IDweek 2020
#322

Evaluation of the BioFire® Bone and Joint Infection (BJI) Panel for the Detection of Microorganisms and Antimicrobial Resistance Genes in Synovial Fluid Specimens

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Background

Bone and Joint Infections (BJIs) present with non-specific symptoms that may include pain, swelling, and fever and are associated with high morbidity and significant risk of mortality. BJIs can be caused by a variety of bacteria and fungi, including anaerobes and microorganisms that can be challenging to culture or identify by traditional microbiological methods. Clinicians currently rely primarily on culture to identify the pathogen(s) responsible for infection. The BioFire® Bone and Joint Infection (BJI) Panel (BioFire Diagnostics, Salt Lake City, UT) was designed to detect 15 gram-positive (seven anaerobes) and 14 gram-negative bacteria (one anaerobe), two yeast, and eight antimicrobial resistance (AMR) genes from synovial fluid (SF) specimens in about an hour.

A prospective clinical evaluation was conducted between May 2018 and Mar 2020 at 10 US and 3 EU sites (Table 1). A total of 1,544 residual SF specimens were successfully enrolled from unique, individual patients. The enrolled population included both adults and children (Table 2). Performance for bacteria and yeast was determined by comparison to Standard of Care (SoC) testing consisting of bacterial culture at each study site (performed according to each site's routine procedures). Performance for AMR genes was determined by comparison to PCR followed by bi-directional sequencing (performed at BioFire).

Summary

90.6% Sensitivity and 99.8% Specificity
for microorganisms compared to culture

100% PPA and 98.8% NPA
for antimicrobial resistance genes compared to molecular methods

Identification of at least one organism in **15.7%** of synovial fluid specimens

Ability to detect multiple types of organisms in a single specimen (i.e. combinations of G+, G-, and yeast)

Potential for higher diagnostic yield than routine culture for on-panel analytes: 76 FP confirmed analyte presence (suggesting the BioFire BJI Panel was correct)

Success rate of **99.6%** for obtaining valid results on initial specimen test

This poster contains data regarding the BioFire BJI Panel which has not yet been reviewed or approved by regulatory agencies for in vitro diagnostic use.

Table 1. Participating Study Sites

Site	Site Name	Location
1	Indiana University	Indianapolis, IN
2	University of Nebraska Medical Center	Omaha, NE
3	Hospices Civils de Lyon	Lyon, France
4	Keck School of Medicine of USC	Los Angeles, CA
5	Jeroen-Bosch Ziekenhuis	Den Bosch, the Netherlands
6	Hospital Universitario Fundación Jiménez Díaz	Madrid, Spain
7	Hospital for Special Surgery	New York, NY
8	Penn State Hershey Medical and Children's Hospital	Hershey, PA
9	Ohio State University Wexner Medical Center	Columbus, OH
10	Geisinger Health	Danville, PA
11	Children's Hospital Los Angeles	Los Angeles, CA
12	Nationwide Children's Hospital	Columbus, OH
13	Primary Children's Hospital	Salt Lake City, UT

Table 2. Demographics and Specimen Characteristics

Demographics	
Enrolled	
1544	
Sex	
Male	878
Female	666
Age	
< 91 days	1
91 days - 4 years	22
5 - 15 years	75
16 - 25 years	35
26 - 64 years	774
65+ years	637
SF Collection Method	
Intraoperative	295
Arthrocentesis	1226
Unknown	23
Joint Collection Site	
Knee	1204
Hip	207
Shoulder	55
Ankle	10
Spine	2
Other	49
Unknown	17
Prosthesis	
Yes	442
No	850
Unknown	252

Table 3. Reference Methods

Analyte Type	Primary Reference Method
Bacterial and yeast	Routine manual and automated microbiological/biochemical methods (performed at source laboratory)
AMR genes	One PCR assay + sequencing (performed at BioFire)

Figure 1. Analyte Prevalence

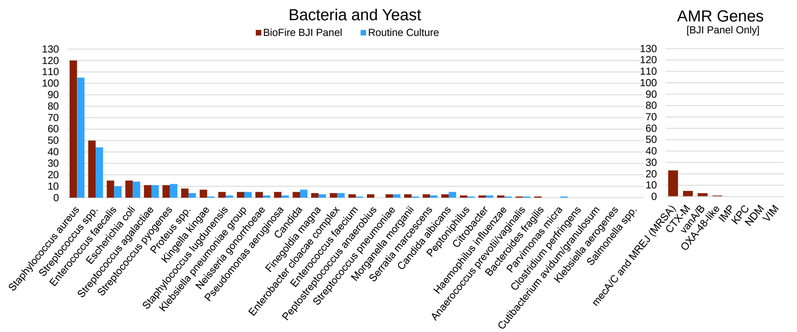

Figure 2. BioFire BJI Panel Detections

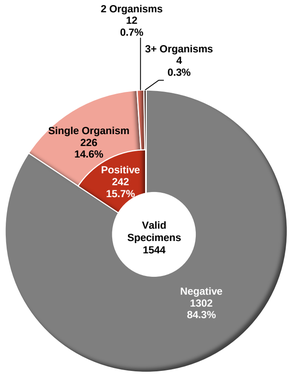

Figure 3. Organism Prevalence in BioFire BJI Panel Co-Detections (n=16)

