Evaluation of chromogenic media for detection of methicillin-resistant 
*Staphylococcus aureus*

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**Running title:** Chromogenic media for MRSA detection

**Key words:** sensitivity, specificity, rapid screening, screening culture, MRSA

**Abbreviations:** Methicillin resistant *Staphylococcus aureus*, MRSA; Limit of detection, LoD; methicillin-resistant staphylococci, MRCoNS; methicillin-sensitive staphylococci, MSCoNS; colony forming units, cfu.

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ABSTRACT

Rapid laboratory diagnosis is critical for treating, managing, and preventing methicillin-resistant *Staphylococcus aureus* (MRSA) infections. We evaluated and compared the potential for MRSA detection of five chromogenic media − *Brilliance* (Oxoid), ChromID (bioMérieux), *MRSA Select* (Bio-Rad), CHROMagar (CHROMagar-Microbiology), and BBL-CHROMagar (BD Diagnostics). Media were tested on log serial dilutions (10<sup>0</sup>–10<sup>6</sup> cfu) of pure isolates of MRSA (n=60), non-MRSA (n=27), and their defined mixtures simulating clinical samples (n=84). Further evaluations were done on pre-enriched nasal and groin screening swabs (n=213) from 165 hospitalized patients. Randomized samples were spiral-plated on each medium and independently scored by 5 investigators for characteristic colonies at 24 and 48 hours incubation. Confirmatory testing was done on up to 5 putative MRSA colonies recovered from each medium. Cumulative average sensitivity on isolates, mixtures and clinical samples was highest for *Brilliance* (97%), and similar for the other four media (≥92%). Cumulative average specificity was highest for BBL-CHROMagar (99%), followed by *MRSA Select* (98%), CHROMagar (97%), ChromID (89%), and *Brilliance* (86%). All media detected MRSA at 10 and 1 cfu, although at these low loads, few MRSA harboring SCC<sub>mec</sub> III- or IV were misinterpreted as non-MRSA by investigators. False-positive results were mainly due to methicillin-resistant *S. epidermidis*. For an arbitrary MRSA prevalence of 5% and based on patient sample evaluations, positive predictive values for BBL-CHROMagar and CHROMagar (≈84%) were highest. Negative predictive values of all media were ≥92% for MRSA prevalence ranging from 5%–30%. In conclusion, BBL-CHROMagar and CHROMagar gave best overall results for detection of MRSA, irrespective of the sample concentration, investigator, or incubation period.
INTRODUCTION

Methicillin-resistant *Staphylococcus aureus* (MRSA) has emerged as a major nosocomial pathogen in the last decade. Patients colonized with MRSA serve as reservoirs of self-infection or dissemination to other patients and to the hospital environment (6,12,22). Hence, screening for MRSA carriage and contact isolation of MRSA carriers is crucial for effective hospital infection control (9). Employing rapid and sensitive screening assays for MRSA detection could help to further improve infection control as well as decrease costs (10,13).

In recent years, use of chromogenic media has become a key method for the rapid identification of microorganisms in clinical samples (20). These media detect key microbial enzymes as diagnostic markers for pathogens through the use of “chromogenic” substrates incorporated into a solid agar-based matrix (20). In contrast to conventional culture media, chromogenic media allow direct colony color-based identification of the pathogen from the primary culture. This reduces the need for subculture for further biochemical testing and hence the time to result.

Currently available chromogenic media for MRSA detection incorporate chromogens to differentiate *S. aureus* from other pathogens and antibiotics for selective growth of MRSA. These media differ in their chromogenic substrates, antibiotic formulations and/or concentrations, factors that impact their sensitivity and specificity for MRSA detection (reviewed in ref. (13). We compared the potential of five of the most commonly used commercial chromogenic media for MRSA detection using pure MRSA and non-MRSA isolates as well as their mixtures at defined concentrations simulating clinical samples. Further evaluations of the media were carried out on nasal and groin screening samples from hospitalized patients.
MATERIALS AND METHODS

