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Evaluation of the FilmArray Blood Culture ID Panel on Biofilms Dislodged from Explanted Arthroplasties for Prosthetic Joint Infection Diagnosis

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The FilmArray Blood Culture ID (BCID) panel (BioFire Diagnostics, Inc., Salt Lake City, UT) is an FDA-cleared multiplex PCR panel for pathogen identification from positive blood culture bottles. We assessed its performance with sonicate fluid for prosthetic joint infection (PJI) diagnosis.

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Definitions of PJI and significant cultures were as previously described (1, 2). Limits of detection from spiking studies with laboratory reference isolates were 7.5×10^2, 9.3×10^5, and 1.15×10^5 CFU/ml for *Staphylococcus aureus* IDRL-6169, *Staphylococcus epidermidis* IDRL-7173, and *Escherichia coli* IDRL-7029, respectively (specimen volume, 250 μl). Clinical performance was evaluated by using 216 nonduplicate hip and knee sonicate fluid samples (98 PJI cases, 118 aseptic joint failures) collected between 20 April 2006 and 14 May 2011, stored at −70°C, and thawed once for analysis. Included were 14 cases of polymicrobial PJI (median, 2 pathogens; range, 2 to 7), 69 cases of monomicrobial PJI, and 15 cases of PJI with no pathogens detected by culture or molecular methods.

The overall sensitivities of the BCID panel and sonicate fluid culture for PJI diagnosis were 53 and 69%, respectively (McNemar's test, $P = 0.004$). Considering only specimens with organisms represented in the panel, sensitivities were not statistically significantly different (sensitivities: BCID panel, 58%; sonicate fluid culture, 69% [$P = 0.09$]). For culture-positive PJI with pathogens represented in the panel, the overall BCID panel sensitivity was 71%. The BCID panel specificity was 99%. A single BCID *Candida parapsilosis*-positive specimen from a patient with aseptic failure grew *Clostridium beijerinckii* (<20 CFU/10 ml, considered a contaminant), suggesting extraneous contamination.

Additionally, we assessed the pathogen-specific performance of the BCID panel. For comparison, we included culture results, as well as those of 16S rRNA gene PCR assay, a 10-assay PCR panel, and PCR-electrospray ionization/mass spectrometry (PCR-ESI/MS) from our previous work (2–4) (Table 1). The BCID panel performed comparably to sonicate culture for most pathogens, missing only two *Enterococcus* infections and one *Pseudomonas aeruginosa* infection, but detected two additional *S. aureus* infections. However, its sensitivity for coagulase-negative staphylococci (SCN) was quite low (54%). Diminished sensitivity for SCN is likely because the panel is optimized for blood culture bottles; its performance is also known to vary with different species of SCN (5).

The BCID panel detected an organism in six culture-negative PJI cases (Table 2). *vanA/B* (for enterococci) and *mecA* (for *S. aureus*) detection or lack thereof was completely concordant with vancomycin and oxacillin susceptibility, respectively. Oxacillin susceptibility and *mecA* status were incompletely concordant for SCN. Of 17 *mecA*-positive specimens, 12 had oxacillin-resistant SCN (OR-SCN), 4 had both oxacillin-susceptible (OS-SCN) and OR-SCN, and one had only OS-SCN isolated in cultures. Of three *mecA*-negative specimens, one yielded OR-SCN. *mecA* positivity may not correlate with oxacillin resistance because of heterotypic expression (6) or potentially mixed infections with multiple strains or species.

A BCID-like approach would possibly be a useful adjunct to PJI diagnosis if sensitivity for SCN detection were improved and additional PJI-associated pathogens (e.g., *Propionibacterium acnes*, *Finegoldia magna*, and *Corynebacterium* species) and possibly a universal 16S rRNA gene target were incorporated. With minimal hands-on time (~2 min) and a short turnaround time (~1 h), rapid etiologic diagnosis and preliminary susceptibility data for major PJI pathogens (e.g., *S. aureus*) may facilitate earlier therapeutic and surgical decisions (e.g., surgical approach, type of antibiotic polymethymethacrylate spacer) and enhance patient satisfaction.

