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LETTER TO THE EDITOR

Comparing BioFire FilmArray BCID2 and BCID Panels for Direct Detection of Bacterial Pathogens and Antimicrobial Resistance Genes from Positive Blood Cultures

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Among molecular assays currently developed for detection and identification of pathogens (and their antimicrobial resistance genes) in positive blood cultures (BCs) (1), the BioFire FilmArray blood culture identification (BCID) panel (bioMérieux, Marcy l'Etoile, France), a multiplex PCR assay with <2 min of hands-on time and an ~1-h turnaround time, allows for syndromic diagnosis of bloodstream infection (BSI) (2, 3). Previously, the panel could identify 24 etiological agents of BSI (11 Gram-negative bacteria, 8 Gram-positive bacteria, and 5 yeast species), as well as three antimicrobial resistance genes (*mecA*, *vanA/B*, and bla_{KPC}, which encodes *Klebsiella pneumoniae* carbapenemase). Now, the BioFire FilmArray BCID2 panel encompasses 43 molecular targets associated with BSI, including 15 Gram-negative bacteria, 11 Gram-positive bacteria, 7 yeast species, and 10 antimicrobial resistance genes (https://www.biomerieux-diagnostics.com/biofire-bcid-panel). The last targets include genes encoding carbapenemases (IMP, KPC, OXA-48-like, NDM, and VIM), colistin resistance (*mcr-1*), extended-spectrum β-lactamase (ESBL) (CTX-M), methicillin resistance (*mecA/C* and, specifically for methicillin-resistant *Staphylococcus aureus* [MRSA], *mecA/C* and MREJ [*mec* right-extremity junction]), or vancomycin resistance (*vanA/B*). Unlike BCID, no published studies to date reported on BCID2 performance. This study evaluated and compared the accuracy of BCID2 with that of BCID to identify bacterial species and relative antimicrobial resistance genes directly from positive BCs.

We used archived samples from positive BCs (1.5 ml thereof mixed with 100 μl of dimethyl sulfoxide and stored at −80°C), which had prospectively been processed with the BD Bactec 9240 (BD Diagnostic Systems, Sparks, MD), BacTAlert 3D (bioMérieux), or BacTAlert Virtuo (bioMérieux) system at two hospital microbiology laboratories from January 2018 to August 2020. For BCID2 testing, samples were thawed and allowed to reach room temperature, and a 200-μl aliquot was lysed and processed following the manufacturer's instructions. We compared BCID2 results with those of conventional identification or detection (i.e., MALDI BioTyper analysis and, relative to antimicrobial resistance genes, PCR sequencing, both performed on microbial isolates subcultured from positive BC samples), which was considered the reference method in this evaluation, or with those of the BCID.

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TABLE 1 BioFire FilmArray BCID2 and BCID panel results compared to reference method results for bacterial organism identification and antimicrobial resistance gene detection from 90 positive blood cultures[a]