Study design

Figure 1 shows the outline of the study. The chromogenic media evaluated were as follows: (i) ChromID MRSA (bioMérieux, Marcy l’Etoile, France), (ii) MRSA Select (Bio-Rad, Nazareth Eke, Belgium), (iii) CHROMagar MRSA (CHROMagar, Paris, France), (iv) BBL-CHROMagar MRSA (BD Diagnostics, Erembodegem, Belgium), and the recently introduced (v) Brilliance MRSA (Oxoid, Basingstoke, UK; marketed as Remel Spectra in the US). As differences in constituents between BBL-CHROMagar and the original CHROMagar formulation are not disclosed, we tested both products. Each medium was challenged with a total of 384 samples that consisted of well-characterized bacterial isolates and their mixtures at various concentrations as well as patient screening samples (see further). Each sample was assigned an Excel-generated randomization code and inoculated on all five media in random order using a spiral plater (Eddy Jet, The Netherlands). All media were incubated for 22–24 hours (referred to as 24 hrs incubation) and then again for another 22–24 hours (referred to as 48 hrs incubation) at 37°C in aerobic conditions. The entire set of inoculated chromogenic media (n = 1920 plates; 384 samples plated on five media) were scored independently by each of the 5 investigators at both time points, i.e., at 24 and 48 hours incubation. Furthermore, putative MRSA colonies were recovered from each of the five media and confirmed on standard biochemical tests.
Samples

Isolates

Forty-two well-characterized MRSA (n = 15) and non-MRSA (n = 27) were inoculated as pure isolates on the five chromogenic media. The MRSA collection included strains of some of the most prevalent clonal lineages that have disseminated worldwide and harboring various known types of SCCmec (staphylococcal cassette chromosome mec, the mobile genetic element that carries the methicillin resistance gene, mecA) (see Table 1). The non-MRSA isolates included methicillin-sensitive *S. aureus* (MSSA, n = 5), methicillin-resistant coagulase negative staphylococci (MRCoNS, *S. epidermidis, S. warneri, S. sciuri*, n = 5), methicillin-sensitive coagulase negative staphylococci (MSCoNS, *S. capitis, S. epidermidis, S. lugdunensis*, n = 3), *Enterococcus spp.* (*E. faecalis, E. faecium, E. casseliflavus*, n = 4), and various gram-negative bacteria (*E. coli, K. pneumoniae, K. oxytoca, Acinetobacter spp.*, and *P. aeruginosa*, n = 10).

Staphylococcal isolates were characterized using coagulase test and speciated on semi-automated biochemical tests (API Staph, bioMérieux, Marcy l’Étoile, France). Non-staphylococci were identified and speciated either on relevant API tests or by standard biochemical tests (23,25).

For testing on chromogenic media, all isolates were subcultured on Mueller Hinton (MH) agar and incubated overnight. A colony suspension in brain heart infusion broth (BHI) with a turbidity of 0.5 McFarland (=10^8 cfu/ml) was made from the pure subculture on MH agar. After appropriate dilutions, 10^5 cfu colony suspension of each of the 42 isolates was spiral-plated on the five chromogenic media and on MH agar, the latter serving as a positive control for bacterial growth. The limits of detection (LoDs) of each of the five media were also
determined. For this, pure colony suspensions of all 15 MRSA, 3 MRCO NS, and 2 MSCO NS were serially diluted (10³, 10¹, and 10⁰ cfu) and spiral-plated on the five chromogenic media. All media were incubated for 24 and 48 hours and were evaluated at both time-points by all five investigators.

Mixtures of isolates
To study cross-reactions due to non-MRSA on the chromogenic media, mixtures of MRSA and non-MRSA isolates were prepared at defined concentrations. Strains used were MRSA (n = 2; 1 hospital-acquired strain with SCCmec type III and 1 community-acquired strain with SCCmec type IV) (Table 1), MRCO NS (n = 2; S. epidermidis and S. warneri), enterococci (n = 2, E. faecalis and E. faecium), and one strain each of MSSA, E. coli, K. pneumoniae, Acinetobacter spp., and P. aeruginosa. To prepare various combinations of ‘parent’ mixtures, 10⁵ or 10⁶ cfu each of a MRSA, MRCO NS, MSSA, and, occasionally, non-staphylococcal species were mixed (n = 20; see Supplementary Table). These parent mixtures were further diluted serially (10¹-, 10³-, and 10⁵-fold) to obtain a total of 80 mixture samples containing MRSA. Similarly, non-MRSA mixtures were prepared by mixing one each of MSSA and MRCO NS isolates at 10⁵ or 10⁶ cfu (n = 4; Supplementary Table) and were inoculated at this single high load without further dilutions. Each of the 84 mixture samples were plated on the 5 chromogenic media, as well as on mannitol salt agar with 4 µg/ml of cefoxitin (MS-CFOX) and MH agar, the latter two media acting as growth controls.