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TABLE 1 Pathogen-specific sensitivities of the BCID panel, culture, 16S rRNA gene PCR, 10-assay PCR panel, and PCR-ESI/MS

Pathogen (no. of isolates)	No. of isolates detected/total (% sensitivity)						
	Sonicate fluid culture (>20 CFU/10 ml)[e]	Intraoperative tissue or fluid culture (≥2 specimens)	Preoperative synovial fluid culture	FilmArray BCID[e]	16S rRNA gene PCR[e]	10-assay real-time PCR panel[e]	PCR-ESI/MS[e]
Pathogens[i] represented in BCID panel[a]							
Candida albicans (2)	1/2 (50)	1/2 (50)	1/1 (100)	2/2 (100)	NA[h]	NA	1/2 (50)
Enterobacter cloacae (1)	0/1 (0)	0/1 (0)	0/1 (0)	1/1 (100)	0/1 (0)	1/1 (100)	1/1 (100)
Escherichia coli (4)	3/4 (75)	4/4 (100)	2/4 (50)	4/4 (100)	4/4 (100)	4/4 (100)	3/4 (100)
Enterococcus species (8)	8/8 (100)	6/8 (75)	5/5 (100)	6/8 (75)[b]	6/8 (75)	8/8 (100)	5/8 (60)
Streptococcus agalactiae (3)	2/3 (67)	2/3 (67)	1/1 (100)	3/3 (100)	3/3 (100)	3/3 (100)	3/3 (100)
Group C *Streptococcus* species (1)	1/1 (100)	1/1 (100)	ND[g]	1/1 (100)	1/1 (100)	1/1 (100)	1/1 (100)
Group G *Streptococcus* species (1)	1/1 (100)	1/1 (100)	0/1 (0)	1/1 (100)	1/1 (100)	1/1 (100)	0/1 (0)[f]
Klebsiella pneumoniae (1)	0/1 (0)	0/1(0)	ND	1/1 (100)	1/1 (100)	1/1 (100)	0/1 (0)
Pseudomonas aeruginosa (4)	3/4 (75)	4/4 (100)	1/1 (100)	2/4 (50)	4/4 (100)	4/4 (100)	3/4 (75)
Serratia species (1)	0/1 (0)	0/1 (0)	0/1 (0)	0/1 (0)	1/1 (100)	1/1 (100)	1/1 (100)
Staphylococcus aureus (20)	16/20 (80)	19/20 (95)	7/9 (78)	18/20 (90)[c]	14/20 (70)	17/20 (85)	19/20 (95)
SCN (40)[d]	32/40 (83)	33/40 (33)	21/28 (75)	20/37 (54)[d]	33/39 (85)	35/38 (92)	34/40 (85)
Viridans group streptococci (2)	1/2 (50)	1/2 (100)	0/1 (0)	1/2 (50)	1/2 (50)	2/2 (100)	2/2 (100)
Pathogens[j] not represented in BCID panel							
Abiotrophia/Granulicatella species (2)	2/2 (100)	2/2 (100)	0/1 (0)	NA	1/2(50)	1/2 (50)	1/2 (50)
Actinomyces species (4)	3/4 (75)	2/4 (50)	1/1 (100)	NA	1/4 (25)	3/4 (75)	1/4 (25)
Capnocytophaga species (1)	1/1 (100)	1/1 (100)	1/1 (100)	NA	0/1 (0)	NA	1/1 (100)
Corynebacterium species (4)	1/4 (25)	3/4 (75)	1/4 (25)	NA	1/4 (25)	1/4 (25)	0/4 (0)
Finegoldia magna (6)	6/6 (100)	5/6 (83)	0/4 (0)	NA	3/5(60)	6/6 (100)	4/6 (67)
Mycobacterium abscessus (1)	0/1 (0)	1/1 (100)	1/1 (100)	NA	0/1 (0)	NA	0/1 (0)
Prevotella melaninogenica (1)	1/1 (100)	1/1 (100)	ND	NA	1/1 (100)	NA	1/1 (100)
Propionibacterium acnes (5)	3/5 (60)	2/5 (40)	2/4 (50)	NA	3/5 (60)	3/5 (60)	5/5 (100)
Veillonella species (1)	0/1 (0)	1/1 (100)	ND	NA	0/1 (0)	NA	0/1 (0)