Reference method (no. of results)	FilmArray BCID2 panel (no. of results)	FilmArray BCID panel (no. of results)
Gram-negative organisms (77)		
Acinetobacter baumannii (3)	*Acinetobacter calcoaceticus-Acinetobacter baumannii* complex (3)	*Acinetobacter calcoaceticus-Acinetobacter baumannii* complex (3)
Bacteroides fragilis (8)	*Bacteroides fragilis* (8)	–
Citrobacter freundii (1)	*Enterobacterales* (1)	*Enterobacteriaceae* (1)
Enterobacter cloacae complex (2)	*Enterobacter cloacae* complex (2)	*Enterobacter cloacae* complex (2)
Escherichia coli (11)	*Escherichia coli* (11)	*Escherichia coli* (11)
Klebsiella aerogenes (9)	*Klebsiella aerogenes* (9)	*Enterobacteriaceae* (9)
Klebsiella oxytoca (3)	*Klebsiella oxytoca* (3)	*Klebsiella oxytoca* (3)
Klebsiella pneumoniae (14)	*Klebsiella pneumoniae* group (14)	*Klebsiella pneumoniae* (14)
Klebsiella variicola (8)	*Klebsiella pneumoniae* group (8)	*Klebsiella pneumoniae* (8)[b]
Ochrobactrum anthropi (1)	–	–
Pseudomonas aeruginosa (1)	*Pseudomonas aeruginosa* (1)	*Pseudomonas aeruginosa* (1)
Salmonella spp. (8)	*Salmonella* (8)	*Enterobacteriaceae* (8)
Stenotrophomonas maltophilia (8)	*Stenotrophomonas maltophilia* (8)	–
Gram-positive organisms (54)		
Brevibacterium casei (1)	–	–
Enterococcus faecalis (9)	*Enterococcus faecalis* (9)	*Enterococcus* (9)
Enterococcus faecium (8)	*Enterococcus faecium* (8)	*Enterococcus* (8)
Staphylococcus aureus (9)	*Staphylococcus aureus* (9)	*Staphylococcus aureus* (9)
Staphylococcus epidermidis (11)	*Staphylococcus epidermidis* (11)	*Staphylococcus* (11)
Staphylococcus haemolyticus (4)	*Staphylococcus* (4)	*Staphylococcus* (4)
Staphylococcus lugdunensis (9)	*Staphylococcus lugdunensis* (9)	*Staphylococcus* (9)
Staphylococcus pasteurii (1)	*Staphylococcus* (1)	*Staphylococcus* (1)
Staphylococcus pettenkoferi (1)	*Staphylococcus* (1)	*Staphylococcus* (1)
Streptococcus salivarius (1)	*Streptococcus* (1)	*Streptococcus* (1)
Total organisms (131)	Total organisms (129)	Total organisms (113)
Antimicrobial resistance genes (53)		
***bla*$_{\text{CTX-M-15}}$** (11)	CTX-M (11)	–
***bla*$_{\text{CTX-M-27}}$** (5)	CTX-M (5)	–
bla$_{\text{KPC-3}}$ (6)	KPC (6)	KPC (6)
bla$_{\text{KPC-31}}$ (2)	KPC (2)	KPC (2)
***bla*$_{\text{NDM-1}}$** (3)	NDM (3)	–
bla$_{\text{OXA-23}}$ (2)	–	–
***bla*$_{\text{OXA-48}}$** (4)	OXA-48-like (4)	–
***bla*$_{\text{VIM-1}}$** (4)	VIM (4)	–
mecA (12)	*mecA/C* (6),[c] *mecA/C*, and MREJ (5)	*mecA* (10)[d]
vanA (4)	*vanA/B* (4)	*vanA/B* (4)
Total genes (53)	Total genes (50)	Total genes (22)

[a]Including results from 55 monomicrobial and 35 polymicrobial blood cultures (BCs) from patients with clinically relevant bloodstream infection (BSI) (Table S1). Boldface indicates all molecular targets identified at the species or genus level (i.e., organisms) or detected (i.e., genes) only in the BioFire FilmArray BCID2 panel. Dashes indicate the absence of detection(s) due to off-panel organisms/genes identified/detected by the reference method and not the BioFire FilmArray BCID2 or BCID panel.

[b]These results were interpreted as correct identifications because the BCID panel's *K. pneumoniae* assay had been designed to detect both *K. pneumoniae* and *K. variicola*, which is a closely related species to *K. pneumoniae*.

[c]The BCID2 panel uses the detection of *mecA/C* alone to identify staphylococci other than *Staphylococcus aureus* (SOSA) such as *S. epidermidis* and *S. lugdunensis* (above listed) or that of *mecA/C* and MREJ together to identify MRSA. However, BCID2 also signals *mecA/C* alone in polymicrobial BCs that grow MRSA together with *S. epidermidis* or *S. lugdunensis*. Thus, we excluded *mecA/C*-positive results of two BCs that grew *mecA*-positive *S. aureus* (correctly detected as MRSA) and *mecA*-negative *S. epidermidis* (Table S1). This allowed inclusion of four *mecA/C*-positive results in total. Additionally, three *mecA* genes in samples that grew *S. haemolyticus* (identified as *Staphylococcus*) were undetected because the BCID2 does not perform *mecA/C* detection for an organism not identified at the species level. These results were considered to be from off-panel genes and, thus, were excluded from the analysis.

[d]The BCID panel signals the presence of *mecA* gene alone also in the case of polymicrobial BCs growing two different *mecA*-positive organisms. Thus, we included two other *mecA*-positive results in the analysis, which regarded two polymicrobial BCs, one growing 1 *mecA*-positive *S. aureus* plus 1 *mecA*-positive *S. epidermidis* and the other one growing 1 *mecA*-positive *S. aureus* plus 1 *mecA*-positive *S. haemolyticus* (Table S1). This allowed inclusion of 12 *mecA* results in total.