Clinical samples
Nasal and groin screening swabs (n = 213) were collected from 165 patients admitted at the University Hospital of Antwerp with prior history of MRSA carriage. Samples were
individually incubated overnight in a selective enriched broth (BHI with 7% NaCl and 4 µg/ml oxacillin) and 50 µl of the broth sample was inoculated on each of the 5 chromogenic media and also on MH agar.

Before the samples were plated on the chromogenic media, the MRSA status of all patient samples was established using culture-based and molecular methods. All pre-enriched broth samples were subcultured on mannitol salt agar, and putative S. aureus colonies were confirmed by tube coagulase, and screened for methicillin resistance on MH agar supplemented with 6 µg/ml oxacillin and 4% saline. Furthermore, oxacillin and cefoxitin MICs were determined according to CLSI guidelines (5). Molecular screening of samples was performed utilizing Hyplex StaphyloResist PCR (BAG, Lich, Germany) and an ‘in-house’ multiplex PCR (11). Based on these tests, MRSA were detected in 87 of the 213 samples. To obtain an overview of the prevalent SCCmec types, one MRSA isolate each from 46 of the 87 MRSA-positive broths was typed for SCCmec types I-V on real-time PCR (Applied Biosystems, Lennik, Belgium), as described previously (8). Of the 46 MRSA isolates typed, 40 (87%) harbored SCCmec IV, 5 (11%) SCCmec I, and 1 (0.02%) SCCmec II.

Confirmatory tests on putative MRSA colonies recovered from chromogenic media

One investigator also recovered putative MRSA colonies from the isolate mixtures and patient samples inoculated on the five chromogenic media for confirmatory testing on latex agglutination (Pastorex Staph Plus, Bio-Rad, Belgium), tube coagulase test, and a subculture on MS-CFOX. Up to 5 colonies showing a characteristic morphology were collected from each chromogenic medium and purified on blood agar. Confirmatory testing was done in succession.
on these colonies and stopped once a colony was confirmed as MRSA. Colonies identified as non-MRSA were analyzed up to genus level using standard biochemical tests (23,25).

Investigator assessment of the chromogenic media

Investigators scored the five media for ease in colony color differentiation between MRSA and non-MRSA and general user friendliness. Investigators also graded the five media in order of preference that were assigned choice-weighted scores with first through the last choice weighted 5 through 1.

Statistical analysis

Investigator response and confirmation test results were collected together with true status of each sample established on a combination of biochemical/phenotypic/genotypic tests. Using a logistic regression model, sensitivities and specificities averaged for five investigators were estimated for pure isolates, mixtures, and patient samples cultured on each chromogenmic medium. A Bayesian paradigm was utilized assuming readouts of the 5 investigators as random effect, and sample concentration, incubation period and the different chromogenic media as fixed effects and the model was fitted using the R software (www.r-project.org). In such an approach, credible intervals (CI) are calculated that are roughly equivalent to confidence interval in classical (frequentist) statistics. Positive predictive value and negative predictive value predictions were made based on MRSA prevalence estimates ranging from of 0%–50.
RESULTS

Detection of pure isolates

Sensitivities of Brilliance (97.6%, 95% CI: 95.13–99.10) and BBL-CHROMagar (97.0%, 95% CI: 93.70–98.97) were consistently high while those of ChromID, MRSASelect, and CHROMagar varied across the four pure MRSA isolate loads tested here (Figure 2A, continuous lines). However, at 48 hours incubation, sensitivities of all five media increased to 95%–100% at all MRSA loads tested (Figure 2A, dotted lines). All five chromogenic media could sustain growth of MRSA strains at loads as low as 10 and even 1 ($10^0$) cfu. Although at lower loads, a few strains were misinterpreted as non-MRSA by investigators. These included MRSA-harboring SCCmec type III on MRSASelect, CHROMagar and ChromID, and SCCmec type IV on BBL-CHROMagar (strains 5, 7, and 12, Table 1). Brilliance showed the highest sensitivity among the five media at MRSA loads of $10^0$ cfu with only one SCCmec type I-harboring MRSA being misinterpreted by two investigators (strain 1, Table 1). However, specificity of Brilliance was lowest because of misinterpretation of 4 of the 5 MRCoNS tested, and one each of MSSA and E. coli at 24 hours incubation by two investigators (Figure 2B). At 48 hours of incubation, all four of the enterococcal strains tested were also misinterpreted by four investigators, thus further decreasing the specificity of this medium to less than 60%. On the other hand, specificities of CHROMagar and BBL-CHROMagar were more than 99% at both 24 and 48 hours of incubation with extremely narrow CIs, indicating a high precision of these estimates (Figure 2B). Inter-investigator variations in observations were negligible for pure isolate samples ($\hat{\sigma}_R^2 = 0.03$, 95% CI: 0.00–0.15).
Detection of defined strain mixtures

