spp. (*S. aureus* 211, *S. lugdunensis* 3, and *Staphylococcus* spp. 444) Overall *Staphylococcus* ID agreement was 98.8% PPA and 99.2% NPA. Of the 6 discordant results by Portrait Staph ID/R PCP, 3 were false positive for *S. aureus*, *S. epidermidis*, and *S. lugdunensis* by sequencing and 3 were false negative *S. epidermidis* or *S. hominis* by sequencing. The overall agreement for detection of *mecA* was 93.1% PPA and 98.6% NPA. Of the 16 discordant mecA results by Portrait Staph ID/R BCP, 15 were false positive and 1 false negative by sequencing.

**Conclusion:** The performance characteristics of the Portrait Staph ID/R BCP compared favorably to reference methods. This multiplex amplification assay provides valuable information beyond the initial Gram stain in less than 2 hrs. of testing. Accurate and rapid organism ID and resistance mechanism could have a positive impact on patient management.

## INTRODUCTION

Staphylococci are a major cause of hospital and community-acquired infections, leading to serious infections associated with significant rates of morbidity and mortality. The Portrait Staph ID/R Blood Culture Panel (BCP) is a qualitative, multiplex, nuclei acid-based assay that simultaneously identifies *Staphylococcus aureus*, *Staphylococcus lugdunensis* and various *Staphylococcus* species to the genius level and the detection of the *mecA* gene for methicillin resistance directly from positive blood cultures. The test utilizes automated hot-start enabled PCR for amplification of specific DNA targets detected by hybridization probes immobilized on a silicon chip surface. The Great Basin PA500 Portrait System is a fully automated system that includes the Portrait Analyzer, single-use Staph ID/R BCP cartridges, and the Portrait data analysis software (Figure 1). The Portrait System is designed to perform automated sample preparation, PCR, and optimal chip-based detection with integrated data analysis in 110 minutes. The purpose of this clinical trial was to assess the performance of the Portrait Staph ID/R BCP compared to reference methods.

## FIGURES

**Figure 1.** Portrait Staph ID/R BCP Automated System

## METHODS

**Blood culture samples.** Blood culture samples were collected from patients and incubated in the BD BACTEC continuous blood culture system. Bottles flagged positive by the instrument were Gram stained and then bottles confirmed to contain gram positive cocci in clusters (GPCC) or gram-positive cocci in singles (GPC) were tested with the Portrait Staph ID/R BCP. A total of 762 compliant samples were used in the prospective study.

**Portrait Staph ID/R BCP assay.** The assay was performed according to the manufacturer's instructions. Briefly, the Portrait Staph ID/R BCP assay is built into an injection-molded card. Reagents are lyophilized and placed in blister packs. The operator inserts 50 uL blood culture into the sample port, inserts the card into the desktop instrument, and initiates the test. The Portrait system is designed to perform automated sample preparation, hot-start PCR, and chip-based detection. Data analysis is completed in 110 min.

**Reference procedures.** (i) *Staphylococcus* identification was compare to biochemical methods; catalase, coagulase and the BD Phoenix instruments. Additional comparison was made with MALDI-TOF MS. (ii) Detection of the *mecA* gene was compared to cefoxitin disk diffusion according to CLSI.

**Discrepant Analysis.** (i) Clinical isolates were sequenced for *rpoB* to resolve discordant species identification between the Portrait Staph ID/R BCP and reference methods. (ii). Clinical isolates were sequenced using PCR *mecA* specific primers to resolve discordant detection between Portrait Staph ID/R BCP and cefoxitin disk diffusion method.

## RESULTS

**Table 1.** Summary of the clinical performance of Portrait Staph ID/R BCP versus reference methods for the identification of Staphylococcus species – 762 prospective blood cultures

| All sites combined | % Agreement | | | |
|---|---|---|---|---|
| Organism detection | TP/TP + FN | PPA 95% CI | TN/TN +TP | NPA 95% CI |
| *S. aureus* | 211/214 | 98.6% 96.0-99.5% | 548/551 | 99.5% 98.4-99.8% |
| *S. lugdunensis* | 3/3 | 100% 43.9-100% | 761/762 | 99.9% 99.3-99.9% |
| Staphylococcus species OTHER than *S. aureus* or *S. lugdunensis* | 444/449 | 98.9% 97.4-99.5% | 307/316 | 97.2% 94.7-98.5% |