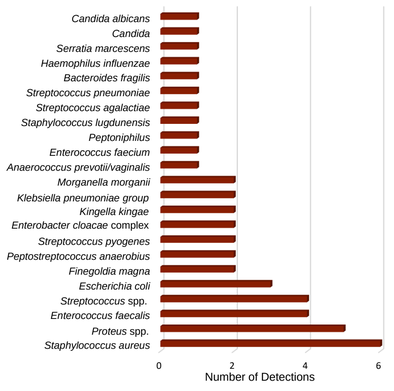

Figure 4. BioFire BJI Panel Detections by Gram Stain Classification

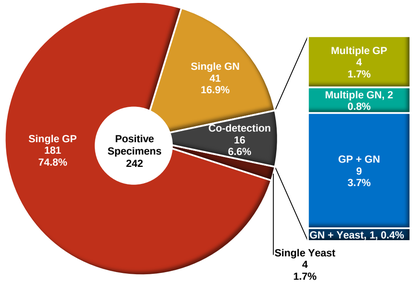

Table 4. BioFire BJI Panel Performance

Analyte	Sensitivity/PPA			Specificity/NPA		
	TP/ (TP + FN)	%	95% CI	TN/ (TN + FP)	%	95% CI
Gram Positive Bacteria						
Anaerococcus prevotii/vaginalis	1/1	100	-	1543/1543	100	99.8-100%
Clostridium perfringens	0/0	-	-	1544/1544	100	99.8-100%
Cutibacterium avidum/granulosum	0/0	-	-	1544/1544	100	99.8-100%
Enterococcus faecalis	10/10	100	72.2-100%	1529/1534	99.7	99.2-99.9%
Enterococcus faecium	1/1	100	-	1541/1543	99.9	99.5-100%
Finegoldia magna	3/3	100	43.9-100%	1540/1541	99.9	99.6-100%
Parvimonas micra	0/1	0	-	1543/1543	100	99.8-100%
Peptoniphilus	1/1	100	-	1542/1543	99.9	99.6-100%
Peptostreptococcus anaerobius	0/0	-	-	1541/1544	99.8	99.4-99.9%
Staphylococcus aureus	98/105	93.3	86.9-96.7%	1417/1439	98.5	97.7-99.0%
Staphylococcus lugdunensis	2/2	100	34.2-100%	1539/1542	99.8	99.4-99.9%
Streptococcus spp.	38/44	86.4	73.3-93.6%	1488/1500	99.2	98.6-99.5%
Streptococcus agalactiae	10/11	90.9	62.3-98.4%	1532/1533	99.9	99.6-100%
Streptococcus pneumoniae	3/3	100	43.9-100%	1541/1541	100	99.8-100%
Streptococcus pyogenes	11/12	91.7	64.6-98.5%	1532/1532	100	99.7-100%
Gram Negative Bacteria						
Bacteroides fragilis	0/0	-	-	1543/1544	99.9	99.6-100%
Citrobacter	2/2	100	34.2-100%	1542/1542	100	99.8-100%
Enterobacter cloacae complex	2/4	50.0	15.0-85.0%	1538/1540	99.9	99.5-100%
Escherichia coli	14/14	100	78.5-100%	1529/1530	99.9	99.6-100%
Haemophilus influenzae	1/1	100	-	1542/1543	99.9	99.6-100%
Kingella kingae	1/1	100	-	1537/1543	99.6	99.2-99.8%
Klebsiella aerogenes	0/0	-	-	1544/1544	100	99.8-100%
Klebsiella pneumoniae group	4/5	80.0	37.6-96.4%	1538/1539	99.9	99.6-100%
Morganella morganii	1/1	100	-	1541/1543	99.9	99.5-100%
Neisseria gonorrhoeae	2/2	100	34.2-100%	1539/1542	99.8	99.4-99.9%
Proteus spp.	4/4	100	51.0-100%	1536/1540	99.7	99.3-99.9%
Pseudomonas aeruginosa	2/2	100	34.2-100%	1539/1542	99.8	99.4-99.9%
Salmonella spp.	0/0	-	-	1544/1544	100	99.8-100%
Serratia marcescens	2/2	100	34.2-100%	1541/1542	99.9	99.6-100%
Yeast						
Candida	4/7	57.1	25.0-84.2%	1536/1537	99.9	99.6-100%
Candida albicans	3/5	60.0	23.1-88.2%	1539/1539	100	99.8-100%
Antimicrobial Resistance Genes						
CTX-M	5/5	100	56.6-100%	33/33	100	89.6-100%
IMP	0/0	-	-	38/38	100	90.8-100%
KPC	0/0	-	-	40/40	100	91.2-100%
mecA/C and MREJ (MRSA)	19/19	100	83.2-100%	90/94	95.7	89.6-98.3%
NDM	0/0	-	-	40/40	100	91.2-100%
OXA-48-like	1/1	100	-	33/33	100	89.6-100%
vanA/B	3/3	100	43.9-100%	14/14	100	78.5-100%
VIM	0/0	-	-	38/38	100	90.8-100%

Figure 5. Discrepancy Investigation Results