Of the 80 MRSA-positive mixture samples, Brilliance, ChromID, MRSASelect, CHROMagar, and BBL-CHROMagar failed to grow 1, 1, 4, 0, and 7 samples, respectively. While all five media showed high sensitivities for detection of MRSA in mixtures inoculated at $10^5$, $10^4$, and $10^2$ cfu, sensitivities of BBL-CHROMagar, ChromID, and Brilliance were decreased for detection of $10^0$ cfu of MRSA (Figure 3A). These either did not grow on these media or the colonies were misinterpreted as non-MRSA by investigators. At 24 hours incubation, the decrease in sensitivity was most pronounced for BBL-CHROMagar (66.7%; 95% CI, 58.88–74.03), followed by ChromID (73.7%; 95% CI, 10.41–99.51), and Brilliance (85.8%; 95% CI, 79.44–91.05) (Figure 3A, continuous lines). False-negative results were due to MRSA harboring SCCmec types III and IV on BBL-CHROMagar and ChromID, and only SCCmec type IV on Brilliance. Specificities of both MRSASelect and BBL-CHROMagar were high and sustained at 48 hours incubation (Figure 3B). However, with the exception of BBL-CHROMagar, at least one of the four non-MRSA mixtures tested was misinterpreted by one investigator on the other four media. Inter-investigator variations in observations were minor for strain mixtures ($\hat{\sigma}_R^2 = 0.02; 95\%$ CI, 0.00–0.10).

In addition, up to 5 putative MRSA colonies were collected by an investigator for further confirmatory testing by standard biochemical methods. Correct MRSA identifications on the first colony were highest for CHROMagar (95%, n = 76), followed by BBL-CHROMagar (86%, n = 69), ChromID (85%, n = 68), Brilliance (79%, n = 63), and MRSASelect (73%, n = 58). However, with two colony analyses, Brilliance, ChromID, and MRSASelect also achieved correct MRSA identifications of $> 95\%$. All remaining samples were correctly identified by the
third colony analysis for all media. Isolates giving identical colony color and morphology as MRSA on all media were identified as MRCoNS (*S. epidermidis*).

**Validation of chromogenic media on screening specimens from patients**

*Brilliance* showed the highest sensitivities and lowest specificities on patients’ samples incubated for 24 and 48 hours (Table 2). Specificities of CHROMagar and BBL-CHROMagar were highest at 24 hours and sustained at 48 hours incubation. Sensitivities of all media increased by ≈ 8% at 48 hours incubation and, expectedly, paralleled a concomitant decrease in specificity except for the two CHROMagars. Inter-investigator variations in observations were small for the patient samples (\( \hat{\sigma}^2 = 0.01; 95\% \text{ CI}, 0.00–0.06 \)).

Diagnostic accuracy of each medium assessed on investigator observations for the patient samples is illustrated on the receiving operator characteristic (ROC) plot (Supplementary figure 1). Areas under the curve (AUC) were highest for BBL-CHROMagar and CHROMagar (0.93) followed by ChromID and MRSASelect (0.90) and *Brilliance* (0.86). Positive predictive values of BBL-CHROMagar and CHROMagar were highest amongst the five media (Supplementary figure 2). At 24 hours incubation and for an arbitrary MRSA prevalence of 5%, positive predictive values of BBL-CHROMagar and CHROMagar were 85% and 83%, respectively, and substantially higher than the other three media. On the other hand, negative predictive values for all five media at 24 hours incubation were uniformly high (≥ 92% with MRSA prevalence up to 30%; Supplementary figure 2).