**Table 2.** Summary of the clinical performance of Portrait Staph ID/R BCP versus reference methods for the identification of *mecA* – 762 prospective blood cultures

| All sites combined | % Agreement | | | |
|---|---|---|---|---|
| Detection of *mecA* with | TP/TP + FN | PPA 95% CI | TN/TN +TP | NPA 95% CI |
| *S. aureus* | 68/72 | 94.4% 86.6-97.8% | 682/690 | 98.8% 97.7-99.4% |
| *S. lugdunensis* | 0/0 | NA | 762/762 | 100% 99.5-100% |
| Staphylococcus spp OTHER than *S. aureus* or *S. lugdunensis* | 243/262 | 92.7% 88.1-97.1% | 481/500 | 96.2% 92.4-98.0% |

**Data Analysis**

- Overall % agreement of Portrait Staph ID/R BCP versus reference methods for the identification of *Staphylococcus* species: PPA 98.8% and NPA 99.2% (Table 1).
- Overall % agreement of Portrait Staph ID/R BCP versus reference methods for the identification of mecA: PPA 93.1% and NPA 98.6% (Table 2)

**Table 4.** Discordant sequencing results for *mecA* (All sites combined).

| # Samples | Portrait Staph IDR BCP | Cefoxitin Disk (Reference) | *mecA* Sequencing |
|---|---|---|---|
| 15 | Present | Absent | Absent |
| 16 | Absent | Present | Absent |
| 8 | Present | Absent | Present |
| 1 | Absent | Present | Present |

**Data Analysis**

- Overall there were a total of 40 discordant *mecA* identification results compared to cefoxitin disk diffusion.
- For 24/40 discordant samples, *mecA* sequencing results were concordant with Portrait Staph ID/R BCP.
- The remaining 16/40 discordant samples consisted of 15 FP *mecA* and 1 FN *mecA* results.

## RESULTS

**Table 3.** *Staphylococcus* species identification discordant sequencing results for rpoB (All sites combined).

| # Samples | Portrait Staph ID/R BCP | BD Phoenix (Reference) | *rpoB* Sequencing |
|---|---|---|---|
| 1 | *S. aureus* in mixed Staph infection (NOT *S. lugdunesis* | *S. hominis* | *S. hominis* |
| 1 | *S. aureus* in mixed Staph infection (NOT *S. lugdunesis* | *S. aureus* | *S. aureus* |
| 1 | Staph species OTHER than *S. aureus* or *S. lugdunensis* | *S. aureus/S. epidermidis/S. hominis* | *S. epidermidis* |
| 2 | Staph species OTHER than *S. aureus* or *S. lugdunensis* | *Coryne. jeikium* | *S. pettenkoferi* |
| 2 | Staph species OTHER than *S. aureus* or *S. lugdunensis* | S. aureus | *S. epidermidis* |
| 1 | Staph species OTHER than *S. aureus* or *S. lugdunensis* | *Rothia mucilaginsa* | *S. epidermidis* |
| 1 | Staph species OTHER than *S. aureus* or *S. lugdunensis* | *R. mucilaginosa Strep gardonii* | *S. hominis/S. epidermidis* |
| 1 | *S. aureus* in mixed Staph infection (NOT *S. lugdunensis*) | *S. epidermidis* | *S. epidermidis* |
| 1 | *S. lugdunensis* in mixed Staph infection (NOT *S. aureus*) | *S. epidermidis* | *S. epidermidis* |
| 1 | Negative | *S. epidermidis* | *S. epidermidis* |

**Data Analysis**

- Overall there were 8 false positive (FP) and 5 false negative (FN) Staph ID/R BCP results compared to BD Phoenix.
- For 7/13 discordant samples, rpoB sequencing results were concordant with Portrait Staph ID/R BCP.
- The remaining 6/13 discordant samples were either FN for *S. epidermidis* or *S. hominis*, or FP for *S. aureus*, *S. epidermidis* or *S. lugdunensis*.

## CONCLUSIONS

- The performance of the Portrait Staph ID/R BCP in this study was found to be highly favorable compared to reference methods.
- The Portrait Staph ID/R system is a small, automated bench-top analyzer with low cost, disposable cartridges for performing on demand testing during any shift. The combination of PCR amplification and chip-based eye visible signal creates a low cost, scalable platform.
- The immediate benefit of the Portrait Staph ID/R system is the minimal sample handling (sample in/results out).
- The Portrait Staph ID/R BCP can identify the most clinically relevant *Staphylococcus* species which are increasingly associated with true infections.
- The decreased time to results has benefits of improved patient outcomes and promote antimicrobial stewardship.

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