Both the reference method and the BCID had been part of a previously implemented laboratory workflow for BSI diagnosis (4). Frozen aliquots of the original BC samples were submitted to subculturing and testing of the organism(s) grown from the aliquots to confirm samples' previous state.

We studied 90 BCs that grew clinically relevant bacterial species, of which 55 monomicrobial (55 species in total) and 35 polymicrobial (77 species in total, including 1 *Candida albicans*) with antimicrobial resistance determinants (53 genes in total) were identified (see Table S1 in the supplemental material). We selected BCs to ensure testing of organisms either belonging to bacterial species (e.g., *Bacteroides fragilis*) or carrying antimicrobial resistance genes (e.g., $bla_{CTX\text{-}M}$) that were not included in the BCID. Both BCID2 and BCID assays were compared with the reference method specified above. Regarding results with on-panel organisms (Table 1), the percent agreement was 100.0% (95% confidence interval [CI], 97.2% to 100.0%) for the BCID2 and 100.0% (95% CI, 96.8% to 100.0%) for the BCID. All off-panel organisms yielded a negative result with the BCID2 (1 *Ochrobactrum anthropi* and 1 *Brevibacterium casei*) or the BCID (8 *B. fragilis*, 1 *O. anthropi*, 8 *Stenotrophomonas maltophilia*, and 1 *B. casei*). Regarding results with on-panel genes (Table 1), the percent agreement was 100.0% (95% CI, 92.3% to 100.0%) for the BCID2 and 100.0% (95% CI, 85.8% to 100.0%) for the BCID. No genes that encode ESBL- or carbapenemase-mediated β-lactam resistance (i.e., 16 CTX-M, 3 NDM, 4 OXA-48-like, and 4 VIM) were detected by the BCID. With respect to organisms targeted by both BCID2 and BCID assays, no discrepancies between the assays' results were observed with the polymicrobial BC samples analyzed as a whole (Table S1).

Regarding apparently discrepant results (all for methicillin resistance genes), three *mecA* genes were not detected by the BCID2, one in monomicrobial and two in polymicrobial BC samples (see IDs 54, 83, and 87 in Table S1). These samples grew *Staphylococcus haemolyticus* (identified as *Staphylococcus*) alone in one sample or together with *S. aureus* (1 *mecA* negative and 1 *mecA* positive) in two remaining samples. This was because the BCID2, contrary to the BCID, does not perform *mecA* detection for an organism not identified at the species level. Furthermore, the BCID2 detected *mecA* genes from two other polymicrobial BC samples that grew *mecA*-negative *Staphylococcus epidermidis* together with MRSA, for which a positive *mecA/C* and MREJ detection signal was provided (IDs 84 and 85 in Table S1). This was because the BCID2 also signals the *mecA/C* gene alone in samples that grow MRSA together with *S. epidermidis* or *Staphylococcus lugdunensis*, the two staphylococci other than *S. aureus* (SOSA) identified by the panel.

Here, we report that the BCID2 panel identified more bacterial species and relative antimicrobial resistance genes in positive BCs than the BCID panel while retaining similar performance for targets already included in the BCID. This was the case for BSI pathogens, such as *Escherichia coli*, *K. pneumoniae* (with the KPC gene), *S. aureus* (with the *mecA* gene), or *Enterococcus faecalis* (with the *vanA* gene), which are the most common bacterial pathogens (5). With the BCID2, the opportunity to identify MRSA (5) or *S. epidermidis* and *S. lugdunensis* (6) among SOSA may be clinically useful (7), whereas the incapacity to identify SOSA such as *S. haemolyticus* or other coagulase-negative *Staphylococcus* species may be detrimental, particularly in the presence of *mecA*-positive isolates (8, 9). Because the reference method helped us to interpret BCID2 (or BCID) results, we believe that the FilmArray BCID2 panel may be a valuable adjunct to culture-based diagnostics.

SUPPLEMENTAL MATERIAL

Supplemental material is available online only.

SUPPLEMENTAL FILE 1, PDF file, 0.2 MB.

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