Of the 87 MRSA-positive patient samples, 5, 8, 10, 11, and 10 samples failed to grow on *Brilliance*, ChromID, MRSASelect, CHROMagar, and BBL-CHROMagar, respectively.
Confirmatory testing by one investigator on putative MRSA recovered from samples growing on the media showed that correct MRSA identification of samples on first colony screening was highest for Brilliance (92%, n = 80), followed by BBL-CHROMagar and MRSASelect (87%, n = 76), ChromID (85%, n = 74) and CHROMagar (84%, n = 73). All remaining samples were correctly identified by the third colony analysis for all media.

Qualitative evaluation of media by investigators

Four of the five investigators graded the media. Both CHROMagar and BBL-CHROMagar scored equal and maximum number of votes for clear colony coloration and easy differentiation between non-MRSA and MRSA colonies (3/4 votes each). CHROMagar also obtained maximum votes for user-friendliness (3/4 votes), followed by BBL-CHROMagar and MRSASelect (2/4 votes each). CHROMagar was the most preferred medium (weighted score, 18) and BBL-CHROMagar the second most preferred medium (weighted score, 15). MRSASelect, Brilliance, and ChromID were on the third, fourth, and fifth place with weighted scores of 14, 10, and 5, respectively.
In the present study, BBL-CHROMagar (BD Diagnostics) and CHROMagar (CHROMagar Microbiology) gave best overall results for detection of MRSA, irrespective of the sample concentration, investigator, or incubation period. Table 3 shows a global comparison of the media performance results obtained in the present study. All five media exhibited excellent negative-predictive-values and are well-suited as screening tests for excluding MRSA carriage with a low risk of false-negative results. However, poor discriminative power or low specificities clearly demarcated Brilliance (Oxoid) and ChromID (bioMérieux) from the other three media. In a clinical setting, this might result in loss of time and higher costs due to unnecessary patient isolation.

To stress the importance of investigator perception and decision-making based on colony characteristics, performance of the chromogenic media was assessed on evaluations by five investigators. Work experience in a microbiology laboratory varied widely amongst these investigators, ranging from a few months to more than 25 years experience. Despite these differences, inter-investigator variations in observations were negligible, underscoring the ease-of-interpretation and the nonessentiality of technical expertise required for all five media.

One potential caveat in our study could be that patient samples were not derived from multiple hospitals or geographical areas thereby limiting variability. Moreover, an overnight sample pre-enrichment/oxacillin selection would also decrease the likelihood of observing cross-reactivity due to cohabitant bacteria and generally enhance media performance. We overcame these issues by also challenging media with defined mixtures of bacteria that are likely to co-exist with MRSA at various sampling sites on the human body in various proportions. Confirmatory
testing of putative MRSA colonies revealed that cross-reactivity on the chromogenic media at 202
24 hours incubation was largely due to other staphylococcal species, especially S. epidermidis
203 (MRCoNS). This would impact medium specificity while screening groin/perineal samples, and
to a lesser extent, also nasal samples (1,2,24). Our confirmation results further suggested that a
definitive identification of an MRSA-positive sample might necessitate screening of up to 2-3
206 putative MRSA colonies from the chromogenic media evaluated here. On the other hand, all
five media could easily detect MRSA strains classified as low-level resistant based on oxacillin
209 MICs of 1.5 to 2 µg/ml. This was because of the high cefoxitin MICs of these strains (32 to 64
210 µg/ml), as cefoxitin is a more efficient inducer of the mecA-encoded methicillin resistance
211 protein, PBP2a, than oxacillin (7), which allowed growth on the cefoxitin- (or other
212 cephapenic analogue-) containing chromogenic media utilized in the present study.
213
214 Issues with sensitivity were mainly evident at lower MRSA loads. Some MRSA harboring
217 SCCmec types III or IV either did not yield characteristic colonies at 24 hours incubation at
218 MRSA loads of 1 and 10 cfu, or the colony color was not specific enough causing some
219 investigators to misinterpret these samples as MRSA-negative. These findings can partly
220 explain the high variability in media performance generally observed between diagnostic
221 studies, which might be influenced both by the predominant circulating MRSA types as well as
222 by the differences in their colonization potential (19). For instance, post-enrichment
223 sensitivities of ChromID and MRSASelect reported in the present study are similar to those
224 found in another Belgian study (17), which are on average 13% lower than reported in a Swiss
225 study (4). A predominance of SCCmec IV-harboring MRSA in the patient samples screened in
226 the present and also in the other Belgian study (Dr. Claire Nonhoff, Hôpital Erasme, Bruxelles,
227 personal communication) (17), might be responsible for the inferior performance of the media.
Whether problems in detecting certain MRSA strains are related to the genetic background of the *S. aureus* that have acquired specific *SCCmec* types or are due to differences in fitness costs incurred by carriage of these *SCCmec* types is not known. Inter-strain differences in colonization potential have been previously reported. We have recently shown a 10,000-fold higher average MRSA yield from nasal swabs collected from patients at the University of Geneva Hospitals in comparison to a previous US-based study (14,26). While other variables cannot be discounted, the predominant MRSA clone recovered from the Geneva samples, ST228-*SCCmec* I, is an efficient colonizer as shown by its aggressively persistent and long-term bronchial colonization in cystic fibrosis patients (15).