[a] The BCID panel targets *Enterococcus* species, *Listeria monocytogenes*, *Staphylococcus* species (including a specific assay for *S. aureus*), *Streptococcus* species (including specific assays for *Streptococcus agalactiae*, *Streptococcus pyogenes*, and *Streptococcus pneumoniae*), *Acinetobacter baumannii*, *Haemophilus influenzae*, *Neisseria meningitidis*, *Pseudomonas aeruginosa*, *Enterobacteriaceae* (including specific assays for *Enterobacter cloacae*, *Escherichia coli*, *Klebsiella oxytoca*, *Klebsiella pneumoniae*, *Proteus* species, and *Serratia marcescens*), *Candida albicans*, *Candida glabrata*, *Candida krusei*, *Candida parapsilosis*, *Candida tropicalis*, *mecA*, *vanA/B*, and bla_{KPC}. PJI was defined as the presence of one or more of the following: synovial fluid or periprosthetic purulence, sinus tract communicating with the prosthesis, and/or periprosthetic tissue histopathology with acute inflammation. Significant cultures were defined as (i) two or more intraoperative periprosthetic tissue and/or synovial fluid samples with the same organism, (ii) a positive preoperative synovial fluid culture and an intraoperative culture that yielded the same organism, and/or (iii) sonicate fluid cultures with an organism detected at a concentration of ≥20 CFU/10 ml. Organisms were considered true pathogens if they were detected in a PJI case and (i) met the definition of a significant culture, (ii) were detected in at least one culture sample and by at least one molecular assay, or (iii) were detected by two or more different molecular assays.

[b] One hundred percent concordance with phenotypic testing: two *vanA/B*-positive isolates, both vancomycin resistant phenotypically; four *vanA/B*-negative isolates, all vancomycin susceptible phenotypically.

[c] One hundred percent concordance with phenotypic testing: six *mecA*-positive isolates, all oxacillin resistant phenotypically.

[d] For the BCID panel, only 37 specimens were assessed for SCN sensitivity, as *S. aureus* was codetected in three specimens.

[e] PCR-ESI/MS was performed with unconcentrated sonicate fluid; the BCID panel, the 16S rRNA gene PCR assay, the 10-assay PCR panel, and culture were performed with concentrated sonicate fluid.

[f] Identified by PCR-ESI/MS as *Streptococcus pyogenes*, with the next best match a group G *Streptococcus* species.

[g] ND, not done.

[h] NA, not applicable.

[i] From 70 cases of PJI.

[j] From 14 cases of PJI.

TABLE 2 Additional pathogens identified in sonicate fluid by the BCID panel and not detected by sonicate fluid culture

Additional pathogen detected by BCID	Conventional culture results for pathogen detected by BCID	Pathogen(s) coisolated by culture	Recent antimicrobial therapy	Corroborative molecular testing result(s)
mecA-negative SCN	Sonicate cultures with <20 CFU/10 ml SCN	None	Fusidic acid until surgery	PCR/ESI-MS, *S. caprae/epidermidis*; 16S rRNA gene PCR, *Staphylococcus* sp.; 10-assay PCR panel, SCN
mecA-negative *S. aureus*	None[a]	Methicillin-resistant SCN	Oxacillin until surgery	16S rRNA gene PCR + 10-assay PCR panel, *S. aureus*
Streptococcus agalactiae (GBS)	Sonicate cultures with <20 CFU/10 ml GBS[b]	None	Penicillin G/ceftriaxone until surgery	16S rRNA gene PCR + 10-assay PCR panel, GBS
Klebsiella pneumoniae	Sonicate cultures with <20 CFU/10 ml *K. pneumoniae*[c]	None	Trimethoprim-sulfamethoxazole–rifampin until 7 days before surgery	10-assay PCR panel, *Enterobacteriaceae*
Enterobacter cloacae	None	MRSA,[e] *Finegoldia magna*, *Corynebacterium* species	Trimethoprim-sulfamethoxazole until 7 days before surgery	10-assay PCR panel, *Enterobacteriaceae*
Candida albicans	None[d]	Methicillin-resistant *S. epidermidis*	Trimethoprim-sulfamethoxazole–levofloxacin until 3 days before surgery	None

[a] Cultures from external institution with methicillin-sensitive *S. aureus* previously.
[b] Preoperative aspirate with GBS (group B *Streptococcus* species).
[c] One of five tissue cultures with *K. pneumoniae*.
[d] None detected in corresponding sonicate cultures; however, *C. albicans* was detected in operative cultures obtained 1 month later when the cement spacer was replaced.
[e] MRSA, methicillin-resistant *S. aureus*.

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