Active screening now forms an integral part of all effective strategies to control MRSA, and a search for the optimal ‘rapid’ screening assay has motivated several studies comparing the utility of molecular and culture-based tests for MRSA detection. These studies show mixed results. One study modeled the impact of a direct detection of MRSA carriage using a chromogenic medium or real-time PCR on capture of patient isolation days (PIDs) (21). Their results showed that real-time PCR could capture up to 22.7% more PIDs, although it also generated more unnecessary PIDs due to slightly lower specificity than a chromogenic medium (21). Another study found the performance of real-time PCR and chromogenic medium to be similar (3), while yet another study showed molecular testing to be superior in terms of rapidity of results and sensitivity (18). Major deterrents to the more widespread use of PCR-based assays have been their higher costs, and for some assays, also the need for technical expertise or sample batching. In contrast, costs of screening on a chromogenic medium are similar to conventional culture once technician time and downstream processing costs are considered, and time to result can vary from 1.4 days to 1.7 days depending on the confirmatory tests required
with each medium (16). While the choice between employing a molecular or a culture-based screening assay is governed by several factors including hospital turnover, available isolation facilities, technical expertise etc, the advantages afforded by chromogenic media should encourage laboratories currently screening for MRSA carriage using conventional methods to adopt these rapid culture-based tools.
REFERENCES


CONFLICT OF INTEREST STATEMENT
SM-K has received a speaker’s honorarium from BD Diagnostics. We declare no other conflict of interest.

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ROLE OF THE FUNDING SOURCE
The sponsors of the study had no role in study design, data collection, data analysis, data interpretation, or writing the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.
LEGENDS TO TABLES

Table 1. Characteristics of MRSA strains tested in the study.

Table 2. Sensitivities and specificities of the five chromogenic media utilizing patient samples. All inoculated media were independently evaluated by five investigators.

Table 3. Summary of comparison of the five chromogenic media. Cumulative average sensitivity or specificity is the average of sensitivity or specificity of each medium for the three sample types (isolates, mixtures, and patient samples).

Supplementary Table. ‘Parent’ mixture samples (n = 20) that contained the highest loads of MRSA and non-MRSA inoculated on the media. The MRSA-containing mixtures were also tested on log serial dilutions. MRSA/non-MRSA colony forming units (cfu) are the absolute loads inoculated on the media.

LEGENDS TO FIGURES

Figure 1. Study design. MS-CFOX, mannitol salt agar with 4 µg/ml of cefoxitin.

Figure 2. Sensitivities and specificities of the five chromogenic media utilizing MRSA and non-MRSA as pure isolates. Figure 2A, X-axis shows the absolute MRSA loads inoculated on the five media. All inoculated media were independently evaluated by five investigators.

Figure 3. Sensitivities and specificities of the five chromogenic media utilizing defined MRSA and non-MRSA mixtures at various concentrations. Figure 3A, X-axis shows the absolute MRSA loads inoculated as mixtures on the five media. All inoculated media were independently evaluated by five investigators.
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<th>Strain No.</th>
<th>MRSA phenotype</th>
<th>Clone</th>
<th>SCCmec</th>
<th>mecA /pvl</th>
<th>Oxacillin MIC (µg/ml)</th>
<th>Cefoxitin MIC (µg/ml)</th>
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*ho, homogenous resistance; **he, heterogenous resistance

Table 1
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<td></td>
<td>Sensitivity</td>
<td>95% CI</td>
</tr>
<tr>
<td>Brilliance</td>
<td>89.9%</td>
<td>87.3 – 92.2</td>
</tr>
<tr>
<td>ChromID</td>
<td>82.8%</td>
<td>79.6 – 85.8</td>
</tr>
<tr>
<td>MRSASelect</td>
<td>80.7%</td>
<td>77.6 – 83.8</td>
</tr>
<tr>
<td>CHROMagar</td>
<td>81.9%</td>
<td>78.6 – 84.9</td>
</tr>
<tr>
<td>BBL-CHROMagar</td>
<td>82.9%</td>
<td>79.6 – 85.8</td>
</tr>
</tbody>
</table>

Table 2
<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Brilliance</th>
<th>ChromID</th>
<th>MRSASelect</th>
<th>CHROMagar</th>
<th>BBL CHROMagar</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cumulative average sensitivity - 24 hrs incubation</td>
<td>96.9%</td>
<td>93.8%</td>
<td>92.4%</td>
<td>94.3%</td>
<td>92.3%</td>
</tr>
<tr>
<td>Cumulative average specificity - 24 hrs incubation</td>
<td>85.9%</td>
<td>88.8%</td>
<td>97.8%</td>
<td>96.7%</td>
<td>99.1%</td>
</tr>
<tr>
<td>Sensitivity of MRSA detection at lowest pure isolate load (10^2 cfu)</td>
<td>97.6%</td>
<td>93.8%</td>
<td>86.9%</td>
<td>93.7%</td>
<td>97.9%</td>
</tr>
<tr>
<td>Specificity of media at highest non-MRSA loads in mixtures (10^5-10^6 cfu)</td>
<td>92.1%</td>
<td>74.5%</td>
<td>97.8%</td>
<td>90.9%</td>
<td>98.2%</td>
</tr>
<tr>
<td>Positive predictive value at 5% MRSA prevalence - 24 hrs incubtion*</td>
<td>27%</td>
<td>54%</td>
<td>60%</td>
<td>83%</td>
<td>85%</td>
</tr>
<tr>
<td>Negative predictive value at 30% MRSA prevalence - 24 hrs incubulation*</td>
<td>95%</td>
<td>93%</td>
<td>90%</td>
<td>93%</td>
<td>93%</td>
</tr>
<tr>
<td>Correct identification of MRSA-positive samples on first colony analysis</td>
<td>79%</td>
<td>85%</td>
<td>73%</td>
<td>95%</td>
<td>86%</td>
</tr>
<tr>
<td>Mixture samples</td>
<td>92%</td>
<td>85%</td>
<td>87%</td>
<td>84%</td>
<td>87%</td>
</tr>
<tr>
<td>Patient samples preenriched in an enrichment/selective broth</td>
<td>92%</td>
<td>85%</td>
<td>87%</td>
<td>84%</td>
<td>87%</td>
</tr>
<tr>
<td>Investigator evaluation of easy colony color differentiation</td>
<td>4</td>
<td>5</td>
<td>3</td>
<td>1</td>
<td>2</td>
</tr>
</tbody>
</table>

*Positive and negative predictive values are shown for an arbitrary 'low' and 'high' MRSA prevalence, respectively.

Table 3
Samples
(n = 384)

Isolates
(n = 42)

15 MRSA at $10^5$, $10^4$, $10^3$ & $10^2$ cfu (n = 60)

Non-MRSA at $10^4$ cfu (n = 27)

MRSA: non-MRSA mixtures & their log serial dilutions (n = 84)

Nasal, groin, perineal swabs (n = 213)

Overnight incubation in enrichment/selective broth

samples randomized and spiral-plated on five chromogenic media

Brilliance  ChromID  MRSASelect  CHROMagar  BBL-CHROMagar

Evaluated by five investigators after 22-24 hrs (24 hrs) and after another 22-24 hrs (48 hrs) of incubation

Five putative MRSA colonies from each plate confirmed for true status on:

Latex agglutination test
Coagulase test
Subculture on MS-CFOX